South Asian and Chinese Medical Systems: Ayurveda and Traditional Chinese Medicine Treatments for *Diabetes mellitus*, Type 2

By

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Abstract

SOUTH ASIAN AND CHINESE MEDICAL SYSTEMS:
AYURVEDA AND TRADITIONAL CHINESE MEDICINE TREATMENTS FOR
DIABETES MELLITUS, TYPE 2

By

Sarah K. Khan

Adviser: Professor Michael J. Balick

Ayurvedic (a South Asian medical tradition) and Traditional Chinese Medicine (TCM) treatments for non-insulin dependent *Diabetes mellitus*, Type 2 were researched to test the hypothesis that if Ayurvedic Management Therapy (AMT) treatments were administered according to traditional and/or traditionally-inspired practices, then a blood glucose lowering effect would be observed.

The results of the pilot clinical research study conducted in Bangalore showed that AMT—any combination of four Ayurvedic formulations (32 plants and one fish species)—did not have a significant effect on reducing the primary FBG parameter by more than 20 mg/dL. Secondary parameters such as weight, LDL, and HDL cholesterol were reduced. The primary result may be due to non-adherence to inclusion-exclusion criteria. In the pilot clinical research study in Shanghai, the TCM base formulation consisted of six plants (plus four substitutes). An additional 21 auxiliary plants were part of the practitioner's repertoire.

The purpose of TCM research in Shanghai was to compare Ayurvedic and TCM treatments, specifically to assess the plants used. A comparison resulted in only two

plants in common: *Curcuma longa* L. and *Cyperus rotundus* L. Both these plants were part of the auxiliary/complementary TCM formulation and were not included in the base formula.

Ayurvedic management therapy was evaluated in order to move beyond a research paradigm that searches for a single, isolated compound. The first step in identifying effective treatment protocols may be the testing of patient outcomes. A shift from identifying bioactive ingredients to identifying formulations, management treatments, or protocol strategies may be a more effective way to help patients who are suffering from disease. An approach that respects the parameters of Ayurvedic and TCM traditions should be developed in collaboration with the Western biomedical paradigm where scientific traditions are rigorously challenged, and potentially improved in the process.

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Introduction

In the following dissertation, I researched Ayurvedic (an ancient South Asian healing tradition) and Traditional Chinese Medicine (TCM) treatments for non-insulin dependent *Diabetes mellitus*, Type 2 (DM2) to test the hypothesis that if Ayurvedic treatments were administered according to traditional and/or traditionally-inspired practices, then a blood glucose lowering effect would be observed.

This dissertation is divided into eight chapters. In the Introduction, I provide a detailed overview of my research hypothesis, my rationale, and the methodology I employed in India and China. In Chapter 1, I review the ethnobotanical literature as it relates to my dissertation research. In Chapter 2, I review the present *Diabetes mellitus* epidemic and how Ayurveda and TCM practitioners have historically treated this ancient illness called "Madhumeha" and "Xiao Ke", respectively. In Chapter 3, I focus exclusively on the history of Ayurveda, and its philosophy. In Chapter 4, I present a review of Ayurvedic basic theories. I then introduce the basic principles of pathology, treatment, and Dravyaguna, that branch of Ayurveda that deals with pharmacology. I discuss how practitioners classify plants in order to treat madhumeha. In Chapter 5, I present the pilot clinical research protocol approved by the Internal Review Boards of City University of New York (CUNY) Graduate Center, New York; St. John's Medical College and Hospital, Bangalore, India; and Hua Shan Hospital, Fudan University, Shanghai, China. In Chapter 6, I present the research findings of my field work in India with an emphasis on the clinical study conducted in Bangalore, India. In Chapter 7, I conclude with a discussion of the research results gathered through a series of case studies conducted at

the Institute of Integrated Chinese and Western Medicine, Hua Shan Hospital, Fudan University, Shanghai, China. Finally in Chapter 8, I summarize the research results and achievements in India and China. I discuss how future research using ethnobotanical and clinical research methods may evaluate non-Western treatment practices and contribute to the improvement of both Western (e.g. allopathic) and non-Western healing traditions. I outline possible future research projects. I conclude with how the evolving ethnobotanical research paradigm may benefit from a shift in focus from the traditional ethnographic and scientific observer to the more active observant-*participant* while at the same applying rigorous clinical research techniques.

Hypothesis

Using comparative ethnobotanical methods, I researched treatments for *Diabetes mellitus* Type 2 (DM2) based upon the South Asian healing system known as Ayurveda (the "science of living") as well as Traditional Chinese Medicine (TCM). More specifically, my research in India culminated in a documentation of the plants and plant formulations used by two Ayurvedic practitioners to treat DM2; my participant-experience as a student at Gujarat Ayurved University; my participation in immersion ethnobotany (participant-observer) in order to experience Ayurvedic treatment in a hospital setting; and the performance of a clinical study to test the efficacy of selected Ayurvedic medicinal plant formulations used to treat DM2. My research in Shanghai, China involved documenting a series of case studies for the treatment of DM2 according to traditional TCM protocol.

My hypothesis is that Ayurvedic antidiabetic plant formulations and treatment protocols, when administered according to traditional knowledge system practices, would decrease the symptoms (e.g., increased blood-glucose levels) associated with DM2.

The comparative ethnobotanical approach (i.e., a comparison of different Ayurvedic practitioners' treatment protocols within India, and a comparison between Ayurvedic and TCM plant treatment protocols) facilitated identifying potentially antidiabetic formulations and treatment modalities that are traditionally prescribed by Ayurvedic and TCM practitioners. These modalities were identified by implementing a prospective and retrospective study in Jamnagar, Gujarat; a small pilot clinical study in Bangalore, Karnataka; and a review of TCM treatment protocol for patients with recently-diagnosed DM2 in Shanghai, China. A small pilot clinical study to test Ayurvedic plant formulations allowed the researchers to evaluate Ayurvedic treatment from two perspectives: Western biomedical and Ayurvedic. Using Western scientific parameters, the primary endpoint was a change in blood-glucose levels from the patients' baseline. Secondary parameters included evaluating lipids and glycated hemoglobin over the course of treatment. In order to evaluate Ayurvedic management treatment, Ayurvedic diagnosis, treatment, and diet protocols were documented.

Rationale

For the clinical study conducted in Bangalore, India, our collaborative team made a conscious choice to focus on Ayurveda as a treatment modality rather than identify a single plant, active ingredient, or lifestyle change among the multiple formulations and modalities. The Ayurvedic treatment modality used in the clinical study included

traditional Ayurvedic examination, diagnosis, and prescription of formulations, in addition to lifestyle changes that comprised diet and exercise regimes. A clinical approach to investigating the efficacy of such formulations and modalities may improve treatment for those who suffer from DM2. It may also provide Western evidence-based data to evaluate centuries-old traditional medical practices and give Ayurvedic practitioners the opportunity to evaluate their own prescribed protocols systematically and build upon those that are found to be efficacious.

The chemical and biomedical potential of less than 1% of the earth's higher plants has been studied or analyzed from a Western biomedical perspective.[1] Due to rapid degradation and loss of natural habitats and the over-harvesting of some species, much of the biological wealth that is intrinsically important to traditional ecological systems of medicine has been destroyed or is currently threatened. The global Red-List of plants produced by the IUCN presents an alarming picture: nearly 34,000 species, or 12.5% of the world's flora, are facing extinction.[2] Although the definition of biodiversity on earth is multifold (it may include genetic, species, cultural or linguistic diversity, etc.) and represents a complex set of interactions, Nabhan argued that most biodiversity today occurs in areas where cultural diversity also is found.[3] According to Maffi, ten out of twelve megadiversity centers (83%) in the world also figure among the top 25 countries for endemic language diversity. The twelve megadiversity centers are listed in descending order; following each country in parenthesis is the endemic language rank: Colombia (23), Peru (18), China (17), Malaysia (15), Zaire (9), Brazil (8), Mexico (6), Australia (5), India (4), Indonesia (2), Ecuador, and Madagascar. The last two countries are major areas

of biodiversity but not of language diversity.[4] According to Harmon, biodiversity and linguistic diversity are correlated due to a process of coevolution of small-scale human groups within their local ecosystems.[5] Maffi stated that traditional linguistic ecologies, for example, encompass not only linguistic and social environments but also the physical environment,[6] and emphasized that when external forces begin to undermine traditional cultures, the wisdom about human-environment relationships begin to lose their relevance. This particular process has been called the 'extinction of experience'. When a particular culture imposes itself on another culture, for example, often local ecological knowledge is at an especially high risk of extinction.[7] This link between biodiversity and linguistic diversity cannot be dismissed and one may conclude that where many cultures have coexisted within the same region, biodiversity has also survived.

Along with concerning itself with rapidly disappearing biodiversity, the World Health Organization (WHO) has determined that up to 80% of the developing world relies on traditional, predominantly plant-based medicines for its primary healthcare needs.[8] To promote public health for all, the World Health Assembly governments called on the Director General of WHO "…to consider the contribution WHO might make to promoting respect for and maintenance of, indigenous knowledge, traditions and remedies, in particular, their pharmacopoeia".[9] In order to understand better traditional healing systems' potential for public health interventions in primary care, I undertook a study of traditional Asian healing practices related to DM2. I chose to study and research

two ancient healing traditions located in two major centers of megadiversity and linguistic diversity in the world: India and China.

The Diabetes Epidemic

Diabetes is a worldwide epidemic that is most prevalent in the following three countries: India, China, and the United States. King et al. estimated that between 1995 and 2025, diabetes will increase 195% in India, affecting some 57.2 million people, 134% in China, affecting some 37.6 million people, and 58% in the United States, affecting some 21.9 million people.[10] One way of meeting the enormous challenge this situation presents is to investigate the efficacy of traditional plant-based therapies. Diverse indigenous healing traditions are found throughout Asia. Ayurveda, the science of life, and Traditional Chinese Medicine (TCM) are two such ancient, codified systems that are widely practiced throughout the subcontinent and China. Both Ayurveda and TCM, as locally available and culturally acceptable modalities, may provide adjuvant and alternative therapies to more expensive pharmaceutical-based treatments for millions of people.

Ayurveda is one of several ancient healing traditions found in South Asia. Scholars estimate the Ayurvedic tradition to be over 3,000 years old, having developed in the South Asian subcontinent. Classical Ayurvedic treatments include not only individualized medicinal plant prescriptions but also encourage diet modification, exercise, and mental balance. The Ayurvedic paradigm of healing has a long and continuous history of use. A substantial body of scientific literature exists on the efficacy of Ayurvedic medicinal plants.[11] Some treatment protocols (i.e. diabetes) for particular diseases are similar with allopathic modalities of treatment.[12] Classical Sanskrit texts

described "*prameha*," an overproduction of urine that includes over 20 subtypes divided into three categories: *kaphaja*, *pittaja*, and *vataja prameha*. "*Madhumeha*," a subtype of *vataja*, is a condition which causes the patient to pass a large quantity of "sweet" urine. Based on detailed descriptions of signs and symptoms, *madhumeha* correlates with modern definitions of NIDDM.[13, 14] Over the centuries Ayurvedic practitioners have developed numerous classical formulations for individual sub-types in order to develop treatments for Madhumeha. Historically classical Ayurvedic preparations, when administered by an Ayurvedic physician according to classically prescribed dosages, are safe, tolerable, non-toxic, and effective.

Modern China's Traditional Chinese Medicine is based on the *Yellow Emperor's Inner Classic (Nei Jing),* compiled by unknown authors between 200 B.C.E. and 100 C.E. It is the oldest major Chinese medical text extant, and serves as the theoretical and philosophical foundation of contemporary TCM. According to basic TCM philosophy, health and illness are described as natural phenomena that occur as natural law operates upon the cosmos, the human body, and the connection between them. The therapeutic modalities include lifestyle counseling, administration of herbs and animal material, acupuncture, diet modification, and particular exercise regimes.[15] There are two words in Chinese for diabetes: the traditional medical name, *xiao ke*, means "wasting and thirsting," and the more modern medical term, tang-niao-bing, means "sugar urine illness." Just as in Ayurveda, the traditional name appears in the ancient texts, including the *Yellow Emperor's Inner Classic*. Historically, *xiao ke* is divided into three types—upper, middle, and lower—with each type corresponding to a disproportionate emphasis

on one of the three main symptoms which are thirst, hunger, and excessive urination. According to TCM terminology, deficient Yin is usually associated with all three types. Just as an Ayurvedic diagnosis of "prameha" may also refer to other illnesses, a TCM diagnosis of "wasting and thirsting" may also refer to illnesses besides the modern definition of DM2.[16]

Both Ayurveda and Chinese medicine (out of which TCM emerged) are ancient traditional knowledge healing systems with long and continuous histories of practice and use. These two healing systems are also becoming more and more available outside their countries of origin. In the United States, research shows that more than one third of the U. S. population reported utilizing at least one non-allopathic therapy to improve their health.[17] [18] Furthermore, Astin reported that such alternatives were more compatible with the patients' values, worldviews or beliefs regarding the nature and meaning of health and illness.[19] People using non-allopathic or integrative therapies are thus searching for healing systems that consider the whole person as compared to a collection of symptoms. Ayurveda and TCM may provide some solutions.

Methodology

Since 2001, I conducted field research in India and in China. From October 2001-June 2002, I conducted the following research in India. I enrolled in an intensive four-month certificate program in Ayurveda Theory and Practice at Gujarat Ayurved University (GAU), Jamnagar, Gujarat (NW India). I also completed a prospective and retrospective survey of individual plant and plant formulations utilized by two Ayurvedic practitioners (Drs. H.M. Chandola and D. Bhatt) to treat DM2 at a local clinic situated in a Hindu

Temple affiliated with Gujarat Ayurved University. I reviewed Ayurvedic texts and regional ethnobotanical databases concerning specific plants and treatments used to treat "sweet urine," as DM2 is called in Ayurvedic texts, in three locations: Gujarat Ayurved University (GAU), Jamnagar, Gujarat (NW India); Arya Vaidya Sala (AVS), Kottakkal, Kerala (SW India); and the Foundation for the Revitalization of Local Health Traditions (FRLHT), Bangalore, Karnataka (South Central India). I admitted myself into AVS in Kottakkal, Kerala for a three-week treatment period in order to personally experience Ayurvedic treatment via immersion ethnobotany.[20]

From October 2003-September 2004, I conducted the following research in India. I enrolled in a four-month certificate course to study the fundamentals of Hindu philosophy (the foundation of Ayurveda) while I also studied the ancient art of yoga at the Bihar School of Yoga (NE India). By studying the Hindu philisophical foundations of yoga, I reinforced and expanded my knowledge of Ayurvedic treatment protocols, since yoga and exercise are integral to Ayurvedic treatment protocols. I organized, planned, and conducted a seven-week, open-label treatment protocol to test the efficacy of Ayurvedic management therapy (AMT) for the treatment of DM 2 (see Chapter 5 for the complete protocol); the protocol included testing the efficacy of AMT for DM2 by measuring the primary parameter—changes in fasting blood-glucose levels. Secondary parameters measured were total cholesterol and glycated hemoglobin. In addition, the Ayurvedic treatment approach was documented and an Ayurvedic guide for nutritional intake for a South Asian population was developed for utilization during the course of the study. The multidisciplinary team included three Ayurvedic practitioners, a phytochemist, a general

practitioner, two endocrinologists, a botanist, a statistician, and me, a public health nutrition specialist botanist-in-training. Among the team members, languages spoken included Kannada, Tamil, Malayalam, Hindi, Urdu, and English.

From September-November 2005, I conducted research in China. For inter-comparative (Ayurveda and TCM) purposes, I conducted a series of case studies at the Institute of Integrated Chinese and Western Medicine, Fudan University, Shanghai, China under the guidance of Professor Wenjian Wang and his graduate student Chunyan He. We documented the TCM approach to treating patients with DM2.

City University Institutional Review Board (IRB) and the respective Review Boards in India and China approved all three studies involving human subjects. (Refer to Appendices A, B, and C to review official IRB approval letter dates and project numbers).

Chapter 1: The Evolving Field of Ethnobotany

Introduction

In the following chapter, I provide an overview of the field of ethnobotany as it relates to my dissertation. First I present a concise review of some definitions of ethnobotany and how the field has become more collaborative, multidisciplinary, and holistic. Basic ethnobotanical research techniques, specifically of the ethnobotanical-directed and comparative ethnobotany approaches to identifying medicinal plants are reviewed. The challenges ethnobotanical researchers encounter when they evaluate traditional healing systems, such as the challenge of properly training botanists to identify different disease states; the lack of detailed ethnobotanical data collected in the field; and the complexity of plants and plant formulations are discussed. I conclude this chapter by demonstrating how a change in approach by Western scientific researchers is needed if they are ever to collaborate effectively with practitioners of traditional practice-based knowledge systems.

Overview of Ethnobotany

Ethnobotany, as a discipline, is evolving into a more holistic and all-encompassing endeavor.[21] This section includes a select review of more recent definitions of ethnobotany as delineated by Davidson-Hunt.[22] I continue with a summary of how ethnobotanical research has been conducted in the past, and who has benefited from the research. I then discuss how continually to develop the field of ethnobotany by employing rigorous research techniques. I complete this section with an overview of the state of ethnobotany today.

Definitions of Ethnobotany

According to Wickens, [23] Stephen Powers coined the term "aboriginal botany" in 1875 in his description of plants used by the Neeshenam Indians of Bear River, California "for medicine, food, textile fabrics, ornaments, etc." North American field workers quickly accepted the use of this term for the next 25 years. The first published use of the term "ethnobotany" was by John Harshberger in 1896, when he defined ethnobotany as "the study of the direct interrelations between humans and plants."[24] [25] According to Davidson-Hunt, Harshberger's definition and vision still form the core of the science of contemporary ethnobotany. Although the definition has been reformulated over the years, only a slight change in emphasis may be noted.[26] Following is a select number of more recent definitions of ethnobotany.

By the late seventies, Ford remarked that ethnobotany had become more cultural than Harshberger had envisioned. Ethnobotany now focused on the "totality of the place of plants in a culture" and the direct interaction of the people with the plants.[27] Ford noted that ethnobotany had matured over the century to tackle a complex web of both applied and theoretical issues of human-plant interactions ranging from cognition to biodiversity conservation. [28] [29] On the other hand, Wickens defined ethnobotany as the study of useful plants prior to their commercial exploitation and eventual domestication. Wickens also noted that ethnobotany now included the use of plants by both tribal and non-tribal communities without any implication of primitive or developed societies.[30] Cotton defined ethnobotany "to encompass all studies which concern the mutual relationships between plants and *traditional peoples*." [31] Balick and Cox in broad terms defined

ethnobotany as the "…study of the relationships between plants and people. The two major parts of ethnobotany are encapsulated in the word itself: 'ethno' the study of people, and 'botany' the study of plants. Between these two points labeled 'ethno' and 'botany' lies a spectrum of interests ranging from archaeological investigations of ancient civilizations to the bioengineering of new crops. However, the field is limited on both sides. On the botanical side of the field, few ethnobotanical studies are concerned with plants that have no connection to people. On the ethno side, most studies are concerned with the ways indigenous people use and view plants." Balick and Cox suggested that, "those uses and those views can provide deep insights into the human condition."[32] Turner defined ethnobotany as the science of people's interactions with plants. While some prefer to restrict the discipline to the study of aboriginal, pre-industrial peoples and their relationships with plants, this definition does not recognize the complex relationships and interdependence between plants and modern societies of all types. Turner emphasized that it should be equally acceptable to study ethnobotany among Canadian Chinese, Canadian Ukrainian, Asian American, and African American cultures as much as among modern Native American groups.[33]

Based on these definitions of ethnobotany, Davidson-Hunt concluded that ethnobotany has changed its focus away from the use of plants by people and towards the relationship between people and plants. This includes use, cognition, and ecology. He noted, however, that there is no consensus as to whether the discipline should focus on all people or just traditional or tribal people.[34] He asserted that neither Cotton nor Balick and Cox provided a clear argument as to why ethnobotany should be limited in its scope.

Although Balick and Cox do provide several reasons for their particular interest in indigenous peoples for the purposes of research,[35] Davidson-Hunt concluded that definitions of ethnobotany such as those proposed by Turner (1995) and Ford (1994), which simply emphasize the dynamic and essential relationship between people and plants, point to the future of ethnobotany as opposed to its past.[36]

Turner summarized and emphasized that the very premises under which Harshberger operated have been shattered. The classification of men into savage, pastoral, agricultural, and civilized, for example, is no longer valid. In fact, a shift in these premises has lead to a more inclusive, respectful, and realistic approach in ethnobotany and its many associated disciplines.[37] The focus of ethnobotanical data collection has also shifted over the years. This is discussed in the following section.

Two Historical Approaches to Ethnobotanical Research

Compared to more recent studies, early ethnobotanical studies were more descriptive in nature. Researchers also tended to work mainly with indigenous communities. In 1996, Alexiades noted that within ethnobotany there were two general approaches: cognitive ethnobotany which focuses on how humans view and classify plants, and economic ethnobotany which focuses on how humans utilize plants. Berlin noted that early linguists and anthropologists engaged in cognitive ethnobotanical research whereas a broader range of specialists engaged in economic botany. [38] [39] Like Berlin, Martin also distinguished two types of ethnobotanical researchers: social scientists and natural scientists. The social scientists tended to focus on local people's interactions with the

local environment and to emphasize folk classification, social rules, and ecological strategies that guide such interaction, whereas the natural scientists acted as the economic botanists.[40] Alexiades argued that cognitive studies (social sciences) provided a theoretical framework that included rigorous data collection and analysis, whereas a large number of early economic studies (natural sciences) were purely descriptive and not situated in a larger theoretical framework, although there are notable exceptions.[41] This lack of a larger framework may have contributed to the criticism of ethnobotany as a non-rigorous science.

Who Benefits from the Ethnobotanical Research?

Early ethnobotanical research and data benefited the modern world. Some scholars, however, have argued that early ethnobotanical studies have had little practical value for the people who provided the information.[42] Although this may be true, Davidson-Hunt noted that this early, basic data-gathering effort can also be seen as a stage in the development of the discipline of ethnobotany.[43]

Alcorn argued that in its early days, ethnobotanical research was shaped by imperialist motives. In so many words, collectors gathered useful plants from areas where traditional cultural groups lived, and these plants were then used for commercial gain by the modern world.[44] Similarly, Davis asserted that Linnaeus, having provided a binomial framework to categorize plants, sent his students on botanical expeditions around the globe to discover plants for Europeans to use as food, textiles, and medicines.[45] Today, however, ethnobotany is more concerned with data collection within a framework where the data

benefits the development of all social and economic classes of people, in particular, the people in and from the region where the data are collected.[46]

Development of the Ethnobotanical Discipline

Plants play an important role in almost every aspect of human life. Ethnobotany encompasses numerous fields including botany, biochemistry, pharmacognosy, toxicology, medicine, nutrition, agriculture, ecology, evolution, comparative religion, sociology, anthropology, linguistics, cognitive studies, history, and archeology. The multidisciplinary nature of ethnobotany encompasses a wide array of approaches and applications. Because of this multiplicity, ethnobotanical research is a challenge for any individual researcher from any single discipline.[47] Today, the ethnobotanical scope has expanded to include modern culture studies and to demand more trans-disciplinary and a greater focus on conservation and sustainable development.[48]

Perhaps because of these challenges, Alexiades argued that, all too often, economic botany studies have not presented data in a larger framework that incorporates the evolutionary, pharmacological, ecological, cultural, historical or social contexts of human-plant interaction.[49, 50] To compound this problem, he added that there exists an intrinsic resistance within "orthodox" science to accept disciplines that challenge traditional boundaries between academic fields and this may also contribute to the perception among skeptics of economic ethnobotany as a "pseudoscience".[51] In order to develop the field of ethnobotany, Alexiades has challenged researchers to develop a sound methodology by defining the research problem, selecting a conceptual model, operationalizing the chosen variables, and choosing adequate field techniques.[52]

Ethnobotany Today

The field of ethnobotanical research has expanded since the days of Harshberger. Hamilton et al., the authors of *The Purposes and Teaching of Applied Ethnobotany*, have noted some of the major, worldwide developments in ethnobotanical research which include the following:

1. Shift of focus from indigenous peoples to embrace all sections of humanity;
2. Greater use of anthropological methods;
3. Awareness that ethnobotanical knowledge is part of wider knowledge-systems;
4. Greater scientific rigor in terms of hypothesis testing and quantification;
5. More emphasis on collaborative research to deal with conservation, sustainable development, and medicine;
6. Greater recognition of intellectual property rights of local and indigenous people, especially with respect to secret medical knowledge, and acknowledgment of the need to provide a fair return of benefits to the local people when research aims at the identification of new commercial products.[53]

Over the last decade in particular, ethnobotanists have become more engaged with questions of conservation, sustainable development, cultural affirmation, and intellectual property rights of local and indigenous people.[54]

A Multidisciplinary Approach

Because ethnobotany is such a vast field, each researcher's area of expertise will determine what types of multi- and transdisciplinary teams will emerge. Most

ethnobotanists encourage a multidisciplinary approach as it is essential to accomplishing quality research.

Davis argued that the old ethnobotanical practices of finding new plants, naming them according to binomial nomenclature, and then incorporating them into modern society has been enhanced by an intellectual view that sees the plants and their utilization as a metaphor for understanding traditional medical knowledge systems of a particular society. According to Davis, anthropologists helped emphasize the dynamic interrelationship between plants and people. The ethnobotanist's task became not one of mere compilation but to understand and evaluate the complex interactions using a biological perspective. He concluded that modern ethnobotany is interdisciplinary and requires an integrative focus and an array of specialists who work as a team. He stated that "no single theoretical or methodological orientation can encompass the breadth of inquiry that is modern ethnobotany. Rather, the ethnobotanist must adopt a problem-solving approach and select a research team and a methodology appropriate to the specific task at hand."[55]

Prance, too, realized the necessity of an interdisciplinary ethnobotanical approach to conducting research on plant chemical activity. For example, he argued that the chemistry of dried plants is often different from the chemistry of a fresh concoction used by a particular healer. Air-dried plants easily lose volatile compounds; and individual plant analysis overlooks the possibility of plant interactions within a mixture. To address these problems and to better analyze the actual medicine utilized by the healer, Prance

suggested that a series of teams conduct ethnobotanical fieldwork with each team made up of an ethnobotanist, an anthropologist, and a chemist. He argued that, in the past, chemical analysis often yielded negative results because analysis was of individual dried plants instead of the medicine used by the healer.[56]

In the case of researching the efficacy of single plants, plant formulations, or treatment modalities of a particular traditional system, Balick supported combining medical and ethnobotanical skills to obtain a proper understanding of plant use in terms of both Western biomedical science and traditional knowledge systems. This involves either an interdisciplinary approach with larger teams that include botanists and medical personnel, or an expanded academic curriculum to train individuals interested in specializing in the medical aspects of ethnobotany.[57]

Finally, Martin envisioned future ethnobotanical research as being fully collaborative. The local community collaborators, he explained, will be full partners in the process: design, research implementation, and application of results.[58] In addition to receiving monetary assistance, local ethnobotanists and scientists will collaborate in analyzing and reinforcing their traditional cultures of interest in various ways, such as by including the testing of local herbal remedies, measuring the sustainability of forest management practices, and designing ways of ensuring that knowledge is passed from one generation to the next.[59]

Within the past decade, Turner noted, ethnobotanists have taken on a more intensive advocacy role to help preserve the integrity of cultures, languages, and the environments in which they are situated. Turner remarked that this role parallels the advocacy roles taken on by conservation biologists and restoration ecologists to protect and enhance the world's biodiversity.[60]

Ethnobotany-Directed and Comparative Ethnobotany: Methods, Problems, and Challenges

Many methods exist for selecting medicinal plants for further study and research. In this section I present general methods for sampling medicinal plants. I focus on the benefits, challenges, and limitations of the ethnobotanical-directed and comparative ethnobotany approaches since these are the methods I utilized in my own research.

Martin described four general methods for sampling medicinal plants:

1. Random sampling method—Collect any plant in sufficient quantity and quality;
2. Chemotaxonomic method—Collect plants with specific documented secondary compounds on the basis of one's knowledge of the distribution of the plant chemicals one wishes to study;
3. Ethnobotanical method—Collect plants that are used as medicine by local people;
4. Comparative ethnobotanical method—Collect plants used by more than one ethnic group living in the same or different regions.[61]

Ethnobotanical Method

If a plant is used by a traditional medical practitioner for years, if not, for decades or centuries to treat a particular disease, one might assume that these plants have a higher incidence of bioactivity than plants chosen randomly from the forest. To test this hypothesis, Farnsworth and his colleagues analyzed information on the 119 known useful plant-derived drugs to determine how many were discovered based on medicinal folklore. In other words, what correlation, if any, existed between the current medical use of the 119 drugs and the alleged medical uses of the plants from which they were derived? Farnsworth found that 74% of the 119 chemical compounds used as drugs have the same or related uses as the plants from which they were derived. This does not mean that 74% of all medical claims for plants are valid, but it does demonstrate that medicinal folklore has significance that was not previously documented. [62]

When Balick evaluated plants submitted to the U.S. National Cancer Institute (NCI) for activity against human immunodeficiency virus (HIV), he found that random plant collections yielded 6% activity, whereas those based on "powerful plants" used by an herbal healer yielded 25% activity. However after dereplication to remove certain compounds such as tannins and polysaccharides (plant compounds already known to have medicinal effect were dereplicated),[63] the percentage fell dramatically and became virtually identical using either random or ethnobotanical-directed collection methodology. Balick added that Gordon Cragg and his colleagues at NCI have shown with a much larger data set that the general ethnobotanical collections do not appear to be advantageous in developing leads for HIV treatment.[64] Balick observed that potentially

significant compounds may be discarded in the dereplication process. He also noted that at least one major research program directed by King and Tempesta has shown that potent antiviral compounds can be isolated from tannins.[65] An additional study by Slish et al. demonstrated that four of 31 ethno-directed species were found to be potent relaxants of vascular smooth muscles whereas none of the 32 randomly collected samples produced a relaxation response.[66] Another point to consider is that traditional healers do not have a history of treating HIV; however, the diseases that they have treated for generations may yield higher levels of active compounds, plants, or plant formulations.[67]

Lewis and Elvin-Lewis argued that traditional knowledge systems provide ample information about plant properties when properly evaluated. For example, Lewis and Elvin-Lewis provided a possible explanation for the lack of activity of ethnobotanical-directed plants as compared to randomly collected samples. Based on their own extensive research, they caution ethnobotanical researchers "not to throw out the baby with the bath water." First, they argued that a medicinal plant often contains more than one bioreactive component that can act additively or synergistically to affect its full healing potential. Therefore, a plant valued as an antiviral agent may yield a weak or moderately weak antiviral substance when tested, but its activity may then be enhanced by the presence of immune modulators and possibly other unidentified healing or physiologically active substances. The same may also be true for certain medicinal plant formulations. These features, valued in holistic traditional knowledge systems such as Ayurveda and TCM, are a challenge to drug discovery strategies involving the isolation of antiviral agents from plants identified by ethnomedicine. This point is especially relevant when

significant clinical antiviral activity does not correlate well with the potencies of the antiviral compounds present in the remedy. Because an important goal of antiviral drug discovery is to identify treatments that are low in toxicity, bioactive compounds derived from efficacious plants should not be discarded out-of-hand without an examination of their toxicities and how they interact.[68]

Balick emphasized that the ethnobotanical-directed approach is most likely to succeed when it is focused on an actual disease system (i.e., diabetes) that is historically treated by healers using specific plants. A smaller study by Slish et al. has already tested this approach with promising outcomes related to potent relaxants of vascular smooth muscles.[69] This concept is being tested by the private sector, and the results over the next decade will enable a proper evaluation of the ethnobotanical-directed approach. [70]

Oubré et al. discussed the ethnobotanical approach used in their research. The team focused on a particular disease state and used a multidisciplinary approach to identifying plants for the treatment of DM2. The team consisted of a Western trained physician-ethnobotanist team and an indigenous healer. By utilizing culturally sensitive interviewing techniques, the physician-ethnobotanist team was able to assess the clinical diagnosis of the disease being treated with a given plant. The team was also able to gather relevant data on the plant parts used, mode and frequency of administration, preparation, expected course of treatment outcome, and other pertinent botanical or medical information.[71] [72]

Farnsworth added that unless ethnobotanical information is collected in greater and more precise detail, then the approach is not better than random selection followed by targeted biological screening. He remarked that Shaman Pharmaceuticals used the detailed approach, which involved a team comprised of an ethnobotanist and a medical doctor who collected information in the field directly from users or healers, with follow-up laboratory studies to verify or disprove the ethnobotanical claims. This approach was unique in the field of drug discovery.[73]

In summary, the ethnobotanical approach is an important tool for identifying plants for bioactivity as long as the ethnobotanical information is collected in appropriate detail; secondary compounds that are dereplicated are not summarily dismissed; a specific disease state is defined during the process of identifying plants or plant formulations for treatment; and compounds are prepared according to traditional medicine prescriptions (e.g., a tea made with water as opposed to an alcoholic extract). It appears Shaman Pharmaceuticals had integrated these important measures to ensure ethnobotanical-directed identification of bioactive plants. According to Farnsworth in 1988, this approach was particularly timely as Western culture was/is in the process of displacing certain traditional healing practices around the world. He concluded that future programs of drug development from higher plants should include a careful evaluation of historical as well as current claims of the effectiveness of plants as drugs deriving from different traditional knowledge systems since such information is rapidly disappearing.[74]

Comparative Ethnobotany

An ethnobotanical-directed approach is a methodology that facilitates identification of plants, plant formulations, or management protocols with potential efficacy. A comparative ethnobotanical approach (comparing more than one different healing tradition) may add additional evidence to the efficacy of certain plants or treatment protocols. Some researchers argue that commonality of use, whether based on independent discovery or interaction between peoples is directly related to the degree of effectiveness of a remedy.[75] [76] [77] Farnsworth said that if, for example, a plant is claimed to be used to treat diabetes in one or more countries or on several continents, this repetition of information would encourage one to believe that the effect was real.[78] Jain and Mudgal reported that a comparative approach may provide information about regional variations of single plant species usage as well as different plant species usage for similar purposes.[79] However, Sensarma and Ghosh cautioned that all communities, in South Asia for example, do not view a specific plant with equal reverence or prescribe a specific plant for the same uses. Utilizing phytoanthropologic tools to research different communities' uses of a particular plant, Sensarma and Ghosh reviewed the varied uses of ten plants in India. India comprises different ethnic, linguistic, and religious groups that often live side by side, yet the authors demonstrated that human-plant relations vary greatly among and between these groups.[80]

Conclusions

As opposed to the random sampling of plants, ethnobotanical and comparative ethnobotanical methods are approaches that are able to identify potentially efficacious traditional knowledge systems' single, multiple plant formulations, or treatment

protocols. But any given one of these approaches is more reliable when data are collected in detail, when secondary compounds are not summarily dismissed, when a specific disease state is defined, and when more than one other knowledge system also demonstrates a history of use.

The Challenges of Ethnobotanical-Directed Method

Limitations exist when one is evaluating the efficacy of single plant or multiple plant formulations for efficacy in the laboratory. The first challenge has to do with the proper training of botanists to identify different diseases states; another is the lack of detailed ethnobotanical data collected in the field; and a third challenge, already alluded to, is the complexity of plants and plant formulations.

Proper Identification of Disease States

One of the major problems evaluating ethnobotanical data noted by Lewis and Elvin-Lewis involves the descriptors applied to disease syndromes by researchers. Many symptoms reported by patients or healers may be too vague to give an indication of what the plant is used for. Part of the solution to this problem is in ensuring the proper training of the interviewer and to provide a clear understanding of both Western biomedical and traditional medical systems.[81] Farnsworth concurred and added that, for the most part, botanists who conduct field work in areas where use of medicinal plants is a way of life are not trained in or do not fully understand the disease state.[82]

Proper Data Collection

The information that ethnobotanists gather is generally inadequate for the laboratory scientist to evaluate in terms of selecting plants for expensive biological investigations, Farnsworth stated.[83] For example the literature in ethnobotany, ethnomedicine, and ethnopharmacology usually documents the following information:

(a) Latin binomial of the plant used;
(b) Common or local names of the plant used;
(c) Plant part(s) used;
(d) Geographical area where used; and
(e) Medical use (often vague with few details).

Data that are required for assessment of the value of the plant medicine but are usually missing from ethnobotanical writings are the following:

(a) Method of preparation of the medicine;
(b) Dosing (amount and frequency of use);
(c) Source of information (e.g., traditional healer, actual user, person who knows someone who uses the plant for medicinal applications, his or her background, age, group);
(d) Route of administration (oral, external, rectal, vaginal, nasal, ophthalmic); and
(e) Specific medical use and/or symptomatology of the disease.[84]

Based on extensive experience in the field, Lewis and Elvin-Lewis stated that the better one understands the disease systems and the etiological agents or physiological events that cause them, the more definitive the assays are and the more significant the results obtained. These results then translate into highly focused and targeted information of enormous potential relevance in natural products research. Many researchers have argued that ethnobotany provides the mechanism for rapid assessments of the pharmaceutical potential of species. This approach is a significant procedure when time and funds are insufficient to test the majority of species.[85 86 87 88 89 90 91]

Complexity of Single and Multi-Plant Formulations

Another problem researchers confront—and one to which Lewis and Elvin-Lewis have already alluded—is the complexity of single and multi-plant formulations.[92] In addition to Lewis and Elvin-Lewis' analysis of the complexity of single plant and plant formulations, Hamilton et al. made three points in this regard:

(1) Testing the efficacy of medicinal plants can be complex. *In vitro* tests may fail to reveal active constituents because these may form only during internal digestion.
(2) Plants or plant formulations active as mixtures may be ineffective or even toxic if administered alone. Practitioners often question the therapeutic value of substituting medicinal plant preparations with single isolated chemicals derived from a plant formulation or from a single plant.
(3) Statistical proof of efficacy may be difficult to determine if medicines are tailor-made for individual needs, as is common in non-Western traditions, rather than prescribed as standardized aliquots, the normal practice with Western pharmaceutical drugs.[93]

Perhaps searching for a single bioactive ingredient from a particular plant is not the most effective approach. Instead of requiring traditional practitioners to fit their approaches into the Western biomedical paradigm, researchers may collaboratively develop innovative methods for testing the efficacy of particular time-tested formulations or treatment protocols. This approach does not limit researchers' ability to test for efficacy based on patient outcome. In fact, this approach allows traditional practitioners to test their medicines or treatment protocols in a controlled setting, and provides the researchers with data to benefit both Western and traditional knowledge systems. (This approach, however, introduces a whole other set of challenges to the modern scientific researcher. A review and discussion of some of these challenges appears in Chapter 6, where clinical research results are presented.)

Conclusions

In summary, most medicinal plant knowledge systems utilize single plant and multiple plant formulations. The point in time at which each plant is harvested, the preparation, and the synergy between individual plants in a multiple plant formulation are often based on years of experiential and observational data. Often, plant formulations modulate the effect of the individual plants, thereby increasing the desired effects and decreasing possible harmful effects. Testing patient outcomes involving traditional plant formulations may be the first step in identifying effective treatment protocols. The shift away from identifying bio-active ingredients and towards identifying effective management treatments or protocol strategies may be one way to help patients who are suffering from disease.

A Shift in the Paradigm?

The following is a summary of the work of several contemporary researchers in the field of ethnobotany who identify issues that challenge western orthodox ideas about how one defines a science.

Contemporary ethnobotanists recognize that knowledge of the language and culture of the people with whom one is working are prerequisites to a full understanding of the uses of plants.[94] According to the same logic, contemporary ethnobotanists often study the philosophical and theoretical foundations of the "traditional knowledge systems" under investigation. Shankar has emphasized that, just like the western biomedical paradigm, many traditional healing systems, whether codified or non-codified, adhere to their own theoretical principles based on philosophical and experiential groundings.[95] For example, Shankar and Majumdar stated that if modern medicine wants to apply the successes of some Ayurvedic treatments, then non-Ayurvedic-trained researchers should be encouraged to take the time to learn Ayurvedic principles, diagnostics, pharmacological, and treatment theories and procedures.[96] However, it should be noted that some traditional practitioners from certain traditions such as Ayurveda and TCM claim that their systems are already scientific, since they are validated by centuries of experimentation.[97] These practitioners argue that their traditional systems do not require the approval of Western biomedical medicine to make the treatments more efficacious.

Anderson asserted that traditional empirical knowledge must first be accepted as science, not just as 'ethnoscience.' According to him many scientists as well as science historians,

tend to dismiss anything non-Western as not "real" science, and therefore unworthy of serious attention. Yet these very same scientists are willing to follow Ancient Greek and Renaissance theorists in referring to their activities as "science," though these sciences were based on very different principles from anything related to contemporary Western biomedical medicine. Anderson proposed using a term to describe non-allopathic healing traditions as "empirical, practice-based knowledge of the world." This term is applied as long as it generates general principles that systematize and extend beyond observations. Anderson strongly argued that we cannot understand Maya science, for example, without understanding its transformation beliefs, any more than we can understand European medical science of the nineteenth century without knowing Galen's equally wrong but equally influential humoral theories.[98]

Cox touched on a sensitive topic when he discussed the limitations of the ethnobotanical approach. Perhaps Western scientists need to confront the fact that indigenous knowledge systems have effectively discovered bioactivity without the tools of Western biomedical science. This realization challenges the epistemology of some Western scientists who may be threatened by this success. Yet Cox asserted that the promise of the ethnobotanical approach is that we may learn not only new pharmacology, but also new ways of caring for the sick and for the planet we share.[99] Hamilton et al. argued that in seeking ways forward, it is important that scientists maintain open minds, that they try to understand the biases of their own scientific traditions, and that they keep in mind the cultures and socio-economic circumstances of those whom they wish to benefit or with whom they wish to collaborate.[100]

Anderson succinctly stated that "we have to see ethnobiology as a science whose ultimate end is not just knowledge but knowledge applied to saving nature, and, as a part of that, to using resources more efficiently in order that humans and other creatures can live decent lives without wiping out the resource base. To do this, and even to understand adequately the actual uses and non-uses of plants and animals that we observe, we have to investigate entire world views: traditional science, religion, arts, stories, languages, and society."[101]

Conclusions

Traditional knowledge systems adhere to their own internal logic and theoretical foundations. Some practitioners asserted that their systems do not require validation from Western medicine. Others argued that as long as a practice-based knowledge system generates principles that systemize and extend beyond observation, it should be considered a science. The limits of strict Western biomedical research methodologies are also challenged since, in many instances, indigenous knowledge systems have effectively identified bioactivity of plants or a treatment protocols without the use of modern-day scientific tools. However, in order to introduce those plants, plant formulations, or treatment protocols from traditional healing systems into the Western medicine paradigm, an approach that respects the parameters of both scientific traditions can be developed. Towards this end in the following chapters, I discuss how as a team we developed and administered a study to test Ayurvedic Management Therapy (AMT) for the treatment of DM2.

Chapter 2: Ayurveda and Traditional Chinese Medicine: Treating "Madhumeha" and "Xiao ke"

In the following chapter, I present data on the worldwide *Diabetes mellitus* epidemic. To better understand Ayurvedic and TCM practice, I review the two systems' historical treatment of DM2.

Diabetes mellitus: A Review

Diabetes is a worldwide epidemic that is most prevalent in India, China, and the United States. King et al. estimated that between 1995 and 2025, diabetes will increase 195% in India, affecting some 57.2 million people; 134% in China, affecting some 37.6 million people; and 58% in the United States, affecting some 21.9 million people.[102] Any number from 85-95% of diagnosed diabetes cases are classified as Type 2. For a map of recent data on diabetes distribution worldwide, see Figure 1 and Table 1.

Prevalence of diabetes, 2003, the World

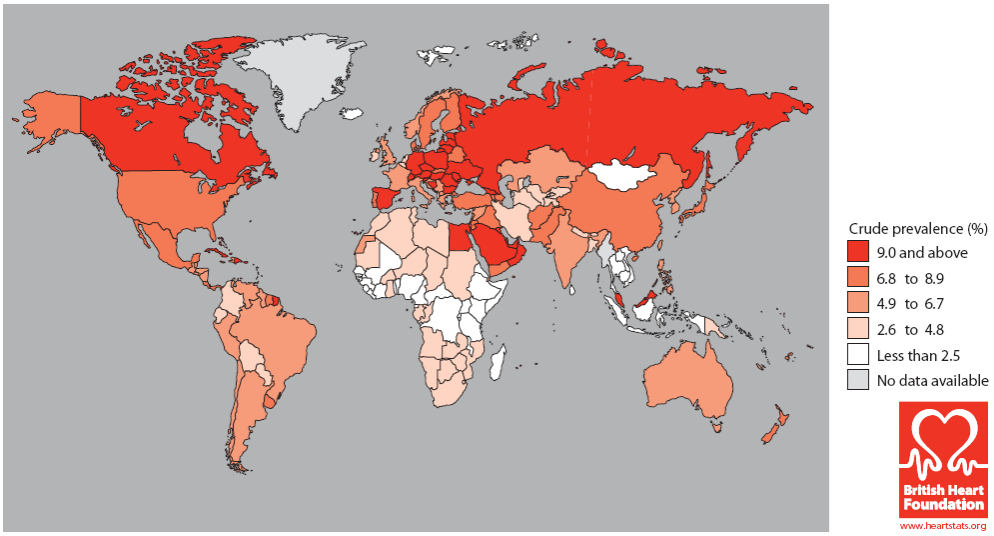


Figure 1. World Diabetes Prevalence 2003 [103]

Table 1. Diabetes and Impaired Glucose Tolerance (IGT) Prevalence [104]

All Diabetes and IGT	**2003**	**2025**
Total world population (billions)	6.3	8
Adult population (billions) (20-79 years)	3.8	5.3
Number of people with diabetes (millions) (20-79 years)	194	333
World diabetes prevalence (%) (20-79 years)	5.1	6.3
Number of people with IGT (millions) (20-79 years)	314	472
IGT prevalence (%) (20-79 years)	8.2	9.0

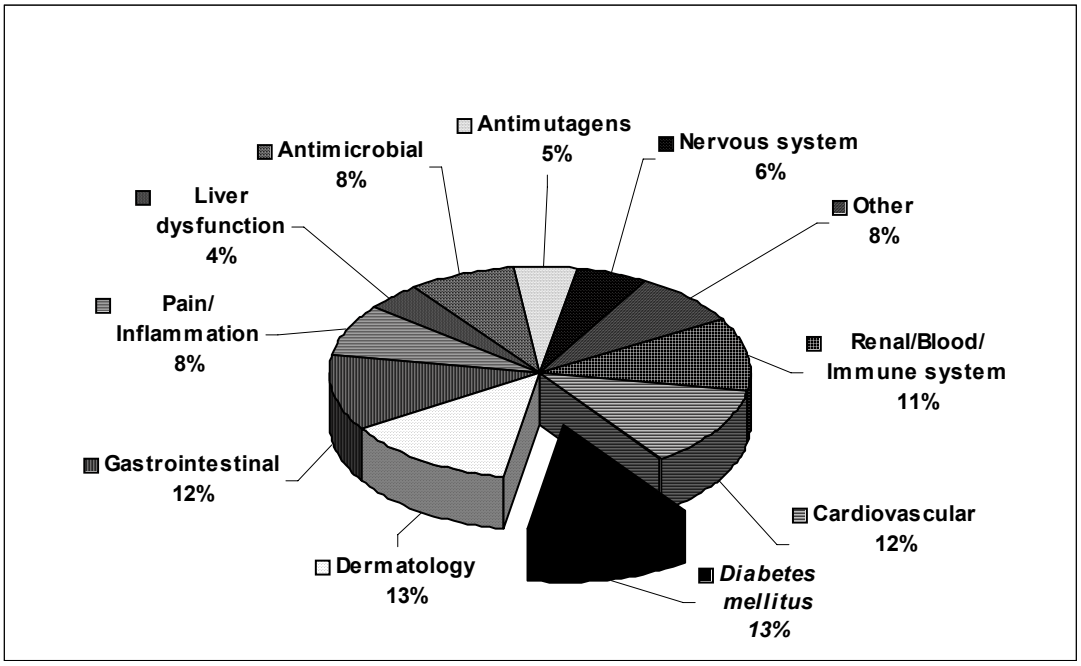
Within the USA, diabetes is one of the most common chronic diseases, with more than 7% of the adult population affected. It is even more common in the elderly, Latino, African-American, Asian and Pacific Island-American, and Native-American populations.[105] In order to address this growing epidemic in Asia and North America, I researched Asian healing systems and their possible contributions to the treatment of DM2.

After reviewing the literature on 166 Ayurvedic plants, Khan and Balick found that 13% of the plants had demonstrated some type of antidiabetic effect in human studies [106] (Figure 2). Of the 166 plants researched, 25 showed some effect in both animal and human studies. These included: *Aegle marmelos* (L.) Correa, *Allium cepa* L., *Aloe barbendensis* Mill., *Capsicum annum* L. *Cassia fistula* L. *Coriandrum sativum* L., *Cuminum cyminum* L. *Eclipta alba* (L.) Hassk., *Eugenia jambolana* Lam., *Ficus benghalensis* L., *Ficus religiosa* L. *Gymnema sylvestre* (Retz.) Schult., *Juniperus communis* L., *Linum usitatissimum* L., *Nelumbo nucifera* Gaertn., *Ocimum sanctum* L., *Oryza sativa* L., *Picrorhiza kurrooa* Royle ex. Benth., *Saussurea lappa* (Decne.) C.B.

Clarke, *Swertia chirata* (Wall.) C.B. Clarke, *Taraxacum officinale* Weber ex. F.H. Wigg., *Tephrosia purperea* (L.) Pers., *Tinospora cordifolia* Miers, *Trigonella foenum-graecum* L., and *Withania somnifera* (L.) Dunal.

Based on this review of the literature, and because both Ayurveda and Chinese Medicine possess a long history of treatment of modern-day DM2, I decided to focus my dissertation research on Asian healing systems' treatments of modern-day DM2. Furthermore, in the subcontinent and Asia, Ayurveda and Chinese medicine, as locally available and culturally acceptable modalities, may provide alternatives to the more expensive conventional treatments.

Figure 2. Percentage of 166 Ayurvedic Plants with Human or Studies Divided into 11 Categories (n = 66) (Khan and Balick 2001)



*Prameha and Madhumeha Descriptio*ns based on Ayurvedic Classical *Texts*

Classical Ayurveda

Classical Ayurvedic treatment not only includes individualized medicinal plant prescriptions based on an individual's Ayurvedic constitution but also encourages diet modification, exercise, and mental balance. The Ayurvedic paradigm of healing has a long and continuous history of use and a substantial scientific literature on the efficacy of Ayurvedic medicinal plants, and is often concurrent with allopathic modalities of treatment.[107] In terms of DM2, the Ayurvedic clinical description, etiology, diagnosis, prognosis, and recommended lifestyle changes are similar to those in Western medical descriptions.[108] Over the centuries, Ayurvedic practitioners have developed numerous classical formulations for individual sub-types to treat madhumeha (sweet urine). Historically, classical Ayurvedic preparations, when administered by an Ayurvedic physician according to prescribed dosages, are considered safe, tolerable, and non-toxic.

Differential Diagnosis of *Madhumeha*

Like Chinese medicine, Ayurvedic practitioners utilize a system of differential diagnosis to treat individual patients. The diagnosis is based on analysis of the signs and symptoms and the differentiation of syndromes. There is an art in selecting the appropriate protocol, and in changing the protocol as the signs and symptoms of a patient change over time. A review of the basic Ayurvedic diagnosis techniques appeared in Chapter 3.

History of *Madhumeha*

In classical Ayurvedic texts, a urinary abnormality is described as *prameha* (over-production of urine). *Madhumeha*, sweet urine, is one of 20 subtypes of *prameha*. According to Bhatia, Charaka described ojameha as a synonym for *madhumeha*, because *ojas* (life essence) is secreted through the urine.[109] [110] [111] Susruta, another important figure in the development of Ayurveda, in particular surgery, described *madhumeha* as *kshaudrameha* where one passes urine that resembles the color of honey.[112] Susruta also explained that all *pramehas*, left untreated, will turn into *madhumeha*.[113] If ulcers occur, *madhumeha* is considered incurable.[114] [115]

Definition of *Madhumeha*

Charaka,[116] Susruta,[117] and Vagbhata[118] all described madhumeha as a subtype of twenty different *pramehas* ('*pra*' means intensity of amount; '*meha*' means to pass urine; '*prameha*' means an overproduction of urine or a urine abnormality). These twenty subtypes are divided into three categories: *kaphaja*, *pittaja*, and *vataja* prameha (Table 2). *Madhumeha* ('*madhu*,' sweet; '*meha*,' to pass urine) means to pass sweet urine. *Madhumeha* falls under the *vataja dosha* category.[119] [120] [121] [122] [123]

Table 2. Types of *Prameha*: *Kapha, Pitta,* and *Vata* (Please note that Ayurvedic scholars differed on the *Prameha* names and categorizations. This is why some names are not listed.) [124] [125]

Types of *Prameha* (As described in Classical Ayurvedic texts)				
Kaphaja Pramehas				
	Charaka Samhita	***Susruta Samhita***	***Vaghbata Samhita***	***Madhava Nidanam***
1	*Udakameha*	*Udakameha*	*Udakameha*	*Udakameha*
2	*Ikshuwa Ikshuwalikameha*	*Ikshuwa likmeha*	*Ikshumeha*	*Ikshumeha*
3	*Sandrameha*	*Sandrameha*	*Sandrameha*	*Sandrameha*
4	*Shuklameha*	*Pishtameha*	*Pishtameha*	*Pishtameha*
5	*Sandraprasadmeha*	*Surameha*	*Surameha*	*Surameha*
6	*Shukrameha*	*Shukrameha*	*Shukrameha*	*Shukrameha*
7	*Shitameha*		*Shitameha*	*Shitameha*
8	*Siktameha*	*Siktameha*	*Siktameha*	*Siktameha*
9	*Shanairmeha*	*Shanairmeha*	*Shanairmeha*	*Shanairmeha*
10	*Alalmeha*		*Lalameha*	*Lalameha*
11		*Lavanameha*		
12		*Phenameha*		
Pittaja Pramehas				
	Charaka Samhita	***Susruta Samhita***	***Vaghbata Samhita***	***Madhava Nidanam***
1	*Ksharameha*	*Ksharameha*	*Ksharameha*	*Ksharameha*
2	*Kalameha*		*Kalameha*	*Kalameha*
3	*Neelameha*	*Neelameha*	*Neelameha*	*Neelameha*
4	*Lohitameha*	*Shonitameha*	*Raktameha*	*Raktameha*
5	*Manjishthameha*	*Manjishthameha*	*Manjishthameha*	*Manjishthameha*
6	*Haridrameha*	*Haridrameha*	*Haridrameha*	
7		*Amalameha*		
Vataja Pramehas				
	Charaka Samhita	***Susruta Samhita***	***Vaghbata Samhita***	***Madhava Nidanam***
1	*Vasameha*	*Vasameha*	*Vasameha*	*Vasameha*
2	*Majjameha*	*Sarpimeha*	*Majjameha*	*Majjameha*
3	*Hastimeha*	*Hastimeha*	*Hastimeha*	*Hastimeha*
4	*Madhumeha*	*Kshaudrameha*	*Madhumeha*	*Madhumeha*

Classification and Causes of *Madhumeha*

Based on detailed descriptions of signs and symptoms, *madhumeha* correlates with modern definitions of DM2.[126] [127] [128] For example, *madhumeha* is further divided into two

types. (1) *Dhatukshaya janya madhumeha* (DJM) is characterized primarily as a wasting of the tissues (*dhatus*) that leads to increased vata. The patient tends to be lean and thin. Genetics play a role; the problem is often compared to modern *Diabetes mellitus* Type 1, and is considered incurable. (2) *Aavrutta janya madhumeha* (AJM), on the other hand, is primarily characterized as relating to an excess of heavy, oily, sour, and/or salty foods, non-aged cereal products, and a sedentary lifestyle. Increased fat leads to excess *kapha* and *pitta*, which obstruct the passage of vata. Lifestyle and diet tend to play a role; this type of *madhumeha* is often compared to modern *Diabetes mellitus* Type 2, and is considered curable or at least manageable. [129] [130] [131] [132] [133]

In his review of classical texts, Shah added that the causes of *madhumeha* include sitting on soft cushions for long periods of time and/or sleeping for long periods of time. This also included excessive intake of curds; domestic, aquatic, or marshy land animal flesh; milk and milk products; fresh grains; fresh water; puddings made of jaggery (unprocessed cane sugar) or sugar; and any kapha-increasing substances.

Charaka added that, according to Shah, mental anxiety and excitement are also predisposing factors of vataja prameha. Susruta reiterated that those who indulge in sleep during the day, have a sedentary lifestyle, or take in excess sweet, cold or fatty foods will also succumb to madhumeha.[134] Vata or vatika pramehas, according to Charaka, included the excess consumption of astringent, pungent, bitter, rough, light, and cold foods. Excess in activities such as sexual intercourse, physical exercise, emesis, purgation, non-unctuous enema, and hard evacuation will also contribute to development of vatika

pramehas. Suppressing natural urges, fasting, injury, exposure to the sun, excitement, anxiety, excessive bloodletting, and unhealthy body postures are other factors that exaggerate the madhumeha and vatika pramehas.[135]

Charaka and Vagbhata described an individual with madhumeha as one who passes excessive urine that is astringent, sweet, pale, and rough. Vagbhata added that the whole body is sweet. Susruta qualified this by noting that the urine of the effected individual resembles honey and acquires a sweet taste.[136]

Vagbhata asserted that all types of food and activities that increase kapha, fat, and urine cause prameha. These include foods that are sweet, sour, salty, unctuous, heavy, slimy, or cold; drugs; fresh grains (new grains); sura (a particular type of wine); flesh of marshy animals; sugarcane; jaggery; and milk products.[137] (For a summary description, see Table 3).

Table 3. Classification and Causes of *Madhumeha* according to Classical Ayurvedic Texts

	Charaka	Susruta	Vagbhata
Definition	Prameha is a type of obstinate urinary disorder.[138]	A pramehi is a person who demonstrates prodromal features of urinary abnormality with a slight or excessive increase in urine.[139] A madhumehi is one who is suffering from boils and has severe complications.[140]	Prameha is a type of polyuria.[141]
Symptoms and Causes	Addiction to the pleasure of sedentary habits, sleep, curds, soup of the meat of domesticated and aquatic animals or animals inhabiting marshy land, milk preparations, freshly harvested food articles, freshly prepared alcoholic drinks, jaggery preparations, and all kapha-aggravating factors are responsible for prameha.[142] Sweating, foul body odor, flabbiness, sedentary lifestyle, a sense that the cardiac region is covered with extraneous material, excretion from eyes, ears, and tongue, obesity, excessive hair and nail growth, desire for cold things, a dry throat and palate, a sweet taste in the mouth, burning sensation in hands and legs, ants swarming on the urine.[143]	There are two types of urinary abnormalities: hereditary ones and those due to indulgence in insalubrious activities. The hereditary types are caused by defects in the paternal and maternal germinal seeds; the insalubrious factors are derived from the intake of non-beneficial diets. People suffering from the former are thin and dry-skinned, eat less, have polydipsia, and have active habits; whereas the people afflicted with the latter type are obese, have polyphagia, are smooth-skinned, and prefer to sit idle, lie down, and sleep.[144]	Early symptoms include an increase in area and rate of growth of nails, matting of the hair, sweet taste in the mouth, dryness of the palate and throat, thirst, increase of waste products on skin exterior and in the orifices of the body, desire for cold, greasiness of the body, perspiration, loss of tactile sensation, burning sensation in the hands and soles of the feet, ants swarming to the body because of excess sweetness, bad smell of urine and body, whiteness of urine, difficult respiration, sleepiness, stupor, and laziness.[145]
Prognosis	Kaphaja pramehas are of ten types and are curable. Pittaja pramehas are of six types and are palliable. Vatika pramehas are of four types and are incurable.[146]	All types of urinary abnormalities, if not treated in time, develop into madhumeha and become incurable.[147]	Those prameha caused by kapha, or by pitta and vata, are controllable and incurable, respectively.[148]
Pathology	Kapha having vitiated medas, mamsa, and kleda of the body located in the urinary tract causes different types of meha. Similarly, pitta aggravated by hot things vitiates those elements and causes different types of meha. When kapha and pitta are in a diminished state, the aggravated vata draws tissue elements such as ojas, majja, and lasika into the urinary tract and vitiates them to cause the third category of pramehas.[149]	Various types of urinary abnormalities are produced based on specific increases or decreases within the combination of doshas, dhatus, malas, and foods.[150]	The cause of all of the pramehas is indulgence in foods and activities that increase the production of kapha, fat, and urine. Prameha is produced from kapha followed by vata, pitta, fat, moisture in the body, muscular tissue, semen, and lymph/plasma getting localized in the urinary bladder. When pitta is associated with kapha, blood and other prameha are produced. When vata is associated with lymph, bone marrow, and ojas (the substance that maintains life), prameha is produced.[151]

Symptoms of Prameha and Madhumeha

Symptoms of prameha appear in descriptions by Charaka and Susruta. Charaka described the symptoms of *prameha* in the following terms: matting of hair; sweetness in the mouth; numbness and burning sensation in hands, feet, and body parts; dryness in the

mouth, palate, and throat; thirst; lassitude; mala accumulation in the body; smearing in body orifices; bees and ants attracted to the body and urine; frequent sleep; and drowsiness.[152] Susruta concurred and described *prameha* symptoms as the following: burning sensation in palms, hands, and soles of feet; body heaviness; urine that is sweet and white; somnolence; lassitude; thirst; bad breath; shortness of breath; a slimy mucous deposit on the tongue, palate, pharynx, and teeth; clotted hair; and the excess growth of finger- and toenails.[153] Vagbhata described *prameha* symptoms in the manner of Charaka.

Symptoms of *madhumeha* may include those listed above for prameha with a particular emphasis on an increased quantity and turbidity of urine, sweet urine that resembles honey, and urine that tastes astringent. Susruta and Vagbhata also described affected urine as sweet like honey. Also included in the symptomatology of *madhumeha* are extreme thirst, hunger, tiredness, and accumulation of waste. Susruta went on to explain that the patient's urine attracts a swarm of flies, and that the patient is struck with lassitude, becomes obese, has no interest in food, experiences indigestion and a burning sensation on the skin, and has thirst, insomnia, body numbness, and constipation.[154] [155]

Prognosis of *Madhumeha*

If the disease is caused by excess *kapha* or *pitta*, it is considered curable. If the disease is due to excess *vata* then it is considered incurable. If not treated, all *prameha* varieties, according to Madhava, an expert on Ayurvedic clinical diagnosis, will ultimately become madhumeha and will perhaps be incurable.[156] Mishra explained in more detail that the *kaphaja* urinary disorders are curable because the causative *dosha* and the affected tissues have the same properties. Because of this, the therapy required is also the same. *Pittaja*

pramehas are controllable, and the disorder may persist because the causative *dosha* is *pitta*, whereas the tissues and waste products are different, requiring a different type of therapy. *Vataja* p*ramehas* are considered incurable because both the *dhatus* and *ojas* undergo deterioration.[157]

Pathology of *Madhumeha*

According to classical Ayurveda, DM2 and all *pramehas* (urinary disorders) begin with the derangement of *kapha* that spreads throughout the body. As *kapha* spreads it mixes with fat that is similar to *kapha*. Once *kapha* mixes with fat, it passes into the urinary system and interferes with normal urinary excretion. Deranged *pitta*, *vata*, and other body fluids may also be involved in this blockage. The blockage is thought to cause the frequent urination that NIDDM patients' often experience.[158]

In summary, the Ayurvedic definitions, classification and causes, symptoms, prognosis, and pathology of *madhumeha* provide insight into an ancient disease and its treatment. To varying degrees, the Ayurvedic assessment of madhumeha parallels many observations and treatment modalities with modern allopathic assessments and approaches. Traditional Chinese Medicine, on the other hand, percieves DM2 from a different lens.

TCM Management of Xiao ke bing (Diabetes mellitus)

According to Liu et al. of the Cochrane Database of Systemic Reviews, medicinal herbs have been widely used for more than 2000 years to treat NIDDM ('*xiao ke bing*' as it is described in ancient texts on Chinese medicine).[159] The term '*xiao ke*', literally, "wasting/melting and thirst," a label used to this day for diabetes, is a compound ideally

suited to signify two obvious symptoms of this disease. Because thirst and 'melting' are so obviously associated with diabetes, the possibilities of parallel observations in other healing traditions in the East (Ayurveda, Unani, Tibetan, etc…) and beyond leading to similar terms and descriptions of the same disease are quite strong.[160]

Based on the *Inner Classic*, Ni translates that xiao ke or diabetic exhaustion "is usually caused by a diet rich in fatty foods, which generates internal heat. Indulgence in sweets also weakens the spleen, leading to chest and abdominal fullness."[161]

According to Dharmananda, two of the traditional herbal formulas most frequently used in modern China and Japan for the treatment of diabetes were described in the book *Jingui Yaolue* (written around 220 C. E.), which is about miscellaneous diseases. The text described symptoms characteristic of uncontrolled diabetes such as thirst, frequent urination, and loss of body weight. One of the formulas described was Rehmannia Eight Formula (*Bawei Dihuang Wan*; also called *Jingui Shenqi Wan*). Originally it was indicated for persons who showed weakness, fatigue, and copious urine excreted soon after drinking water. Dharmananda suggested that in some cases this may have been diabetes as we know it today. The other formula described was a ginseng and gypsum combination (*Baihu Jia Renshen Tang*); originally it was indicated for severe thirst and fatigue and is considered ideal for diabetes of recent onset.[162]

The Chinese medical classic *A Collection of Diseases* written by Wang Shou and published in 752 C. E., described sugar in the urine as one of the most important

symptoms of diabetes. Choate stated that for the first time in Chinese medical history, diabetes was listed among the eleven hundred diseases. The author recommended pork pancreas as treatment for the disease, and also recommended a special method of testing sugar in the urine: the patient was asked to pass urine on a wide, flat brick to see if ants gathered to collect the sugar.[163] Ayurvedic practitioners would also check to see if ants gathered, and tasted the urine for sweetness (as in Tibetan medicine).

Dharmananda reported that Liu Wansu (ca. 1120-1200 C. E.) supported the theory that diseases are usually caused by heat in the body, which should be countered by herbs that had a cold nature. One of his published formulas for diabetes, Ophiopogon and Trichosanthes Combination (*Mainendong Yinzi*), is traditionally described as clearing heat and nourishing yin. It is comprised almost entirely of herbs that have been shown by modern research to lower blood sugar. Another of his formulas, Siler and Platycodon Formula (*Fangfeng Tongsheng San*), is recommended by many Japanese doctors for treatment of obesity and accompanying type 2 diabetic syndrome. [164]

By the latter half of the 20th century, there were about 200 standard prescriptions recorded as suitable for treating diabetes.[165] The majority of these may be viewed as combinations that rely primarily on about two dozen anti-diabetic ingredients plus a small number of auxiliary herbs. Over time, the main traditional prescriptions brought forward came to include Rehmannia Eight Formula and its simplified version, Rehmannia Six Formula; Ginseng and Gypsum Combination; and Ophiopogon and Trichosanthes Combination. [166]

In the late 1970s, clinical investigations were reported on the use of herbal medicines (both different single herbs and mixtures of herbs) as a means of treating diabetes and its

complications. The mechanism of action of the herbal medicines involves regulating glycemic metabolism, decreasing cholesterol levels, eliminating free radicals, increasing secretion of insulin, and improving microcirculation. Until March 1999, 14 herbal medicines (13 mixtures of herbs and one extract of a single herb) were officially approved for the treatment of diabetes by the State Drug Regulatory Authority of China; thirteen herbal medicines were listed in the National Essential Drugs directory issued by the State Drug Administration of China. Almost all the herbal medicines are so-called 'Chinese proprietary medicines,' i.e., they are usually based on well-established and longstanding recipes and formulated tablets or capsules for commerce, convenience, or palatability. However, active ingredients of these formulations are largely unknown and they are combined to formulate herbal medicines. A number of clinical trials have been reported on the subject in Chinese medical journals during the past 20 years. The first randomized trial was reported in 1991.[167]

According to TCM generally *xiao ke bing* is attributed to three main factors: improper diet, emotional disturbance, and a constitution that is yin deficient:

- Improper diet refers to irregular eating and drinking habits in the form of over-consumption of fatty, greasy, pungent and sweet foods, and hot drinks and alcohol that damage the transporting and transforming functions of the spleen and stomach. The accumulated food in turn generates internal heat that consumes the fluids, thus bringing on wasting and thirsting.
- Prolonged emotional disturbance contributes to wasting and thirsting by hindering the flow of qi. Over-thinking damages the spleen. Anger, resentment and

frustration lead to constrained liver *qi*, which transforms into heat and fire and consumes the *yin* of the lung and stomach. Excessive worry damages the kidneys and weakens the *qi*.

- When an individual is constitutionally yin deficient, factors such as prolonged stress or illness, overwork, and/or excessive sexual activity can consume the essence. The result is kidney *yin* deficiency that can be mixed with lung and stomach *yin* deficiency symptoms as well as with kidney *yang* deficiency.[168] [169]

According to Choate, *Diabetes mellitus* is classified as upper, middle or lower *xiao ke bing* (wasting and thirsting syndrome) and is generally characterized by thirst, hunger, frequent urination, and wasting. Cloudy urine and sugar in the urine may also accompany these symptoms, each of which is said to have a predominant symptom: excessive thirst in the upper *jiao* (lung), excessive appetite in the middle *jiao* (stomach), and excessive urination in the lower *jiao* (kidney). In reality there is usually a mixture of all the symptoms, although one often predominates slightly. By his or her analysis of the symptoms, one should be able to determine which organ—lung, stomach or kidney—is most *yin* deficient, and should therefore have a focus for treatment.[170]

Upper burner

Upper *xiao ke* syndrome is characterized by the drying up of body fluids by lung heat, which leads to great thirst, restlessness, dry cough, dry skin, hoarseness, dry red tongue with or without cracks, a thin yellow tongue coating, and a forceful rapid pulse, especially at the distal position.[171]

Middle burner

Middle *xiao ke* syndrome is characterized by stomach fire which leads to excessive appetite and constant hunger, desire to drink cold liquids, a burning sensation in the epigastrium, constipation, a red tongue with a thick yellow coating, and a slippery, forceful rapid pulse.[172]

Lower burner

Lower *xiao ke* syndrome is characterized by kidney yin deficiency where there is excessive urination (clear or turbid), dry mouth at night, night sweating, sore back and aching bones, red-peeled tongue, and a deep, thread-like rapid pulse. [173]

Lower *xiao ke* syndrome with deficiency of both kidney *yin* and *yang* (with the latter more pronounced) is characterized by frequent urination of turbid urine, especially at night; soreness and weakness of the lower back and knees; aversion to cold; lassitude; impotence; a pale red tongue with teeth marks and a white coating on the tongue; and a deep, thread-like weak pulse.[174]

Pathogenesis of Xiao Ke

> Huang Di said, You mentioned previously that in febrile disease or diabetic exhaustion, one should not consume fatty, sweet, or rich foods: the doctor should not use aromatic herbs or heavy minerals. Fragrant herbs can cause manic reactions, and heavy minerals can cause epilepsy.

> The typical patients who suffer from these two conditions are often wealthy. You ask them to refrain from a rich diet, which they may resist; yet you also do not use expensive aromatic and mineral herbs How do you proceed then?
>
> Qi Bo answered, Aromatic herbs may be too dispersing. The dispersing can cause the pathogen to enter the orifices. Heavy minerals are too strong and have a rapid-acting and harsh quality. Unless the patient is on a calm nature, one should not prescribe these herbs."
>
> Huang Di asked, Can you explain this further?
>
> Qi Bo replied, Heat conditions are already harsh. The use of harsh herbs will inure the spleen qi. The spleen is the earth and disdains domination by wood. The use of these herbs on jia yi days will surely cause the condition to worsen.[175]

Liu and Tseng summarized the pathogenesis of *xiao ke*. The imbalance begins with a *yin* deficiency and dry heat. Over a period of time, this state will damage *qi* and *yin*. A damaged *yin* affects *yang*. This sustained imbalanced state ultimately results in both a *qi* deficiency and a *yin* deficiency. In addition, damp-heat, blood stasis, and heat toxins may exacerbate the disease process.[176]

In summary, DM2 is at epidemic proportions worldwide. Ayurveda and TCM as locally available adjuvant therapies may provide valuable treatment modalities to treat such an ancient disease.

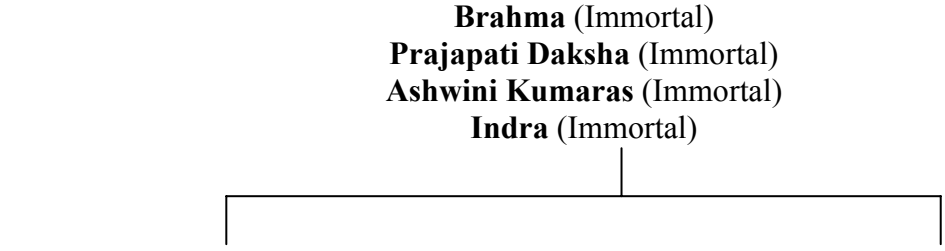
Chapter 3: A Brief History of Ayurveda

Introduction to a Brief History of a South Asian Medical Tradition:[177] Ayurveda

Ayurveda, one of a number of South Asian medical systems, began its development in ancient times (other South Asian codified traditions include the Siddha,[178] Tibetan,[179] and Unani [180] [181] traditions, for a few examples). Tracing Ayurvedic history up to the present is a challenging task. Furthermore an unbroken series of delineated developments does not exist. Instead one must regard the evolution of modern-day Ayurveda as a series of phases.[182] In this section, I present Ayurvedic history and development up to the present. First I will present a brief overview of the developmental phases of Indian medicine. These phases may be divided into the Mythical, Pre-Vedic and Pre-Harappan, Vedic, and Classical Samhita phases (it should be noted that the classification of Ayurvedic history in these phases is disputed), and A Select History up to the Present. I will conclude this section with an overview of contemporary Ayurveda.

Mythology

I begin with a brief overview of the mythological development of Ayurveda. Kutumbiah described how Charaka, one of the fathers of classical Ayurveda, described the development of this healing art (Figure 3).



Divodasa Dhanvantari (Immortal) **Dhanwantari** (Mortal, King of Varanasi) --Many disciples: Aupadhenava, Vaitarana, Aurabhara, Poushakalvata, Gopurakshita --Developed School of Surgeons 9-6th B.C.E. Centuries --Developed School of Physicians 8-6th centuries B.C.E.	**Bharadwaja** (Rishi) **Purnavsu Atreya** (Mortal) --Many disciples: Ksharapani, Parashara, Harita, Jatukama, Bhela, Agnivesha
Susruta --Wrote first well accepted standard textbook of Ayurveda: Susruta Samhita (Palm Leaf Manuscript), 5-4th century B.C.E.	**Charaka** --Revised Agnivesha Samhita, 1st century C.E.
Susruta II --Nagarjuna, 1st century C.E. Anonymous writer --Wrote Uttara-Tantra and completed the work of Susruta-Samhita	**Vagabhata** --Astanga Hridaya --Commentary and summary of Charaka and Susruta, 7th century C.E.

Figure 3: Important Figures in the Development of Ayurveda[183]

As humans began to get sick and experience disease, holy seers met on the slopes of the Himalayas and decided that Indra, the king of gods, would reveal to Bharajdeva the keys to wellness, Ayurveda, in a condensed form. Bharajdeva then passed this knowledge on to Punarvau Atreya, who taught Ayurveda to six disciples: Agnivesa, Bhela, Jatukarna, Parusara, Harita, and Ksirapani.[184] When diseases arose that impeded the austerity, fasting, study, continence, and vows of humans in general, the great sages, the doers of good who were foremost imbued with compassion for all creatures, met together on the sacred Himalayan slope. Saraswati tells the story of this gathering:

Health is the supreme foundation of virtue, wealth, enjoyment, and salvation. New diseases are the destroyers of health, of the good life, and even of life itself. Thus has arisen the great impediment to human progress. What will be the means to remedy this?

Having observed this, they sat in meditation. Then they saw with the eye of understanding, their refuge in Indra. He the Lord of immortals shall tell us rightly the means of overcoming disease. Who will go to the abode of the thousand-eyed Indra in order to inquire and learn from him? "I should be charged with this mission." The first to speak these words was Bharadvaja. Hence he was commissioned by the sages.

Diseases have arisen that are the terror of all human beings. Tell me O'Lord of the immortals! The appropriate means of remedying them. Unto the sage, the great Lord Satakrtu (Indra) knowing his wide understanding, propounded in a few words, the science of life.

He taught the science of causes, symptoms and medication, the supreme refuge of both—the healthy and the ailing, the tripartite science, eternal and holy, that the Great Father Brahma knew.

> Bharadvaja thereby acquired unmeasured life endowed with happiness, and in his turn, taught the science to the sages, without either adding or withholding any part.
>
> The great sages perceived this science in its true nature with the eye of discernment; the nature of the general and the particular; the substances, their qualities, actions and coexistent relation; and understanding it and conforming to the rules laid down in the system, they attained the highest happiness and enduring life.[185]

According to Susruta, sages approached Lord Divodasa Dhanvantari, King of Benares. The sages asked the Lord to relay the healing arts to preserve their own lives and for the benefit of mankind. Lord Dhanvantari explained to the sages that Brahma composed one hundred thousand slokas (concise Sanskrit verses) and a thousand chapters on Ayurveda. But due to a human's limited lifespan and intellectual capacity, he simplified Ayurveda and divided it into eight chapters: *Salya chikitsa* (surgery), *Salakya* (eye, nose, and throat), *Kayachikitsa* (general medicine), *Butavidya* (psychiatry), *Kaumarabhrtya* (pediatrics and gynecology), *Agada tantra* (toxicology), *Rasayana tantra* (rejuvenation), and *Vajikarana tantra* (sexual disorders). Lord Dhanvantari further explained to the sages that Brahma had revealed Ayurveda to Prajapati, who taught it to the two Asvini-Kumars. The Asvini-Kumars represented the principles of duality and aided the Vedic gods. From these twins, Indra learned the subject, and Dhanvantari learned from Indra. [186, 187]

With the understanding that this knowledge was too vast to pass on to a single person, Indra decided to impart the knowledge to four great Rishis or teachers: Atreya and Bharadvaja learned general and internal medicine; Kashyapa acquired pediatric knowledge; Dhanvantari mastered mainly surgery. Agnivesha, Atreya's best student, formalized Ayurvedic philosophy and practice in the *Agnivesha Tantra*. This tantra formed the basis for Charaka's later classical treatise.[188]

Although slight variations exist among the descriptions of the mythological development of this ancient healing art, scholars generally agree on the history summarized above.

Pre-Vedic and Pre-Harappan

There are numerous perspectives on the Pre-Vedic and Pre-Harappan civilizations. Indian historian Romila Thapar described six main races that comprise the Indian subcontinent according to ethnological studies: Negrito, Proto-Australoid, Mongoloid, Mediterranean, Alpine, and Aryan. Thapar delineated that the Proto-Australoid race formed a basic element in the Indian population and that this race's speech derived from the Austric linguistic group. Among certain tribes, elements of the language survive in Munda speech. The Mediterranean strain is associated more with Dravidian culture in the South, and people of Mongoloid descent were concentrated in the northeast and the northern fringes of the subcontinent with their speech conforming to the Sino-Tibetan group. The last people to arrive were those referred to commonly as the Aryans. Thapar clarifies that "Aryan" is in fact a linguistic term describing a speech-group of Indo-European origin, and not an ethnic term.[189] According to Kochhar, more recent research revealed that South Asia may not be the home of the Rigvedic people.[190] He asserted that

the Indo-Aryans actually began composing the Rigveda when they were still in Central Asia, Iran, or Afghanistan, and that they probably then completed it in the subcontinent.[191]

One area of pre-Harappan society is thought to have existed at Mehrgarh, a site in the Kachi Plains of Baluchistan (modern day Pakistan).[192] [193] Little is known about the people's migration patterns during the pre-Harappan period. Based on linguistic studies, Jha postulated that the Aryans' homeland was in the steppes stretching from southern Russia to Central Asia. Perhaps one of the Aryan branches migrated to different parts of Europe, Asia, and Iran. Different Iranian tribes then migrated in successive waves, it is thought, over several centuries southeast towards India.[194] Other scholars challenged the notion of an Aryan invasion from the north that caused a transition from the Indic to the Indo-Gangetic cultural tradition. Erdosy asserted that based on linguistic and archeological evidence, "the model of 'Aryan invasions' is firmly rooted in nineteenth-century attitudes about the civilizing mission of European powers, combined with a desire to find a non-Semitic past for themselves. That it survived for so long may be attributed to its utility for both imperialists and nationalists in South Asia: to the former, it provided historical justification for their mission; to the latter it afforded the prestige of common descent with the very power that ruled over them."[195] Kochhar argued further that the establishment of a common Indo-European heritage at the outset of European rule provided the British with a powerful tool with which to reach out to the upper-class Hindus.[196] It is important to note that these debates still exist and that over time, certain suppositions about history are reinterpreted. These historical controversies aside, the first

documented presence of people in the South Asian continent was from Harappa and was also known as the Indus Valley Civilization. It is clear that vibrant medical traditions did develop in South Asia, and the possible influences behind them will now be discussed.

There is a dearth of information on what exactly influenced the development of the Ayurvedic medical tradition. Filliozat, for example, discussed at great length the possible influences of the Indo-Iranian period on the later development of Ayurveda. He concluded that although a complete medical system that the successive Aryan migrants may have brought with them from Iran to the northern sub-continent did not appear to exist, several general ideas about the nature of water, fire, and wind had already been developed. These emerging principles may have contributed to and shaped the later development of Ayurveda.[197]

Indus Valley Civilization or Harappan Civilization

The Indus Valley Civilization or Harappan is the earliest civilization documented in South Asia (Figures 4 and 5). A significant amount of evidence exists about the Harappan civilization even though the script has yet to be deciphered. The Harappan culture was contemporaneous with the Old, Middle, and New Egyptian kingdoms and with Sumer and Akkad in Mesopotamia.[198] In addition, according to Keswami, these Harappan excavations have similarities to those of Elam, Sumer, and Crete.[199] Kutumbiah also added that the Harappan civilization was contemporaneous with Mesopotamia, Egypt, and Crete, and that intimate contact occurred. He described in more detail the prevalent views on illness and disease in these three areas. He concluded that these systems and the ancient Indian system were magical-religious and possessed

characteristics similar to those of the systems used by contemporary civilizations of the time.[200] According to Zysk, magical-religious thinking was understood to have been grounded within the belief that "the causes of disease are not attributed to physiological functions, but rather to external beings or forces of a demonic nature who enter the body of their victim and produce sickness. The removal of such malevolent entities usually involved an elaborate ritual, often drawing on aspects of the dominant local religion and nearly always necessitating spiritually potent and efficacious words and actions."[201] This is similar to classical shamanic disease theory.

Zysk and Sharma described the Harappan settlements as comprising a highly developed and urbanized culture that existed principally along the Indus River (modern Pakistan) from the Arabian Sea to the Punjab and as far south as Gujarat. This vast civilization was nearly twice as large as the Egyptian civilization and four times greater than Sumer and/or Akkad. The main centers or capitals were Mohenjo-Daro (near modern Sukkur) in the south and Harappa (near Lahore) in the north.[202] [203] Keswami noted that the Indus Valley cities' public health facilities were unique in that they far surpassed the facilities found in other ancient civilizations in organization, complexity, and hygiene. The attention to sanitation indicated a high level of advancement in the health and medical fields.[204] More evidence is needed, however, on public health facilities during this time period.

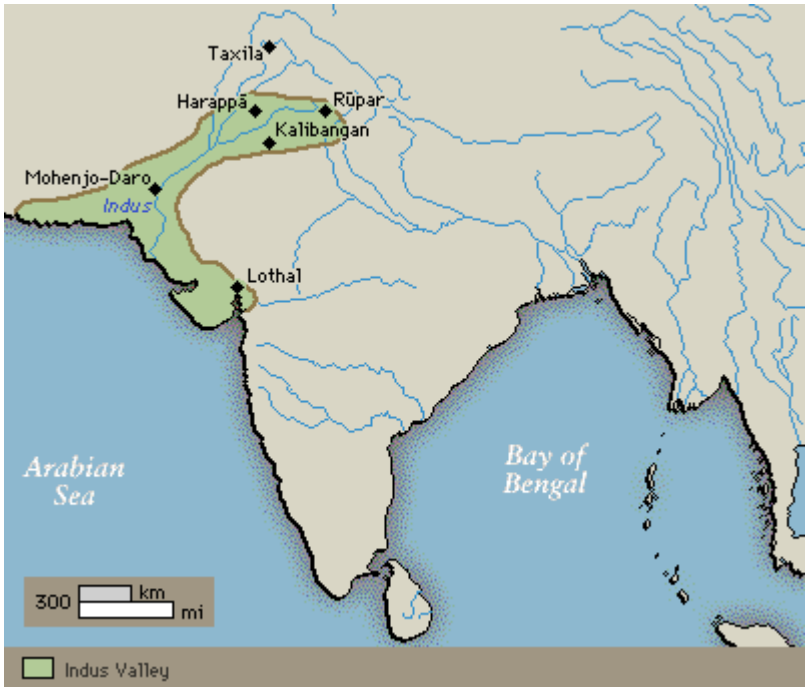


Figure 4. General Indus Valley Civilization Map (www.harappa.com)

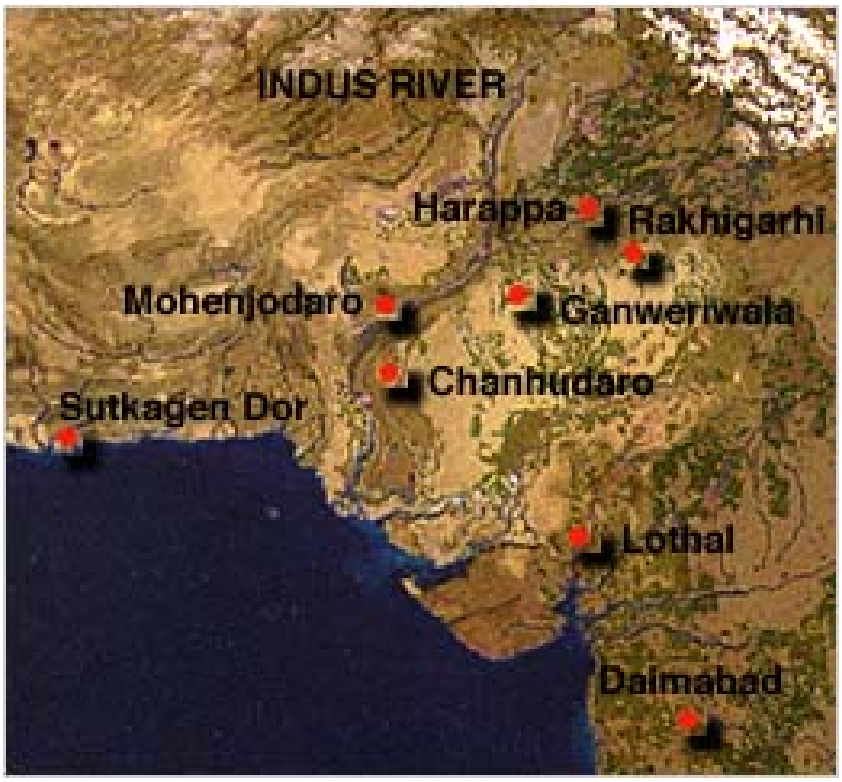


Figure 5. Map of Major Indus Valley Civilization sites (www.harappa.com)

The architecture of the sites was also unique for its time. Harappan cities had wide, paved streets that were planned on a north-south and east-west grid, aqueducts, public baths, and extensive drainage systems. Houses were usually two stories and made of baked brick. Many homes contained a bathroom with sloped floors to facilitate drainage, and some even had latrines similar to modern-day bathrooms.[205] (Figures 6, 7, 8, and 9) Both Svoboda and Zysk found that these architectural designs represented a concern for public health and sanitation, and suggested a belief in ritual purity and pollution that became apparent in later Indian thought.[206] [207] Apparently, a strong emphasis was placed on personal hygiene and the miraculous attributes of water. In later Vedic thought, too, water played a central therapeutic role.[208] For example, the Great Bath at Mohenjo-Daro symbolized not only water's power to cleanse and purify, but also its value to maintaining physiological body fluids.[209]

Figure 6. Mohenjodaro Great Bath (www.harappa.com)

Figure 7. Great Bath Floor (www.harappa.com)

Figure 8. Mohenjodaro Bath (www.harappa.com)

Figure 9. Artist's Conception of Harappa Indus Valley Civilization (www.harappa.com)

Although no concrete evidence exists, the Harappan civilization probably possessed a system of medicine. Zysk suggested that the Harappan healing system was connected with the culture's religious beliefs and practices.[210] Keswami stated that one can only postulate on what kind of medicine the Indus Valley people practiced in the fourth millennium B. C. E. (Before the Common Era). Their medicine must have been made up of a combination of religious and empirical practices. A few substances found at these sites are part of the Ayurvedic pharmacopoeia today.[211] Svoboda stated that the discovery of deer antler, bitumen, and cuttle bone remains, for example, supports this hypothesis, since these substances are used in classical Ayurveda.[212] Sharma further explained that vegetable, animal, and mineral remains exist demonstrating the use of drugs. Evidence also exists of tree-worship, indicating the importance of plants and plant materials to human existence. Various methods of sudation and anointment of the body were in evidence, as was the use of collyrium to prevent and cure eye diseases. It is thought that the Indus people used seals and amulets that depicted animals to ward off

negative spirits. Sharma noted that this practice may have served as a nucleus for bhutavidya, one of the eight branches of Ayurveda.[213] Like Sharma, Zysk proposed that the depictions on some of the seals represent a deep reverence for the earth and the medicinal plants the earth produces. This reverence is also found in Vedic medicine and in later Ayurvedic medicine where the pharmacopoeias detailing the medicinal value of plants become a central foundation of the medical tradition. But Zysk stated that the seals' usage will remain shrouded in mystery until the pictographic Harappan script is deciphered.[214]

On the other hand, Filliozat asserted that the use of similar products for therapeutic purposes proves nothing concerning the medical knowledge of the Harappan civilization. What one may safely assert, he claimed, is that medical knowledge could have been at an advanced stage, and that scientific exchanges probably occurred between the Indus Valley and Mesopotamia before the appearance of the Aryans.[215] Zysk did conclude that Harappan culture demonstrated a concern for public health and a medical tradition that revered plants that were probably in religious ceremonies, and that the spiritually based method of healing was characteristic of medical practices documented in ancient Egypt and Mesopotamia.[216] The cause of the gradual decline and eventual collapse of the Harappan civilizations over the course of two hundred years is unclear. Perhaps the invading Aryans from the north or repeated natural disasters such as the flooding of the Indus contributed the decline. Nevertheless, the culture ceased to exist around 1500 B. C. E.[217]

Before the Vedas, Hindu society developed sciences that had to do with their worship: astronomy, mathematics, geometry, gross anatomy, and medicine. The Sanskrit language also developed.[218] According to several authors, Indian cultural history and chemical knowledge and practice developed during the Vedic period. The Indo-Aryans appear to have settled in the northwest of India and to have interacted with the earlier non-Aryan inhabitants. When the Aryans arrived in the Indus Valley they brought their religious and medical traditions with them. The Indus civilization also contributed to the invading Aryans' culture through assimilation.[219] Thapar emphasized that religious worship in the north followed both Aryan and non-Aryan forms as aspects of both traditions are evident in today's Hinduism. Thapar explained that the Harappa people worshipped fertility symbols such as the mother goddess, bulls, horned deities, and trees, and these practices have continued in Hindu worship. Thapar further asserted that the more abstract Brahmanical belief system, founded on the Vedas, appealed to a limited few.[220]

Vedic Period

The earliest textual evidence of Indian medicine is found in the Vedic texts. According to Kochhar, the Vedic texts comprise priestly religious books that were composed over a long period of time by a large number of authors and the majority of the Vedic texts were completed before the Buddha's time (563-483 B.C.E.). Kochhar stated that the Vedic texts fall into three distinct categories:

1. Four *Vedas* or *Samhitas* and *Brahmanas*: Together these texts are known as *Sruti* (which means "heard," implying revelation). The *Brahmanas* are prose texts attached to the *Samhitas* and are considered to be interpretations of rituals.

2. *Aranyakas* and *Upanishads*: Together these texts are called *Vedanta* (the end part of the *Vedas*). The Aranyakas are concerned with ideas of mysticism and symbolism and form a natural transition to the more philosophical Upanishads.

3. *Kalpasutras*: These contain detailed instructions for performing rituals and are divided further into four categories.[221]

People recited sacred hymns and practiced sacred rituals according to the *Vedas*, the *Brahmanas*, the *Aranyakas*, and the *Upanishads*.[222] It is thought that the Rishi Vedavyasa collected and compiled the four *Vedas* during this period.[223] The four major *Vedas* are the following:

1. The *Rigveda* contains the hymns of the Gods.
2. The *Samaveda* contains the priests' chants.
3. The *Yajurveda* contains sacrificial formulae in prose.
4. The *Atharvaveda* contains chants.

Most scholars believe the oldest *Veda*, the *Rigveda*, was compiled during the second millennium B. C. E. and Svoboda supported this assertion. This version has been preserved by many generations over the centuries. In the purely religious Vedic texts, there are numerous hymns reflecting anatomical, physiological, pathological, psychological, and therapeutic ideas.[224] According to scholars, the *Rigveda* is considered

the source of Hindu medicine, with its hymns and prayers to different deities, extolling their medical and surgical skills. Unnikrishnan asserted that the *Ausadhi sukta* in *the Rigveda* is the oldest document available on medicinal plants, and that brief descriptions of medicinal plant morphological characteristics, habitats, therapeutic classifications, and uses are described.[225] The *Samaveda* and *Yajurveda* are closely related to the *Rigveda* and contain sacrificial prayers and ritual texts.

According to Svoboda, the *Atharvaveda* contains the seeds of Ayurveda with the probable incorporation of indigenous Harappan medical knowledge. The *Atharvaveda* appears to be the first record available of medical knowledge during the Vedic period. It includes prayers, incantations, spells, and charms to protect people from disease and natural disasters.[226] Also known as the *Brahma Veda*, the *Atharvaveda* was current in nine different collections. Only the *Paippalada* and *Saunakiya* recensions are available. The *Saunakiya School* has the *Gopatha-brahmana* as its brahmana as well as five sutra works: *Kausika*, *Vaitana*, *Naksatra-Kalpa*, *Angirasa-kalpa* and *Santi-sutra*. These are known as the five kalpas. Of these, the *Kausika-sutra* is probably the earliest and the most important, since all the others depend on it.

Kutumbiah stated that only a few medicines, such as *jangida*,[227] *guggulu*,[228] *kastha*,[229] and *satavara* [230] are mentioned in the Atharvaveda. These plants, in the form of amulets, provided protection from illness and enemies. Kutumbiah further stated that the *Kaushika Sutra* of the *Atharvaveda* directs the use of these medicines either internally or as amulets. In fact, the medicines were used as internal amulets. But on the whole, although

the *Atharvaveda*, along with the practices provided in *Kaushika Sutra*, provide insight into the medical knowledge base during the Vedic period, there is little information on the substances' therapeutic value.[231, 232, 233]

In fact, the fundamental principles of Ayurveda were not elaborated or documented during this time period. [234, 235] Majumdar stated that the *Atharvaveda* has references related to Ayurveda, but that nowhere in the text is the word Ayurveda mentioned. He concludes that Ayurveda developed as a systematic science at a later date, although some material from the *Atharvaveda* was incorporated.[236] However, later texts such as the *Ramayana*, *Mahabharata*, and *the Puranas* mention the word "Ayurveda." Thakar concluded that Ayurveda most probably developed as a branch of knowledge between the Vedic and Puranic periods.[237]

Present-day Ayurveda derives mainly from the later classical texts of Charaka and Susruta dated from around the first century of the Common Era (C.E.).[238] These and later texts contain detailed information on all aspects of health and disease. According to Kutumbiah, at this point, a transition occurred in the development of the Indian medical tradition. There is an emergence of a science with a greater emphasis on empirical thought than on religious practices.[239] Sharma added that there is a general decline in incantation therapy and an increase in drug (plant) therapy by the end of the Vedic age and into the post-Vedic age.[240] After the *Vedas*, approximately between 800 and 600 B. C. E., a time of intellectual ferment occurred that not only led to the establishment of two new faiths, Jainism and Buddhism, but also to the rise of six Indian philosophical

systems.[241] *Vedas* were later organized into the encyclopedic *Samhitas* that have commentaries attached and with which scholars and practitioners are familiar today such as *Charaka*, *Susruta*, and *Vagbhata Samhitas*.[242]

As is often the case, debate and controversy exist as to the development of and influences on Ayurveda. According to Kutumbiah, for example, few medical records existed between the close of the Vedic collections and the development of the schools of medicine.[243] But Wujastyk claimed that he did not include in his own book any material from earlier religious Indian literature, such as the Vedic *Samhitas* or the *Brahmanas* because these texts are not about medicine as it is classically conceived, but about religion. They form the surviving liturgy of extremely ancient Indo-Aryan ritual practices. Wujastyk admitted that there are parts of these texts, especially of the *Atharvaveda*, that bear on the early history of medicine in India. For example, there are prayers and charms aimed at bringing health and staving off the malevolent intentions of disease deities. However, if one looks more closely at the medical ideas and practices preserved in the early Vedic religious literature, one finds that for the most part they do not form an obvious precursor to the system of classical Ayurveda. Wujastyk asserted that such medical material as is recoverable from the Vedic literature is remarkable more for its differences from classical Ayurveda than for its similarities to it. To cite but one example, there is no clear mention in Vedic literature of the system of the three humors or dosas, one of the centerpieces of Ayurveda (see Chapter 4). Of course there are some areas where similar ideas are expressed, but the overall sense is that, culturally speaking, Ayurveda comes from somewhere else. Wujastyk concluded that Ayurvedic texts' claims

to 'derive from' the *Veda* are not evidence for medical history, but rather evidence of a bid by medical authors for social acceptance and religious sanction.[244]

Wujastyk next focused on recent scholarship and studies that have addressed aspects of the problem of what Ayurveda's distinctive roots really are, and how it evolved into the full-fledged classical system we find in the classical *Samhitas*. He refered specifically to Zysk, who he claimed has provided concrete evidence along with a persuasive interpretative framework for a new understanding of the historical roots of Ayurveda. Zysk interpreted Ayurveda as a medical tradition emerging from the ascetic milieu that existed in North India in the fifth century B. C. E. Zysk found evidence in the earliest literature preserved by Buddhist monks who were part of this milieu that almost perfectly fits with early Ayurveda as represented by the *Charaka* and *Susruta Samhitas*. The Buddhist evidence, however, is still embedded within a religious discourse.[245]

It is important to take note of the above controversies surrounding the development of Ayurveda. On a less controversial note, however, most scholars agreed that present-day Ayurvedic practitioners' training is based on the classical *Samhitas*. The *Samhitas* represent an attempt to systematize diverse treatises and opinions on medicine during the time period. And it is this classical period that we will turn to now.

Classical Samhita Period

As the number of diverse treatises on Ayurveda increased, the need arose to systematize the existing medical knowledge. The *Samhitas* represented such an attempt.[246] According to Filliozat and other scholars, the main and oldest classical Indian texts are the *Bhela,*

Charaka, and *Susruta Samhitas*. The first, *Bhela Samhita*, is available in one single incomplete manuscript and the others are not available in their original forms, though more recent revisions of them exist.[247] Although there are no longer any original texts on the Indian medical tradition, the *Charaka* and *Susruta Samhitas* contain a large amount of information. Originally written about 1000 B. C. E., these are considered the most authentic representations of classical Ayurveda. [248, 249]

Charaka

Charaka, Susruta, and Vagbhata form the famous ancient triad of classical texts (*vrddha-trayi*) (Table 4). According to medical tradition, Atreya had six pupils: Agnivesa, Jatukarna, Parasara, Bhela, Harita, and Ksirapani. All wrote medical treatises called tantras. What is known as the *Charaka Samhita* is actually the work of three authors: Agnivesa, Charaka, and Drdhabala. It is important to note that this compilation belongs to several different centuries. So the present *Charaka Samhita* is replete with limitations and difficulties. Agnivesa lived around the 6th Century B. C. E. Charaka's placement in time is controversial. And the entire *Samhita* as revised by Drdhabala came into existence only after Madhava (around the 7th or 8th Century C.E.).[250]

Brihat Trayi: Three major texts
Charaka Samhita
Susruta Samhita
Astanga Hridaya and *Astanga Samgraha*

Laghu Tray: Three minor texts
Madhava Nidana
Sarangadhara Samhita
Bhava Prakasha

Table 4. Important Classical Ayurvedic Texts [251]

Susruta

Susruta is the main, if not the only, source on medical surgery. The original work by Susruta the elder is the *Salya-tantra* (surgical treatise). Susruta's original work contained five sections and deals mainly with surgical matters. At a later date, an anonymous writer composed a supplement entitled *Uttara-tantra* that included all the topics that the elder Susruta did not mention. Nagarjuna is thought to have been that writer. Some identify him as the Buddhist patriarch contemporary with King Kanishka around the second century CE.[252]

It should be noted that the *Samhitas* are not the earliest medical literature. An earlier stage existed during which different branches of knowledge were presented in separate tantras, treatises, kalpas, or monographs. Subsequently, different practitioners compressed and compiled the *Samhitas*. One may conclude from all this data that the oldest texts are probably Atreya's six tantras, the *Charaka Samhita*, the *Susruta Salya-tantra*, followed by the *Susruta Uttara-tantra*, and finally the *Bhela Samhita*.

Vagbhata and Madhavacharya

It is well-known that there were two Vagbhatas. The first Vagbhata wrote a compendium on general medicine and divided it into six sections (*sthanas*). He named it *Summary of the Octopartite Science* (*Astanga Sangraha*). He worked to combine the current conflicting medical traditions into a harmonious whole with a focus on Charaka and Susruta. The *Astanga Sangraha* is more closely connected with Charaka and especially Susruta than is the *Astanga Hrdaya* of Vagbhata the second. The *Astanga Sangraha* is

thought to have been composed either in the late 6th or early 7th Century C.E.[253] Madhavacharya wrote an excellent treatise focusing solely on disease diagnosis. Also known simply as *Nidana* (pathology), it is one of the most popular of all Indian medical works probably written in the 8th Century C.E.

In summary, Madhavacharya is considered the foremost authority on diagnosis, Vagbhata is an authority on medical principles, and Charaka and Susruta are unrivalled in the knowledge of therapeutics and of surgery and anatomy, respectively. Charaka and Susruta creatively accomplished the final synthesis of Ayurveda. Later works, although informative, provide little original material, and instead interpret and expand upon the knowledge already laid out by Charaka and Susruta.

According to Unnikrishnan, the major *Samhitas* include *Caraka Samhita*, *Susruta Samhita*, *Astanga Samgraha*, and *Astanga Hrdaya*, and were all written before the seventh century C.E. Charaka in particular provides an exhaustive description of approximately 600 plants and their medicinal uses. Furthermore, there are ample details about the plants in terms of the following: nomenclature, identification, biological properties and actions, habitat, and regional specifications for substitutes. Information is also provided that details the following: plant collection methods and classification, combination and processing at various stages, incompatibility, contraindications, recipes, and information on poisons.[254] (Table 5)

Text Name	Time Period	Author	Region of Origin
Caraka Samhita	1500 BCE*-400 CE**	Agnivesa, Caraka, Drdhabla Susruta	Himalaya, Kashmir
Susruta Samhita	1500 BCE-500 CE	Nagarjuna Vagbhata	Kasi Sindhudesa
Astanga Samgraha	500 CE	Vagbhata	Sindhudesa
Astanga Hrdayam	600 CE	Vagbhata	Sindhudesa
Astanga Nighantu	800 CE	Madhava	
Paryayaratnamala	900 CE	Unknown	Silahrada
Dhanvantari Nighantu	200-1000 CE	Cakrpanidatta	Unknown
Cakradatta	1075 CE	Cakrpanidatta	Vangadesa
Dravyaguna Samgraha	1075 CE	Madhava	Vangadesa
Madhavadravyaguna	1250 CE	Sarngadhara	Unknown
Sarngadhara Samhita	1300 CE	Hemacandra	Devagiri
Nighantu Sesa	1200 CE	Kesava	Unknown
Siddhamantra	1210-1247 CE	Bopadeva	Unknown
Hrdayadipaka Nighantu	1260-1271 CE	Madanapala	Unknown
Madanapala Nighantu	1374 CE	Bhavamisra	Kasthanagara
Bhavaprakasa	1550 CE	Bhavamisra	Kasi, Kanyakubja
Bhavaprakasa Nighantu	1550 CE	Naraharipandita	Kasi, Kanyakubja
Raja Nighantu	1700 CE	Saligramvaisya	Kasmira
Saligrama Nighantu	1896 CE	Krsnarama Bhatta	Muradabad
Siddhabhesajamanimala	1896 CE		Jayapura

*B.C.E.=Before the Common Era; **C.E.=Common Era
Source: Research Department, FRLHT

Table 5. Major Ayurvedic Authors and Commentaries[255]

Select History up to the Present

During the *Arsha* period (the period of the rishis) two great universities existed in India where astronomy, mathematics, philosophy, and medicine were taught. By the sixth century B. C. E., Taxila had a concentration of scholars and their disciples who all lived near each other to facilitate the exchange of ideas and debate. Located west of the Jhelum River (modern-day Pakistan), Taxila recruited Atreya and Charaka to teach. Another famous physician of this period was Jivaka.[256] As the royal physician of King Bimbisara of Magadha, Jivaka was appointed to supervise the health of Gautama Buddha and all his followers. Because the health of the king also reflected the political stability of the community, kings had a vested interest in maintaining their health. Jivaka became so

famous that, at one point, almost all of Magadha's citizens joined the Buddhist community in order to benefit from his treatment. The other famous university was located on the banks of the Ganga in Benares, where Susruta headed the medical section.[257] [258] [259]

In 326 B. C. E. Alexander the Great invaded northern India. This invasion was the first documented exchange, though it is very likely that Indian medical knowledge had already spread to Greece. Impressed with the Ayurvedic practitioners' acumen, Alexander ordered that Ayurvedic physicians treat all the cases of poisoning among his men. On his departure, he also enlisted some of these physicians as members of his entourage.[260]

According to Sharma, the Buddhist tradition flourished along side the Vedic tradition under the royal patronage of leaders such as Ashoka, Kaniska, and Sri Harsa. As Buddhism spread to other Asian countries, the South Asian medical tradition accompanied the monks and nuns. Medical manuscripts from excavations as far as Central Asia support this argument.[261] In the third century B. C. E., for example, Ashoka, the emperor of most of northern India, converted to Buddhism. With his conversion, he supported and built charitable hospitals that specialized in surgical, obstetric, and mental facilities throughout his realm. The famous Ashoka rock edicts attest to his commitment to a Buddhist philosophy as do the many emissaries he sent to neighboring countries. According to Sharma, Emperor Ashoka established hospitals and dispensaries for the sick, and ordered the planting of medicinal plants along avenues and other public places.[262]

The Bower manuscript, written in the fourth century C. E. and found in Central Asia, documented the continuance of the medical missionary activity long after Ashoka's time. In the later Gupta and Maurya empires, private medical practitioners continued to coexist with state-employed practitioners. The state supported medicinal herb gardens, established hospitals and maternity homes, and punished those who tried to practice without state permission.[263]

The Golden Age

Established in the fourth century, Nalanda University was established by the Buddhists located in what is now the Indian state of Bihar. Nalanda endured until about the twelfth century. Medicine was a compulsory subject within the curriculum. The best documentation on Nalanda is from Chinese travelers (such as Fa-Xian) who visited India as students over the course of several centuries. It appears that only twenty percent of all the applicants passed the admission examinations, instruction was free, senior students acted as teaching assistants, and teaching occurred throughout both day and night. The campus covered half a square mile, and it housed as many as 10,000 students and 1,500 teachers at a given time, along with support staff. The Nalanda brothers appear to have developed an old-boys network. [264, 265]

Mughals (1526-1857)

Muslim invaders ended this Golden Age. In addition, Buddhism had gained popularity as a reaction against the empty rituals developed by the priestly Vedic class. The Hindus responded with isolated violence against Buddhist temples and with the development of their own reformist movement from within the tradition. Various Mughul rulers further

destabilized Ayurveda by systematically accusing the monks as infidels, destroying universities and burning the libraries. Some of these Ayurvedic practitioners were able to escape to Tibet and Nepal, where Ayurveda was first introduced in the eighth century. This is why some Ayurvedic texts are preserved only in Tibetan translation.[266] The Muslim conquerors, however, introduced their own style of medicine, called Unani Tibb. Unani (which means Greek in Arabic) combines Greek medicine with Ayurveda. The Muslims learned about Ayurveda from texts that had been translated into Persian. Ayurveda continued to grow despite the support of Unani Tibb tradition by the new Muslim rulers. For example, in the thirteenth or fourteenth century, another Ayurveda treatise emerged: it was *Sharngadhara Samhita*, which introduced new diseases and treatments.[267] Of the Mughul emperors, Akbar proved to be the most enlightened. He ordered the compilation of all Indian medical knowledge so the best of all traditions would be studied and preserved under his rule.[268]

Colonial and Post Colonial Period

According to Shankar, European attitudes towards indigenous sciences fall into two phases. From the seventeenth to the early eighteenth centuries, Europeans sought useful knowledge on healing from the non-European world to add to their own knowledge base. For example, they searched for information concerning smallpox inoculation and all types of surgical techniques, especially rhinoplastic surgical procedures.[269] During the first half of the period of British rule of South Asia, however, indigenous surgery such as smallpox vaccination was legally prohibited. Shankar emphasized that this was just one example of a deliberate strategy by the British to undermine indigenous medicine and reliance on local, affordable, and culturally available practices. By the mid-nineteenth century,

allopathic medicine became the dominant and state-patronized medical system. Naturally, this lead to a decline of indigenous medical systems and adversely affected the practitioners' morale. Shankar reinforced the understanding that this political move favored Western knowledge systems in general and the Western biomedical model to the detriment of indigenous knowledge systems and indigenous systems of medicine. [270] Although the pre-independence movements attempted to restore an Indian identity, many indigenous social, political, and economic institutions assumed Western models. Shankar noted that this was evident in ideological debates that occurred about how to revitalize Ayurveda.

Ayurveda Today

According to Shankar, today, Indian indigenous systems of medicine fall under five categories: (1) Grassroots level efforts in villages; (2) non-governmental organizations (NGOs); (3) official Indian government centers; (4) the private sector; and (5) professional practitioners associations. These systems can be summarized as follows:

1. Grassroots level efforts in villages: Based on rough estimations, there are approximately 700,000 midwives, 60,000 village bonesetters, and 60,000 herbal healers (excluding spiritual healers) in India out of a population of approximately a billion.
2. Non-governmental centers: there are no statistics available on these.
3. Official Indian government institutes at the national and state levels: There are about 300 undergraduate teaching colleges and seven post-graduate centers. There also exist the Central Research Councils for Ayurveda and Siddha (90 centers)

and the Central Research Council for Unani (29 centers). Thirteen state-run pharmacies exist in different Indian states, and production is exclusively for supplying state-run health services. The quality of official institutions, teaching, research, and services is poor compared to the private or voluntary sector. Traditional Indian systems of medicine as opposed to allopathic teaching, research, and service institutions, receive only three percent of the national health budget.

4. Private sector: By the end of 2001, there were approximately 500,000 Ayurvedic, Siddha, and Unani registered practitioners. The private sector invests the most capital in the pharmaceutical area. By the end of 2001, about 9,300 licensed pharmacies existed. The majority (about 6,000) have a turnover of less than 10 million rupees (the exchange rate between Indian Rupees and US dollars is approximately 45-50 Rupees = $1.00). Although the number of pharmacies has increased, quality control has not improved. In June 2002, however, a Good Manufacturing Practices code was introduced.
5. Professional practitioners' associations: Since Independence, professional associations have not articulated a larger vision of how traditional Indian systems of medicine may contribute to Indian national health goals.[271]

Based on 1999 figures, there were 2,258 Ayurvedic, 196 Unani, and 224 Siddha hospitals in India.[272] According to an All India Ethnobiological Survey by the Ministry of Environment and Forests, conducted by the Government of India (1985-1995), approximately 8,000 wild plant species are used in the rural and tribal health-care

communities. These make up nearly fifty percent of the known, Indian flowering plants species. In addition, local animals, metals, and minerals are utilized.[273]

Indian Philosophical Basis of Ayurveda

Introduction

There are six major Indian philosophical systems (*Sad-Darshana*). Achaya claimed that with the emergence of three Indian philosophical systems, in particular, *Samkhya* and *Nyaya*, and *Vaisesika*, a profound conceptual turn occurred.[274] Without at least an overview of these philosophies, one cannot gain a clear understanding of Ayurvedic foundations and fundamentals.[275] Athavale claimed that these three schools, in particular, explain the composition of the universe. [276, 277]

The Particularist School—*Vaisesika*

The Vaisesika system is considered one of the oldest schools of Indian philosophy and was first expounded in the form of aphorisms in the *Vaisesika Sutra* by Kanada. The composition of the *Vaisesika Sutra* can probably be placed in a two-hundred-year period from 200 B. C. E. to the beginning of the Common Era.

The *Vaisesika* School expresses an interest in examining and classifying fundamental realities. The school espouses the reality of the external world, propounded an atomic theory of matter, and was understood by many as a prototypical example of early 'scientific' speculation in ancient South Asian culture. The school is primarily concerned with the analysis of nature, and takes its name from its preoccupation with particularity

(*visesa*). The *Vaisesika* School demonstrates an interest in investigating the fundamental categories of reality. In short, the *Vaisesika* can be seen as an early attempt to provide a comprehensive ontological classification or 'inventory' of existence.[278] Based on the *Vaisesika* philosophy of Kanada, Athavale concluded that the entire universe is composed of seven characteristics:

1. Substance (*dravya*)
2. Quality (*guna*)
3. Action (*karma*)
4. Common generic property (*samanya*)
5. Specificity (*visesa*)
6. Constant inseparable relation or connection (*samavaya*)
7. Absence of non-existence (*abhava*) [279]

The School of Reasoning—*Nyaya*

The *Nyaya Sutra* was traditionally ascribed to Aksapada Gotama (c. 250-450 C.E). These sutras are better organized than those of the Vaisesika School. Some aphorisms from the *Vaisesika Sutra* are repeated with slight variations in the Nyaya Sutra. It is unlikely that the *Nyaya Sutra* in its final form is the work of only one author.

The primary focus of the *Nyaya* School shifted away from the ontological orientation of the slightly earlier Vaisesika towards a concern with the nature of knowledge itself: How do we know what we know? What sources of knowledge are valid? The *Nyaya Sutra* demonstrated a keen interest in the nature of perception and the ways in which truth is

established. A particular area of concern was with the nature of inferential reasoning (anumana). *Nyaya* also constructed a system of rules for conducting debates. The school shared many presuppositions with the *Vaisesika* and defended a form of pluralistic realism that is grounded in the reliability of common-sense perceptions.[280] The most important contribution made by this school is its methodology. This was based on a system of logic that has subsequently been adopted by most of the other Indian schools (orthodox or not), much in the same way that Western science, religion and philosophy can be said to be largely based on Aristotelian logic.

But *Nyaya* philosophy was not merely interested in logic for its own sake. Its followers believed that obtaining valid knowledge was the only way to obtain release from suffering. They therefore took great pains to identify valid sources of knowledge and to distinguish these from mere or false opinions. According to the *Nyaya* School, there were exactly four sources of knowledge (*pramanas*): perception, inference, comparison, and testimony. Knowledge obtained through each of these can of course still be either valid or invalid, and the *Nyaya* scholars again went to great pains to identify, in each case, what it took to make knowledge valid, in the process coming up with a number of explanatory schemes. In this sense, *Nyaya* was probably the closest Indian equivalent to contemporary Western analytical philosophy. [281]

Nyaya-Vaisesika

With the passage of time, the *Nyaya* and *Vaisesika* Schools merged into a single philosophical doctrine. The *Nyaya-Vaisesika* philosophy was based on reason and analysis. The external and material worlds were received by the mind, but also existed

independent of it.[282] The six irreducible substances (*padarthas*) made up the world. These were: taste (*rasa*), color (*rupa*), odor (*gandha*), touch (*sparsh*), sound (*shabda*), movements (*karma*), sameness (*samanya*), perceived differences (*visesha*), and inseparable principles (*samavaya*).[283]

The School of Enumeration—*Samkhya*

The history of *Samkhya* philosophy may be roughly divided into three periods: an early period of proto-*Samkhya* ideas (c. 900 B. C. E.-300 C. E.); the classical period, when *Samkhya Karika* was composed, and the tradition flourished as an independent school (350-1000 C. E.); and later *Samkhya* as exemplified by the composition of the *Samkhya Sutra*, that was a period of relative decline for the philosophy (1000 C. E. onwards).

Samkhya thought represented some of the most ancient strands of Indian philosophical thinking and occurs in a variety of forms. As a school, *Samkhya* supported a radical dualism between consciousness and matter and sees the final purpose in life in terms of the separation of the two and the attainment of isolation for the pure consciousness (*purusa*). Although the goal was to disengage oneself from the activities of the material world, *Samkhya* did not reject the reality of this world (as is the case in the *Advaita* school). Consciousness and matter constituted the two basic ontological principles that underlie the manifestation of the universe.[284] Based on perceptual observation and conceptual knowledge, nature's phenomena could be understood. *Samkhya* philosophy, as Majumdar explained, was based on the theory of transformation. A creator or any act of creation was not acknowledged. Instead, the existence of all things was based on the relationship between two principles: spirit (*purusha*) and matter (*prakriti*).[285]

According to *Samkhya* philosophy, a relationship exists between the elements of nature and those of humankind. There is a relationship between the intellect (*mahat*), the ego (*ahamkara*), and the mind (*manas*), and between the five cognitive and five connative organs that are the *panchabhutas* and their subtle states. Nature and humanity are both represented by three qualities (*gunas*): all that is noble and good (*sattva*), all that is energetic (*rajas*), and all that is inertia (*tamas*).[286]

The classical Ayurvedic texts, such as Charaka and Susruta, were compiled, revised, and rewritten over several centuries. Therefore, discrepancies exist and should be noted. According to Kutumbiah, for example, the *Samkhya* chapter in Charaka does not appear to fit in with the rest of the *Samhita*, nor is it referred to in other parts of the *Samhita*. Perhaps this chapter was somehow later inserted from some other treatise. In another case, Charaka's *Samkhya* description bears little resemblance to traditional accounts by *Israra-Krishna' Karika* and in the *Samkhya-sutra* and may be based on an earlier *Samkhya* version. Nevertheless, Kutumbiah did admit that most of Charaka's medical theories are strongly based on the *Nyaya-Vaisesika* philosophy. Susruta, on the other hand, did not enumerate the Vaisesika categories in great detail as Charaka does, but his account of the *Samkhya* was faithful to the traditional version given by *Israra-Krishna's Karika* and in the *Samkhya-sutra*.[287] Majumdar asserted that Ayurvedic philosophy is explained mainly in classical texts and claimed that Charaka's philosophy closely adheres to the *Vedanta* and early *Samkhya* philosophies, whereas Susruta follows later *Samkhya* philosophy. And Vagbhata, the third in the Great Trio (*Brihat trayi*), who wrote about

Ayurveda and compiled the works of Charaka and Susruta, was mainly influenced by Buddhist thought.[288]

Chapter 4: Ayurveda Fundamentals

Introduction to Contemporary Ayurveda: Fundamental Concepts (Basic Theory)

The foundations of contemporary Ayurveda are based on three, main classical Sanskrit texts known as the *Brihat-Trayi*: The *Charaka* and *Susruta Samhitas* and the *Astanga Hridaya* by Vagbhata (Table 1). As previously discussed, the basic theory and philosophy of Ayurvedic medicine derive from the Hindu *Samkhya* and *Nyaya-Vaisesika* philosophical systems. After the classical period, Ayurveda was classified into the eight following areas:

Kaya-Chikitsa	Medicine
Shalya-Tantra	Major Surgery
Shalakya-Tantra	Minor Surgery: eye, nose and throat
Agada-Tantra	Toxicology
Bhuta-Vidya	Psychiatry
Kaumara-Bhritya	Pediatrics and Gynecology
Rasayana-Tantra	Geriatrics-Rejuvenation
Vajikarana-Tantra	Reproductive Disorders [289]

In this section I present a general overview of the fundamental ideas that define contemporary Ayurveda. I begin with definitions of Ayurveda based on classical texts. To clearly represent the development of the tridosha theory, I have chosen the *Samkhya*

philosophical system, as have many other scholars and practitioners,[290] to represent basic concepts in Ayurveda theory. This overview allows the reader to gain a better understanding of the derivation of the subtle five elements (*tanmatras*) and how they are transformed into the five gross elements (*panchabhutas* or *panchamahabhutas*) that then evolved into the tridosha theory of health and disease, the foundation of contemporary Ayurvedic practice. After presenting this introduction to the tridosha construct, I give an overview of Ayurvedic principles. This includes a review of the *doshas*, sub-*doshas*, seven tissues (*sapta dhatu*), and metabolic or excretory products (*malas*). After providing this overview of the foundations of Ayurveda, I review the Ayurvedic concept of *Prakriti*, Ayurvedic pathology, and dravyaguna (Ayurvedic pharmacology).

The Definitions of Ayurveda

Charaka defined Ayurveda as

> The science which imparts knowledge about life, with special reference to its definition, and the description of happy and unhappy life, useful and harmful life, long and short spans of life and such other material along with their properties and actions as promote and demote longevity will be described in the entire treatise [Chapter 30, Verse 23].[291]

> That (science) is designated as Ayurveda where advantageous and disadvantageous as well as happy and unhappy (states of) life

> along with what is good and bad for life, its measurement and life itself are described [Chapter 1, Verse 41].[292]

Kurup and Raghunathan summarized the main aim of Ayurveda according to Charaka as

> …that knowledge of life which deals elaborately and at length with conditions beneficial or otherwise to the humanity, and to factors conducive to the happiness, or responsible for misery or sorrow, besides indicating measures for healthful living for full span of life.

Living in balance in order to ensure health or a disease-free state (*arogya*) is strongly emphasized. The ancient texts call attention to healthy living as a prerequisite to achieving the four supreme goals of life: righteousness[dharma #0], wealth (*artha*), cultural and artistic values (*kama*), and spiritual freedom (*moksha*).[293]

Ayurveda defines life [ayu #0]as the union of body (*sharira*), senses (*indriyas*), mind (*sattva* or *manas*), and soul (*atma*). The living human, the person of action (*karma purusha*), is a composite of the three humors (*tridoshas*), seven tissues (*sapta dhatus*), and three metabolic products (*trimalas*), i.e., feces, urine, and sweat.[294]

The Samkhya Philosophy: Purusa-Pure Consciousness

Scholars employ different terms to describe and define the Ayurvedic knowledge system. In order to present clearly the basis of Ayurvedic theory, many scholars represent the

Samkhya system in a diagrammatic format (Figure 10). This representation of the *Samkhya* system is based largely on a composite of several scholars.[295] [296] [297] [298]

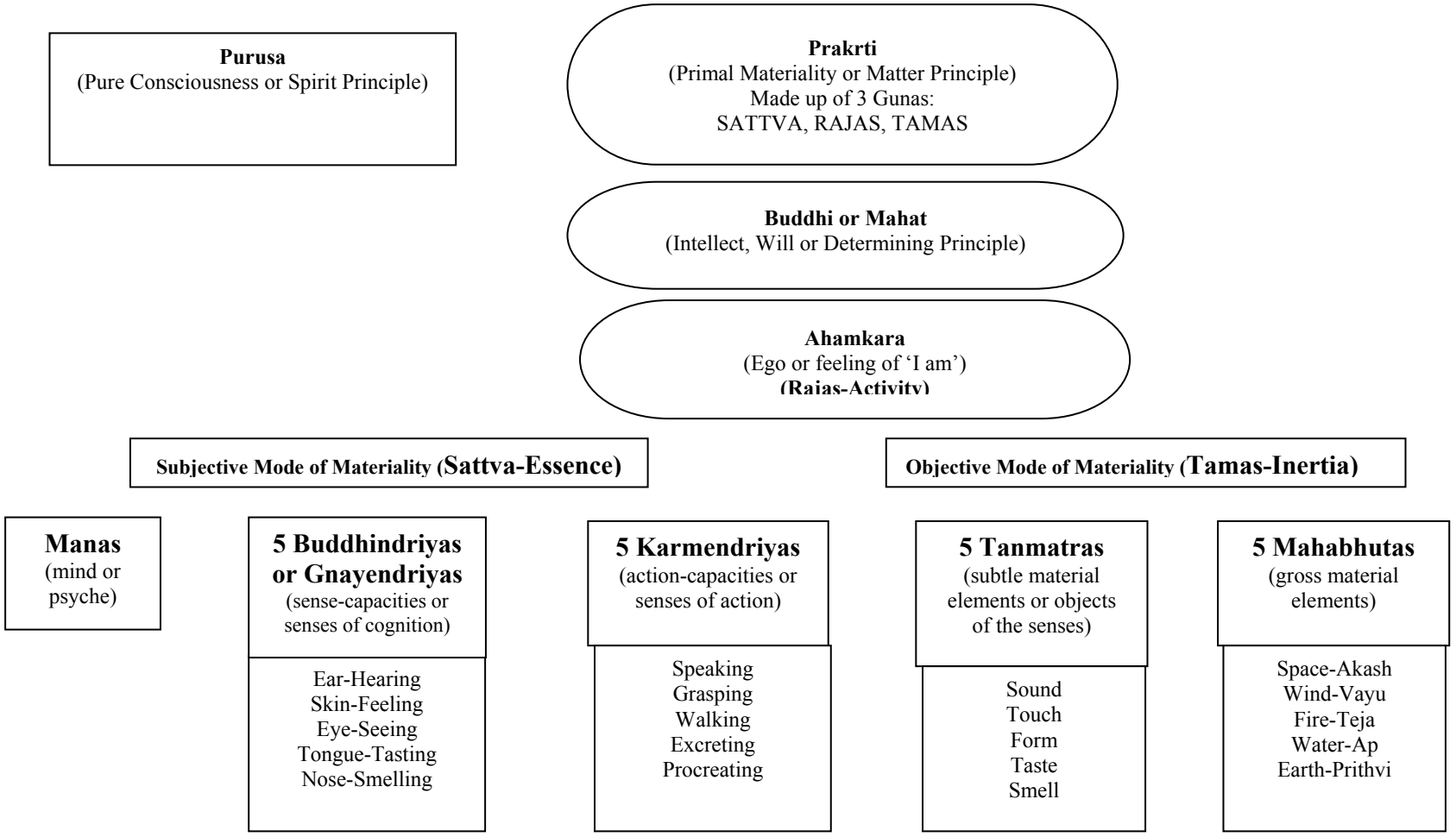


Figure 10. *Samkhya* Overview [299]

Svoboda stated that from Purusha (absolute reality), a relative reality *prakriti* (nature) evolves. The only difference between these two realities is that absolute reality (*purusha*) understands itself to be identical to nature (*prakriti*), whereas nature believes itself to be different from absolute reality.[300] As nature becomes aware of its own existence, it evolves into the state of intelligence or cosmic consciousness. From this intelligence, the ego (*ahamkara*) emerges, a type of atomized form aware of its individuality and difference.[301] Majumdar described Purusha as soul (*atman*) or life (*jiva*) and is conscious of its universal spirit principle. Prakriti, on the other hand, is a dynamic principle, the womb of all biological knowledge, and is unmanifest and unconscious in nature. Majumdar further stated that the matter principle (*prakriti*) possesses three qualities (*gunas*), whereas the spirit principle (*purusha*) does not possess these qualities.[302] Unlike King and Majumdar, Svoboda stated that it is ego (*ahamkara*) that has three qualities (*gunas*): equilibrium (*sattva*), activity (*rajas*), and inertia (*tamas*).[303, 304]

King believed that the development of the subjective and objective manifestations of being is activated by *rajas guna*. *Rajas* denotes movement, activity, and energy in motion. Without *rajas*, creation could not have occurred.[305] Svoboda defined *rajas* as waves of kinetic energy, the 'I' as action; *tamas*, on the other hand, produces objective particles of potential energy (also known as matter), the 'I' as unconscious being; and *sattva* as the subjective consciousness that perceives and manipulates matter, the 'I' as conscious being.[306] Athavale, on the other hand, concluded that *sattva guna* gives rise to the sense capacities (*gyanendriyas*); *raja guna* gives rise to the action capacities (*karmendriyas*); and *tamas* gives rise to the objects of the senses (*tanmatras*).[307]

The subjective manifestations of being

According to Figure 10, *sattva* gives rise to the subjective manifestations of being that include the mind (*manas*), the five sense capacities (*buddhindriyas* or *gyanendriyas*), as they are often called, and the five *karmendriyas*. *Manas* is often defined as the mind. The *gyanendriyas* are described as the five sense capacities: hearing, feeling, seeing, tasting, and smelling. The five *karmendriyas* are defined as action capacities: speaking, grasping, walking, excreting, and procreating. These are precursors and subtle manifestations of the objective manifestations of being.

The objective manifestations of being

Rajas gives rise to the objective manifestations of being that include the five subtle elements (*tanmatras*) and the five gross elements (*mahabhutas* or *panchamahabhutas*). The subtle elements include sound, touch, form, taste, and smell. The five gross elements include ether (*akasha*), air (*vayu*), fire (*agni*), water (*jala*), and earth (*prithvi*). The five elements each represent different states of matter. Each and every substance in the universe is made up of a combination of these five elements with a single element predominating in each substance. Human bodies are also composed of the five elements. The universe is composed of the same five great elements that form the human body. In fact a human is a microcosm within the larger macrocosm or universe. The five senses that humans possess enable them to have subjective contact with the objective universe.[308]

Life embodied is defined as the sum total of all the principles that compose the universe: the five elements, the five cognitive senses with their objects, the five active senses, the thinking mind, the ego, the intellect, the individual soul, and a fragment of the cosmic *purusha* that is also called the *purusha*.[309]

The five gross elements give rise to the doshas

As previously discussed, all matter in the universe is composed of a combination of ether, air, fire, water, and earth (Table 6). These 'building blocks' of the universe represent states of matter as opposed to elements in the Periodic Table. Ether is the source of all matter and the space in which it exists; air represents the gaseous state; fire represents the power to transform the state of any substance; water, the liquid state; and earth, the solid state.[310, 311] These building blocks work together in such a way so that earth helps the other four elements by providing support; water helps by moistening; fire helps by ripening; air helps by drying; and space helps by providing room.[312] According to Ayurvedic theory, the different combinations of the five elements are precursors to the doshas. Sharma and Clark, for example, defined *doshas* as the first manifestations of consciousness in matter.[313]

Table 6. ***Panchamahabhutas*: Five Gross Elements**[314]

	Space (Akash)	**Air (Vayu)**	**Energy (Agni-Tejas)**	**Water (Ap-Jala)**	**Earth (Prithvi)**
Properties	Light Smooth Soft Inactive Clear Minute Neither hot nor cold Separation Differentiation	Light Rough Clear Minute, atomic Neither hot nor cold Active movement	Light Rough, sharp Clear Minute, atomic Hot Dry Luminous Active spread Fast speed	Heavy Fluid Soft Inactive Slimy Cold Dense Large molecules Viscid Wet Movement towards gravity	Heavy Rough Hard Slow, inactive Steady, firm Neither hot nor cold Clear Dense Large, bulky
Movement	Absent	Centrifugal	Upward	Downward	Downward
Taste Predominant Associated taste	 Taste not manifest	 Astringent Slightly bitter	 Pungent Slightly salty and sour	 Sweet Slightly astringent Salty and sour	 Sweet Slightly astringent
Sense Special sense Sense organ	 Sound Ear	 Touch Skin	 Vision Eye	 Taste Tongue	 Smell Nose
Location Body Body parts	 All body activities All large openings, passages and cavities	 All body activities, pulsations and gases All body movements, inspired and expired air	 Entire body in manifest and unmanifest forms Pitta, heat, luster	 All fluids in the body Body fluids, blood, fatty tissue, kapha, pitta, urine, stool, sweat, semen	 All organs, large and steady body Nails, bones, tendons, teeth, muscles, skin, stool, hair, spinal cord

Doshas

The five basic elements form the foundation of the *doshas*. The *doshas* constitute the structural and functional units of all living cells, tissues, organs, and the body as a whole. Combinations of the five elements condense into the three *doshas* (*tridosha*): *vata* (space and air), *pitta* (fire and water), and *kapha* (water and earth). Of the two elements that are prominent in each *dosha*, one predominates. Thus *vata*, *pitta*, and *kapha* are best represented by air, fire, and water, respectively. Majumdar further explained that according to the classical texts, the three *doshas* are the bioregulating principles that control various physiological functions inside the body and the cells. These three bioregulating principles acquire different names depending on the condition of the body. When a body is in a perfect state of balance, these principles are called *dhatus*. But this perfect state is never achieved and so the three principles are referred to as *doshas*: *vata, pitta*, and *kapha*. When these principles produce wastes and are excreted they are called *malas*. [315] When these three principles are in perfect balance, they are called *tridhatu*. However, this perfect state is never achieved within the body. Thus principles are called *dosha*.[316]

> Dosha, dhatu and mala, form the fundamental (functional) units of the body. *Vagbhata A.H. Su. 11:1*[317]

Classical Ayurvedic texts describe the doshas in the following manner:

> Just as the moon, the sun and the wind sustain the world by the act of giving, taking and distorting, so do kapha, pitta and vata

> sustain the body. In brief, vata, pitta and kapha are the three doshas. Vata, pitta and kapha alone are the causes of (basis of) the formation of the body. By them alone when acting ('not dead'-functioning) this body is sustained. *Susruta Su. 21:8, Vagbhata A.H. Su. 1:6, Susruta Su. 21:3*[318]

A *dosha* is any fault or error, any transgression against the rhythm of life that promotes imbalance. (Popular books on Ayurveda do not define dosha as a transgression. According to classical Ayurveda, however, an individual is never in a state of balance. If an individual was in a state of balance, there would not be any vitiated doshas. The doshas would not exist because there would be no imbalance or transgression). The three *doshas* regulate different functions in the body. Life is inconceivable without these three activities, and any imbalance may result in disease. [319] The definition of health according to Ayurveda is that all doshas and *dosha* sub-types are functioning normally, the gunas of the doshas are normal, and the doshas are in the proper proportions quantitatively. The same applies to *dhatus* and *malas*. The well-being of the soul (*atma*), senses (*indriya*), and mind (*manas*) are equally important to the Ayurvedic definition of a state of health.[320] To facilitate healing and balance, a practitioner selectively administers medicinal plants, herbs, animal products, and minerals to treat a disturbance in the equilibrium of the three *doshas*.[321]

In Table 7, the different qualities (*gunas*) associated with each *dosha* are listed. These are considered subtle as opposed to gross qualities. *Dosha* qualities are more abstract. They are

used to categorize the effects of different treatments and regimens for balancing the doshas.[322]

Table 7. *Dosha* Qualities [323] [324]

Dosha	Qualities	Effects
Vata	1. Dry, rough (rooksha)	Dryness, emaciation, broken or hoarse voice, insomnia
	2. Light (laghu)	Light, inconsistent digestion, movement, and gait
	3. Mobile (chala)	Unstable, constantly moving joints, eyes, etc.
	4. Abundant (bahu)	Talkative; prominent tendons and veins
	5. Cold (sheeta)	Intolerant of cold; feels cold quickly
	6. Coarse, brittle (khara)	Rough, dry skin, rough hair
	7. Non-slimy (vishada)	Limbs and joints 'crack'
Pitta	1. Slightly oily (sasneha)	Smooth skin
	2. Hot, warm (ushna)	Intolerance for heat, excessive hunger, thirst; skin problems; early wrinkles, graying, and baldness
	3. Sharp (teekshna)	Physical strength, strong digestive power, sharpness
	4. Liquid (drava)	Loose, soft joints and muscles, tendency to sweat, more frequent urination than usual, tendency to loose bowel movements
	5. Sour (amla)	Fewer progeny, low sperm count
	6. Pungent (katu)	Fewer progeny, low sperm count
Kapha	1. Heavy (guru)	Stable gait; tendency to heavy build
	2. Cold (sheeta)	Slow, non-intense hunger, thirst, and perspiration
	3. Soft (mrdhu)	Pleasing appearance, milky, soft complexion
	4. Oily (snigdha)	Unctuous skin, organs
	5. Sweet (madhura)	Sweetness of speech and behavior
	6. Stable, steady (sthira)	Slow to anger, and to initiate actions

Vata

The word *vata* is derived from the verb '*vā*,' which means to move, enthuse, make known, and become aware of. *Vata* initiates and promotes biological activity. *Vata* is air or wind and is derived predominantly from space and air elements.[325] [326]

Pitta

The word pitta is derived from '*tap-santape*,' which means to heat, burn or warm up. *Pitta* represents energy, heat or fire in the body. In general *pitta* is responsible for the generation of body heat and for certain physiological attributes of the individual, and it is derived predominantly from energy and water.[327] [328]

Kapha

The word *kapha* is derived from the two letters that spell '*ka*,' which means water, and '*pha*,' which means to flourish. Thus kapha is that which flourishes in the presence of water and is derived predominantly from two elements: earth and water.[329] Another term that is often used in the texts to describe *kapha* is *shleshma*. This word is derived from '*shlish alingane*,' which means to keep together, or to cohere.[330] (Table 8)

Table 8. *Dosha* Characteristics for Humans [331] [332]

Vata	***Pitta***	***Kapha***
Light, thin build	Moderate build	Solid, heavier build
Acts quickly	Acts with medium speed	Slow, methodical
Averse to cold weather	Averse to hot weather	Averse to damp weather
Irregular digestive power, irregular appetite	Strong digestion, sharp appetite	Slow digestion, mild appetite
Quick to learn	Medium time to learn	Slow to learn
Quick to forget	Medium memory	Slow to forget
Tendency to worry	Tends to anger	Tranquil, steady
Tendency to constipation	Regular elimination, sometimes loose or frequent stools	Regular elimination
Vivacious, always moving		
Light, interrupted sleep about six hours	Sound sleep, medium length	Heavy, long sleep
Tend to fatigue, less physical stamina	Enterprising, sharp	Stamina, strength
Curly hair more likely	Thin, fair hair	Dark, full hair
Dry skin	Reddish complexion, moles and freckles	Oily, smooth skin
Prominent, joints, tendons, and veins	Early graying or balding	

Among the three *doshas*, *vata* controls the movements and actions of *pitta*, *kapha*, all the body tissues, and waste products in the body. In short, *vata* is responsible for the origin, maintenance, and destruction of life.[333]

For example, Svoboda and Lade explained that *vata* represents all motion in the body and mind, such as the movement of food and blood; *pitta* represents any type of transformation, such as the progressive digestion of food; and *kapha* represents stability by providing lubrication to the joints. Life is inconceivable without these three activities, and any imbalance may result in disease. [334]

Majumdar further elaborated that *vata* or *vayu* is responsible for inhalation, exhalation, and general body movements. For example, chyle, blood, and the seven tissues (*sapta dhatus*) are dependent on *vayu*. *Pitta*, on the other hand, transforms chyle into blood, maintains memory, and is integral in heat preservation. *Kapha* acts as a binding agent for joints, and it helps in body formation and preservation by cooling digested matter and by separating waste material.[335]

The achievement of health means that the five elements are in balance when the three *doshas* are also in a state of balance. When the *doshas* are balanced, health ensues. Svoboda summarized that a healthy organism produces just enough *doshas*, and an unhealthy organism is that which produces either too much or too little doshas. When this imbalance occurs, the body's vitality, adaptability, and immunity is compromised.[336] Sharma and Clarke countered that 'balancing the *doshas*' actually has nothing to do with amounts, but rather with fostering the normal, healthy functioning of each *dosha*.[337]

> The act of achieving the equilibrium of the dosha, is the objective of this science. *Caraka Su. 1:53* [338]

> The equilibrium of dhatu is said to be normal health. The equilibrium of dosha is declared to be freedom from diseases (absence of diseases). *Caraka Su. 9:4 and Vagbhata A.H. Su. 1:20* [339]

The sage Atreya Punarvasu summarized the *doshas* as follows:

> Gentlemen, all of you have told the right thing, only your remarks are exclusive. All the three, air (vata), bile (pitta) and phlegm (kapha), when they are in their normal state make the faculties of a man intact, provide him with good health, amicable luster and happiness, and thus add to his long life in the same way as the morals, interests and pleasures, rightly practiced make man attain the utmost happiness in this world and the world to come. But if they are abnormal, they put the man into an adverse abyss, in the same way as the three seasons when they become abnormal lead the world to calamity in their respective periods.[340]

The Seat of the *Dosha*: *Sub-doshas*

Classical Ayurveda describes five types of each of the three *doshas* (*vata*, *pitta*, and *kapha*) in the following manner:

Vata: Prana, udana, samana, apana, vyana (Table 9). [341] [342] [343] [344]

Pitta: Pachaka, ranjaka, sadhaka, alochaka, bhrajaka (Table 10). [345] [346] [347] [348]

Kapha: Kledaka, avalambaka, bodhaka, tarpaka, shleshaka (Table11). [349] [350] [351] [352]

Table 9. Five *Vata*

Five *Vata*	***Prana vata***	***Udana vata***	***Samana vata***	***Apana vata***	***Vyana vata***
Location	Brain, head, throat, heart and respiratory organs	Navel, lungs, throat	Stomach, intestines	Colon, bladder, navel, thighs, groin, sexual organs, rectum	Diffused throughout the body in the skin, nervous and circulatory systems
Functions	Respiration; clarity of mind and reasoning; supports memory and enthusiasm; supports feeling; governs perception via the senses, especially hearing and touch; responsible for respiratory dysfunctions such as sneezing and belching	Physiology of speech and singing; relates to energy; ability to make an effort; strength; swallowing	'Fans' the pitta that digests food; responsible for peristaltic motion	Elimination of wastes; sexual discharge; menstruation; colon is considered the principal seat of Vata	Circulation; blood pressure; sense of touch
Conditions that result from imbalance	Respiratory disorders, cognitive problems, neurological disorders, tension headaches. Worry, anxiety, overly active mind, insomnia, hiccups, asthma	Speech disorders, diseases of the throat (dry coughs and sore throats), fatigue	Irregular or weak digestion, anorexia, bloating	Constipation, diarrhea, flatulence, colitis, lower back pain and spasms, sexual dysfunction, menstrual problems, genitourinary diseases	Circulatory and heart diseases, such as high blood pressure and heart arrhythmia, nervous diseases, often involved in other pathological processes

Table 10. Five *Pitta*

Five *Pitta*	*Pachaka pitta*	*Ranjaka pitta*	*Sadhaka pitta*	*Alochaka pitta*	*Bhrajaka pitta*
Location	Stomach, small intestines	Liver, spleen, duodenum, red blood cells	Heart	Eyes	Skin
Functions	Digestion of food, separation of waste products	Formation of red blood cells, balances blood chemistry, aggravated by toxins	Emotion, contentment, memory, and intelligence	Eyesight	Skin metabolism
Conditions that result from imbalance	Digestive weakness, heartburn, hyperacidity, ulcers	Anemia, blood disorders, jaundice, certain skin problems, anger and hostility	Depression and other psychiatric disturbances, heart disease, memory loss, indecisiveness	Visual problems in general, bloodshot eyes	Skin diseases, especially those of a pitta nature such as boils, rashes, and acne

However, Majumdar found that Charaka mentioned one type of *vata* but gave it five different names depending on its location in the body. Furthermore, Charaka did not mention the five different *pitta* or *kapha*. Susruta, on the other hand, described five *vata* and five *pitta* but failed to mention the names of the five *kapha*. Only Vagbhata and later authors described and named the five types of *vayu*, *pitta*, and *kapha*.

Table 11. Five *Kapha*

Five *Kapha*	*Kledaka kapha*	*Avalambaka kapha*	*Bodhaka kapha*	*Tarpaka kapha*	*Shleshaka kapha*
Location	Stomach	Chest, heart, lungs, and lumbar regions	Tongue, throat	Head, sinuses, and cerebrospinal fluid	Joints
Functions	Moistening and initial digestion of food	Supports heart and lumbar region, gives strength and stamina, especially in these regions and the upper torso	Moistening the tongue, secretion of mucus in the mouth, taste perception	Moistening the nose, mouth, and eyes; maintaining spinal fluid; nourishment of the mind and of the sense and motor organs	Lubrication of joints throughout the body, cohesion and binding all over the body
Conditions that result from imbalance	Dull digestion, imbalances of kledaka affect all the other kaphas	Back pain, heart problems, chest congestion, asthma, wheezing, lethargy	Disruption of taste and salivation	Sinus problems, nasal congestion, cough coming from upper respiratory tract, sinus headaches, problems with the senses, especially smell	Joint problems

The dhatus, ojas, malas, srotas, and 13 agnis

> The person who has doshas, 'agni,' dhatus and mala kriyas in equilibrium and who has sound soul, senses and mind, is declared to be healthy. *Susruta Su. 15:45*.[353]

Dhatus

The three *doshas* digest food and give rise successively to the seven tissues and the three waste products (*malas*): sweat (*sweda*), urine (*mutra*), and feces (*purisha*). *Dhatu* is derived from the Sanskrit root '*dha*,' which means to sustain and to nourish, so that anything that sustains and nourishes the body is called a *dhatu*.[354] Ayurveda described six types of tissue (*dhatu*) in the body: body fluids (*rasa*), blood (*rakta*), muscular tissue (*mamsa*), adipose tissue (*meda*), bone (*asthi*), nerve tissue and bone marrow (*majja*), and generative tissue (*shukra*). *Ojas* (the essence of life) is the final extract from the seven tissues. (Figure 11)

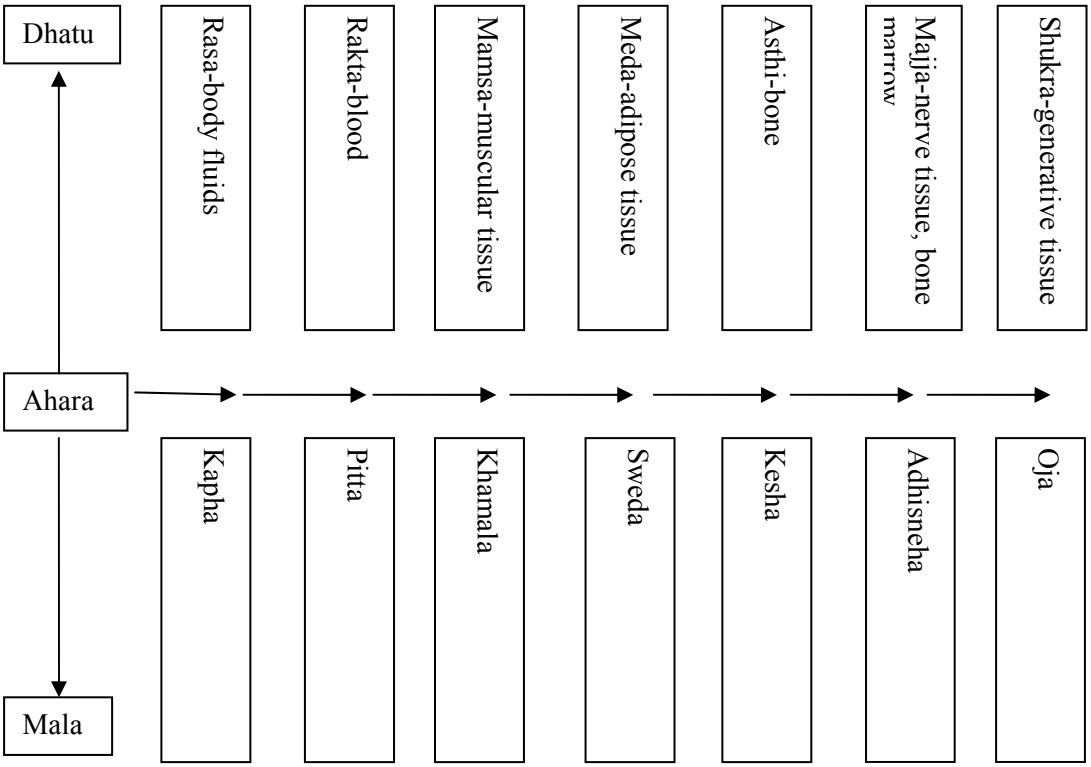


Figure 11. *Dhatu* Movement [355]

These tissues are fundamental principles that successively support each of the bodily tissues. According to Figure 3, the tissues exist in a particular order of importance relative to one another. All the tissues receive nutrients: first from the tissues of the body fluids, then from

the blood tissue in a progressive order. And finally the generative tissue is the last to receive nutrients from the six preceding tissues. The quality of a previous tissue influences the health of the next tissue. For example, as nutrients are assimilated, constitutional changes occur inside the tissues, and three products are formed: the first product contributes to the growth of the tissue; the second contributes to the formation and growth of the next tissue; and the third contributes to the formation of metabolic end products (*dhatu mala*).[356] [357]

> From rasa, rakta is derived from (rakta) mansa (is derived) from mansa, meda is formed, from it (meda) asthi (is derived) from asthi, majja is formed, from it (majja) shukra, and from shukra, embryo is formed. *Caraka Chi. 15:16* [358]

> With (the help of their) own srota, dhatu, is nourished by another dhatu. Dhatu are ahara (nourishment) for dhatus. If the previous dhatu is old and undernourished it would likewise affect subsequent dhatu. *Charaka Chi 8:37; Charaka Su. 28:3; Vagbhata A.H. Su. 11:35* [359]

Sharma and Clarke added that just as the doshas are central to Ayurvedic diagnosis, so too are the *dhatus*. One may classify a patient's constitution based on the *dhatus*. The *dhatus* also give rise to certain symptoms and diseases when they are vitiated. And just as certain factors may vitiate specific doshas, dhatus are vitiated and balanced.[360]

Ojas

As each tissue develops, a particular type of *ojas* (the essence of the tissues) is made. In between each tissue and the next, a specific type of ojas is formed, out of which the next tissue is created.[361] Kurup and Raghunathan equated *ojas* with power and consider it to be an extract of the seven basic tissues. *Ojas* is located in the heart and mixes with the plasma (*rasa*) tissue and then circulates and permeates the entire body. *Ojas* represents the essence of the activity of life, and is a source of strength and power that resists both decay and disease.[362] [363]

Malas

The word '*mala*' means to purify or to clear out. The body creates by-products that are a result of digestive and metabolic activities. The *malas* are the body's metabolic waste products. *Malas* are formed as a by-product of the *agnis* in metabolizing and transforming food and the tissues. The principal *malas* are urine (*mutra*), stool (*purisha*), and sweat (*sweda*); others include mucus, ear wax, and nails. The malas eliminate not only the by-products of the metabolism of food, but also waste products, toxins, and impurities. The *malas* contain all five gross elements and each *mala* is related to a specific tissue. For example, mucus is related to the waste products of body fluid tissue and is associated with the *kapha dosha*; bile is a waste product of blood tissue and associated with *pitta dosha*.[364] [365] [366]

Srotas

Srotas are subtle channels that transport the tissues and excretory products throughout the body. According to Kurup and Raghunathan, *Charaka Samhita* makes it clear that no structure in the body is able to grow, develop, eliminate waste, or atrophy without these

channels. The *srotas* are responsible for transporting body tissue nutrients that are constantly being metabolized. Numerous srotas are present in the body, and each has a specific function.[367] There are thirteen types of *srotas*. When there is any functional impairment, the srotas may be affected in four ways: restriction of flow, excessive flow, diverted flow, and structural change to the srota. An example of restricted flow is atherosclerosis, an example of excessive flow is dysentery, one case of diverted flow is improper shunting of blood, and structural change is an atheroma that develops in atherosclerosis. Any vitiation to the *srotas* results in vitiation of the *dhatus* and vice versa. The doshas may vitiate the srotas and the tissues. Improper food or diet regimens—such as overeating, eating before one's previous meal is digested, taking in unwholesome foods or foods that are incompatible with each other, overexercising, insufficient exercising, excess heating or chilling, excessive worrying, concussion or shock—also aggravate the *doshas* and *dhatus*.[368] [369]

Dhatus **and the thirteen** ***agni***

The word *agni* means fire and not only represents an important feature of the *dosha pitta* but also is involved in the transformation of food substances. The first of the thirteen *agnis* is *jathar agni*, the digestive fire, which metabolizes food and also supports the other twelve *agnis*. The five *bhuta agnis* are those *agnis* that metabolize the five gross elements (*panchamahabhutas*): *akasha agni, vayu agni, tejas agni, jala agni, and prithvi agni*. The qualities of the five gross elements are transformed by the *bhuta agni*. Following the *bhuta agnis* are the dhatu agnis: *rasagni, raktagni, mamsagni, medagni, asthagni, majjagni,* and *shukragni*. Each of these *agnis* metabolizes the formation of each of the tissues from the previous ones.[370] (Figure 12)

Food (ahara)

↓ Gross digestion by the jatharagni (digestive fire in the stomach and intestines)

↓

Ahara rasa

↓ Intermediate digestion by the five bhutagnis:
Akasha agni Vayu agni Tejas agni Jala agni Prithvi agni

↓

20 gunas (qualities) of food

↓ Tissue metabolism by the seven dhatu agnis:
Rasagni Raktagni
Mamsagni Medagni Asthagni Majjagni Shukragni

↓

The seven dhatus

Figure 12. *Dhatu* and 13 *Agni* [371] [372]

Ayurvedic Constitution: Prakriti

The three bioregulating principles, the doshas, also determine basic human character. The dominant *dosha* determines the psychosomatic character of an individual. A *vata prakriti* constitution, for example, is a person who has possessed a dominant *vata dosha* since inception and remains unalterable throughout life.[373] The characteristics of the dominant *dosha* types are described in Tables 12 and 13. In addition to the three dominant types described previously, an individual may possess a constitution due to the preponderance of two *doshas*. Or an individual may possess a constitution that has a predominance of the three *doshas*. Although the constitution is determined at birth and persists until death, one may alter one's constitution by utilizing substances with the opposite qualities to those that are inborn. Based on a detailed diagnostic procedure, the skilled Ayurvedic practitioner is

trained to treat the individual *prakriti* accordingly in order to balance the *doshas* and achieve health.

Table 12. Signs of Balanced *Doshas* [374]

Vata	***Pitta***	***Kapha***
Exhilaration	Contentment, courage, dignity	Affection, generosity
Alertness	Sharp, clear intellect	Stability of mind
Normal formation of tissues	Normal heat and thirst mechanisms	Normal joints
Normal elimination	Good digestion	Muscular strength
Sound sleep	Lustrous complexion	Vitality

Table 13. Signs of Imbalanced *Doshas* [375]

Vata	***Pitta***	***Kapha***
Dry or rough skin	Rashes, inflammatory skin diseases	Oily skin
Insomnia		Excessive sleep, lethargy, mental dullness
Constipation	Inflammatory bowel disease	Slow digestion
Common fatigue (non-specific causation)	Visual problems	Sinus congestion, nasal allergies
Tension headaches	Peptic ulcers, heartburn	Asthma
Intolerance of cold	Excessive body heat	
Degenerative arthritis	Premature graying or baldness	Cysts and other growths
Underweight		Obesity
Anxiety, worry	Hostility or irritability	

Prakriti-Constitution

An individual's characteristic physical and mental constitution is called *prakriti*. The personal constitution is fixed and determined by the parent's constitution at conception. The *vikriti*, on the other hand, is an individual's state of health from moment to moment. Ayurveda describes eight principal constitution types: [1 #0] balanced, (2) *vata*, (3) *pitta*, (4)

kapha, (5) *vata-pitta* or *pitta-vata*, (6) p*itta-kapha* or *kapha-pitta*, (7) *vata-kapha* or *kapha-vata*, and (8) imbalanced.[376]

Ayurvedic Pathology

Introduction

In this section on pathology, I present an overview of how an Ayurvedic practitioner understands the disease process. Classical texts have described in great detail the definition and classification of disease, causative factors, pathology, diagnostic methodology, and treatment principles. These different aspects of pathology and diagnostics will now be presented in a systematic way.

Definition and Classification of Disease

As previously noted, a state of health is achieved when the *doshas* are balanced. If disequilibrium arises, disease ensues. Classical Ayurvedic texts define disease in the following manner:

> Any disturbance in the equilibrium of *dhatu* is known as disease and on the other hand the state of their equilibrium is health. Health and disease are also defined as pleasure and pain respectively. Charaka 9:4 [377] [378]

In Majumdar's review of classical texts, he concluded that diseases are classified primarily as bodily (*sarira*) and mental (*manas*). There are other methods of classification, such as

dividing them as having internal causes versus external causes or as being curable versus non-curable.

> Roga (disease) is said to be of two kinds, Nija (organic, arising from the body itself) and agantu (traumatic, arising from external causes). *Astanga Hrdayam* 1:20 [379]

> Their (of diseases) adhisthana (seat, nidus, residence) is also two: kaya (the body) and manas (the mind). Rajas and tamas are enumerated as the dosas of the manas (mind) *Astanga Hrdayam* 1:21 [380]

Susruta classified those diseases into two broad groups: surgical and medical. He then stated that anything that afflicts the body, including the mind, is a disease and is further classifiable into three types:

Adhyatmika—There are three types. *Adibalapravritta* originates from a primary inherent cause; *janmabalapravritta* is congenital; and *doshabalapravritta* is due to a derangement of any of the *doshas*.

Adhibhautika—There is one type and it is due to any disturbance of the physical environment. *Samghatabalapravritta* is caused by extraneous conditions such as those created by an instrument or by an animal.

Adhidaivika—There are three types. They are due to an act of nature or God. *Kalabalapravritta* is seasonal. *Daivabalapravritta* is providential. *Swabhavabalapravritta* is due to natural causes such as hunger, thirst, and old age.[381]

Causative Factors of Disease

Charaka described the causes of disease in the following *sloka*:

> The causes of the diseases relating to both (mind and body) are three-fold—wrong utlisation, non-utlisation and excessive utlisation of time, mental faculties and objects of sense organs. Charaka 1:54 [382]

Svoboda and Lade noted that there are many factors that cause disease. There are breakdowns from within the body, external attacks, and mental factors that all play major roles. In addition, matters of time play a significant role in disease causation such as the changing seasons, the time of day, age, and speed of the digestive process.[383] Majumdar elaborated on the three types of disease-causative factors as follows:

1. *Asatmendriartha-Samyoga*: This type involves cases in which any of the five senses are used improperly. Improper use is defined as use in excess, non-use, or wrongful use. Overexposure to loud music, not smelling anything, staring at minute objects all day, exercising too much, and not eating enough are just some examples of improper use of the senses.

2. *Pragyaparadha*: This type includes cases in which an individual partakes in excessive activities of speech, mind and/or body. Non-activity in relation to speech, mind, and body are considered unhealthy as well. Suppression of natural urges falls under this category too.
3. *Parinama*: This type of case arises when seasons change, and when cold, heat, moisture, and dryness all affect the proper functioning of the body. Time of day and individual age are additional contributing factors.[384]

In the following section, I describe how a disease manifests in the body.

Pathology

According to Sharma and Clark, the causes of pathogenesis are mistakes in diet, regimen or thinking that lead to abnormalities in the *doshas*, *agni*, and *srotas*. When these are vitiated, fertile ground for the disease to take root and flourish is established. Simply stated, a trained practitioner strives to locate, treat, and remove the causes that led to these abnormalities.[385] Ayurveda describes six stages (*Sat Kriyakalas*) in the pathogenesis of disease, and they are described as follows:

1. *Sancaya*—accumulation of the doshas
2. *Prakopa*—aggravation or excitation
3. *Prasara*—dissemination or spreading
4. *Sthana samshraya*—localization
5. *Vyakti*—manifestation
6. *Bheda*—disruption or complications [386] [387]

7. *Upadrava*—complications (Dahanukat and Thatte add this seventh stage)[388]

Once it is established that a disease is present, the stage of development of the disease is to be determined. The skilled practitioner, while utilizing a series of diagnostic techniques, will determine the stage of the disease. In the next section, I will present the Ayurvedic diagnostic methodology.

Diagnostic Methodology: *Nidana*

The diagnostic methodology in Ayurveda has developed and expanded over the centuries. Once these or various portions of the process are completed, only then does a practitioner prescribe a treatment protocol. According to Majumdar, the Ayurvedic diagnostic toolkit included the following twelve steps:

1. *Nidana*—causes (personal history)
2. *Purva Rupa*—podromal symptoms
3. *Rupa*—symptoms and signs
4. *Upasaya*—therapeutic tests
5. *Samprapti*—pathogenesis
6. *Upadrav*—complications
7. *Sapeksha Roga Nidana*—differential diagnosis
8. *Sadhya-Sadhyata*—prognosis
9. *Arista Lakshanam*—signs of death
10. *Aptopadesh*—authoritative classical and other texts
11. *Anusandhpan*—investigations
12. *Chikitsa*—therapy [389]

Charaka described three aspects of diagnosis: observation (steps 1-6), inference (steps 7-8), and sayings of the seers in authoritative texts (steps 10-11). Susruta emphasized both the use of the five senses during patient examination and the importance of proper examination of the patient and the disease. It was not until much later that Madhava mentioned the first five diagnostic procedures systematically described above.[390]

For example, Svoboda and Lade explained that an Ayurvedic diagnosis starts with an assessment of the tissues. The health of the tissues is reflected in the complexion, the tone of flesh and fat, bone solidity, the nervous system, and the skin and eyes. What cannot be perceived directly must then be assessed through logical inference, analogy, and expert testimonials. Sight, touch, and sound are the main methods of direct perception, especially regarding feces, urine, the pulse, the tongue, and the face. Once the patient is assessed, the particular *dosha* that is responsible for the vitiation is identified, and treatment follows.[391] It should be noted that the process whereby an Ayurvedic physician diagnoses a patient is not unlike the same procedure utilized by Western-trained physicians.

General Principles of Treatment: Chikitsa

Majumdar described the three basic principles of treatment:

1. *Samshodhana Therapy* focuses on expelling increased doshas in the body via emetics, purgatives, and enemas.
2. *Samsamana Therapy* focuses on calming disturbed doshas by the use of the six tastes (*rasas*) and medicines (*dravya*).
3. *Ahar and Vihar Therapies* focus on balanced and nutritious diet (*Ahar*) and a daily routine (*Vihar*) that includes focusing on the appropriate time to wake up; how to clean

the mouth, eyes, and face; how to clean the teeth; gentle oil massages for the head, body, nose, ears; physical exercise; meditation; appropriate clothing to wear; study; work; and sexual activity.

Body Purification Therapy: The *Pancha Karma* Therapy

A detailed and rigorous purification therapy developed over the centuries and is extensively discussed in *Charaka*, *Susruta*, and *Vagbhatas Samhitas*. Charaka described the following procedure: 1. *Vamana* (emesis), 2. *Virechana* (purgation), 3. *Anuvasana Vasti* (one type of enema), 4. *Niruha* (another type of enema), 5. *Shirovirechana* (or *Nasya*—an errhine). Susruta used the single term "v*asti*" to include both *anuvasana* and *niruha vasti* and added *raktamokshana* (blood-letting) as the fifth process of *Pancha Karma Therapy* for its surgical importance.[392]

At present Pancha Karma Therapy involves the following five procedures:

1. Emesis
2. Purgation
3. Enema
4. Errhine
5. Blood-letting

Each patient is unique and therefore requires specialized treatment. After identification of what doshas are vitiated, a program of *Pancha Karma* (five purifications) procedures is delineated. Each procedure requires specific medications depending on the diagnosis.[393]

Massage is an integral part of the type of Ayurveda practiced in the south western state of Kerala.

Ayurveda: Dravyaguna (Pharmacology)

Dravyaguna Vigyana-Historical Development

Ayurvedic pharmacology, called *dravyaguna vigyana* (science), developed during the South Asian subcontinent's medieval period, approximately between the eighth and fifteenth centuries. Unnikrishnan described the many lexicons, treatises, and commentaries written during this time period that elaborated upon and contribute to the development of Ayurvedic pharmacology over the centuries. For example, he listed the following commentaries: *Ayurveda Dipika* by Cakrpanidatta for *Caraka Samhita* (11 C. E.), *Nyaya Candrika* by Gayadasa for *Susruta Samhita* (11 C. E.) *Nibandhasamgraha* by Dalhana for *Susruta Samhita* (12 C. E.), *Sarvanga Sundari* for *Astanga Hrdaya* by Arundatta (13 C. E.), *Sasilekha* by Indu for *Astanga Samgraha* (13 C. E.), and *Tattvapradipika* by Sivadas Sen for *Caraka Samhita*.

More modern treatises were also written in the seventeenth, eighteenth, and nineteenth centuries. As the dravyaguna literature was updated periodically, Unnikrishnan noted that information exchanged between different cultures concerning medicine, such as useful non-indigenous plants and new substances, were incorporated into the dynamic Ayurvedic pharmacology's canon (such as potatoes and chili peppers), thereby enhancing the Ayurvedic therapeutic arsenal.[394]

Unnikrishnan pointed out that a number of regional Ayurvedic works exist that are important to a particular ecosystem. For example, many oral traditions in various parts of South Asia have yet to be documented, and there are approximately 230 manuscripts that focus exclusively on dravyaguna in libraries all over the world, but they are not yet readily available to the larger Ayurvedic community of practitioners and researchers.[395]

Introduction to *Dravyaguna*

Svoboda summarized the principles of Ayurvedic pharmacology in the following statement:

> The principles of Ayurvedic pharmacology differ from those of modern allopathic medicine as much as they resemble those of Chinese medicine. Both Ayurveda and Chinese medicine lay emphasis on the innate characteristics of a substance's effect on a living system, with a view to enhancing positive qualities and eliminating negative ones, rather than on the 'active principles' that modern researchers seek to isolate from medicinal plants. Ayurvedic and Chinese prescriptions use assistant herbs and processing techniques to perfect the action of the main substance in a compound, rather than taking individual chemical fractions out of context and refining them to chemical purity at the cost of their life-force.[396]

Basic Definition

Unnikrishnan defined dravyaguna as the special branch of Ayurveda in which the qualities and biological actions of food and medicine are described. Plant and non-plant substances are defined based on promotive, preventive, and curative properties and applications. *Dravyas* or drugs are defined according to origin: plant, animal, or mineral.[397]

Gogte described *dravyaguna* as a branch of knowledge that deals with dravyas (drugs as well as diet) that aid in the maintenance of health and the alleviation of disease in the human body, the body being made up of the five gross elements and the soul. *Dravyaguna* also includes the properties, actions, proper doses, proper times of administration, and different preparations of these dravya.[398]

According to Sharma, dravyaguna is the science of drugs (*dravya*) and their properties (*guna*) and actions (*karma*). *Dravyaguna* is divided into the following four categories:

1. Pharmacognosy (*namarupa vijnana*) involves the names of and synonyms for drugs and morphological characteristics;
2. Pharmacology (*gunakarma vijnana*) deals with the properties and actions of drugs;
3. Therapeutics (*prayoga vijnana*) is based on properties and actions of drugs, drug usage, dosage, and vehicles; and
4. Pharmacy (*bhesajakalpana*) involves proper drug collection, processing, and storage[399]

Dravya in *dravyaguna* has a more specific and definite meaning. *Dravyas* are those substances that originate from the *panchamahabhutas* and by definition inherently possess both property (*guna*) and action (*karma*). *Dravyas* cannot be perceived directly and so their attributes are inferred on the basis of their properties. A *dravya* has no existence without *gunas*. Therefore, by definition, a *dravya* is a combination of both *guna* and *karma*.[400]

The *Pancha Bhuta theory* that all matter is made up of various combinations of ether, air, water, fire, and earth is also applicable to dravyas. *Dravyas* are also panchabhautik. The *dosha-dhatu-mala* of the body is panchabhautik and if the natural balance is in any way disturbed, then the remedies that are administered also have to be panchabhautik. Furthermore, there is no substance that is not panchabhautik, so there is no substance that cannot be used as a medicine. This includes everything from metals such as gold and mica to biological animal wastes such as urine, feces, soil, and ash. In other words, the human body that is formed from the external universe may also be treated by all the substances represented in the universe, either internally or externally.[401]

Basic Principles of *Dravyaguna*

The ideological foundations of classical Ayurveda are based on the five gross elements (*Pancha Bhuta Theory*) and the tri-dosha theories. Gogte emphasized that the idea that all material things derive from the gross elements is also the key to the development of dravyaguna.[402] A drug acts predominantly on the *doshas* but also on the *dhatu*, *mala*, and *srota*. In a disease state, the type of effect desired is determined before there is any drug administration. For example, if there is an increased kapha dosha, a drug to remove kapha or decrease kapha is administered (*shodhana* or *shamana*, respectively).[403]

Although the effects of a drug on the doshas are inferred, the inferences are based on both logic and observation. According to Ayurvedic pharmacology, drug action is mediated totally or partially via one or all of the following seven attributes: substance (*dravya*), taste (*rasa*), property (*guna*), potency (*virya*), post-digestive rasa (*vipaka*), specific potency (*prabhava*), and action (*karma*).[404]

The Seven Attributes of a Drug: Padartha Vigyana: Dravya, Rasa, Guna, Virya, Vipaka, Prabhava, and Karma [405]

Each and every *dravya* or drug possesses the aforementioned seven qualities or attributes. Based on these attributes, a well-trained Ayurvedic practitioner prescribes drugs that will affect an individual's *doshas*, *dhatus*, *malas*, and *srotas* and thereby balance the doshas. For example, if the dhatus are strong, the doshas remain in balance despite any vitiation. Therefore, a *dravya* utilized for disease treatment must reduce the vitiating capacity of the *doshas* and bring about an equivalent increase in *dhatu bala* (tissue strength).

In the following section, I review in detail the different aspects of each of the seven attributes since these attributes form the paradigm of Ayurvedic pharmacology. In addition, this classification method allows the researcher to analyze in greater detail the specific attributes of individual plants. In Chapter 4, I will present a detailed look at some of the plants utilized in the four Ayurvedic formulations that were used in the clinical study based on dravyaguna classifications.

Dravya

A *dravya* is a drug or substance that is comprised of the five gross elements and acts as an abode for *guna* (property) and *karma* (action). The property (*guna*) represents the quality inherent in substances (*dravya*). Both property and action are inseparable from a substance.

Rasa

Rasa represents the basic taste of a substance. Taste is sensed due to the presence of the five gross elements in differing proportions. Taste is perceived on the tongue and in the oral cavity. Ayurveda describes six tastes:

Madhura	sweet
Amla	sour
Lavana	salty
Tikta	bitter
Katu	pungent
Kasaya	astringent [406]

For example, an individual's chooses food based predominantly on taste (*rasapradhan*). However, the effect of taste on the body takes time because the vibrations of taste are not as strong as the impact of other attributes.

Guna

Guna is the property of a substance. It is an attribute that is inseparable from the *dravya* and does not have any action of its own. The twenty properties of substances that are paired in the following manner:

1. *guru* (heavy) *laghu* (light)
2. *shita* (cold) *ushna* (hot)
3. *snigdha* (unctuous) *ruksha* (dry)
4. *manda* (dull) *tikshna* (sharp)
5. *sthira* (immobile) *sara* (fluid)
6. *mridu* (soft) *kathina* (hard)
7. *vishada* (clean) *pichchila* (mucilaginous)
8. *shlakshna* (smooth) *khara* (rough)
9. *sukshma* (fine) *sthula* (gross)
10. *sandra* (viscous) *drava* (fluidity) [407]

Virya

Virya is the potency or the dynamic property of a substance that evokes a reaction in the body. It is accepted by most practitioners that there are only two types of *virya*: hot (*ushna*) and cold (*shita*). Medicines, as opposed to mere foods, possess a *virya* that is stronger in vibrations (*viryapradhan*) than *rasa*, and therefore have a potential for acting faster upon the body. Most individuals are habituated to a *rasapradhan* diet (based on taste) but not to those *viryapradhan* medicines (based on potency). This increases the potency and efficacy of virya

drugs. But it should be noted that once the body gets habituated to *virya* drugs, the effectiveness of the medicine may diminish.[408]

Vipaka

Vipaka is the taste of a substance after digestion. The *vipaka* is predicted based on inference and knowledge of the action on dosha-dhatu-mala. There are two ways of classifying *vipaka*:[1 #0] heavy (*guru*) and light (*laghu*) and (2) sweet (*madhur*), sour (*amla*), and pungent (*katu*).[409]

Prabhava

Prabhava is defined as the specific property of a substance.

Karma

The *karma* of a substance is action. The effect of a substance that produces changes in the human body due to *rasa*, *guna*, *virya*, *vipaka*, and *prabhava* is the *karma* of a substance.

Sanskar is a process that involves changing the properties of a drug. A particular desired property that was originally absent in the drug may be induced, and an undesired property may be deleted, by the process of *sanskar*. Numerous medicinal preparations have been formulated on this basis. For example, *samyoga* is a combination, and *bhavana* is a process in which a medicine is impregnated with the juice or decoction of another *dravya* so that its properties and actions add to the medicine. The goal is to make the *bhavana dravya* reach the smallest particles of the medicine. An *anupan* is a *dravya* that has to be taken along with the main medicine because it enhances the medicinal action.[410] As another example, if a *dravya* is subjected to a sanskar with another *dravya* having similar *gunas*, then it will lead to an

increase in the quality of the *dravya*, and better quality brings about better action. A *dravya* can also bring about a decrease in the undesirable attributes of a *dravya*.[411] Drugs before *sanskar* and drugs after *sanskar* are two different entities, even though they may be called by the same name for the sake of convenience. The sciences of cooking and pharmacology are extensions of the concept of *sanskar*. Therefore, a serious Ayurvedic practitioner must be well-versed in the science of dietetics as well as in pharmacology.[412]

Chapter 5: Clinical Research Protocol: An Open Label Study to Evaluate Ayurvedic and TCM Management Therapies (AMT) of Non-Insulin Dependent *Diabetes mellitus* (DM2)

Please note that this pilot clinical research protocol or a summary was presented to the respective Institutional Review Boards for approval. This is the original proposal that was presented for approval. A modified version of this protocol was used in Shanghai, China where the length of the study was increased to eight weeks and the number of patients was reduced to 20.

Indication

This study will support the indication for use of Ayurvedic Management Therapy (AMT) for the reduction of hyperglycemia in patients with DM2. AMT is defined as complete Ayurvedic evaluation of disease etiology, individualized prescription of formulations, diet, and exercise regimens. Anticipated completion date: August 2004; Country study conducted in: Bangalore, India

Background

The World Health Organization (WHO) has determined that up to 80% of the developing world relies on traditional medicine for their primary healthcare needs.[413] To promote public health for all, the World Health Assembly governments called on the Director General of the WHO "to consider the contribution WHO might make to promoting respect for, and

maintenance of, indigenous knowledge, traditions and remedies, in particular, their pharmacopoeia".[414]

Diabetes is a worldwide epidemic that is especially prevalent in India, China and the United States. King et al.[415] estimate that between 1995 and 2025, diabetes will increase 195% in India affecting some 57.2 million people, 134% in China affecting some 37.6 million people, and 58% in the United States affecting some 21.9 million people. One way of meeting the enormous challenge this situation presents is to investigate the efficacy of traditional plant-based therapies. This subject has been receiving increasing attention over the past 20 years. Diverse indigenous healing traditions are found throughout Asia. Ayurveda, the science of life, and Traditional Chinese Medicine (TCM), are two such ancient codified systems that are widely practiced throughout the subcontinent and China. Both Ayurveda and TCM, as locally available and culturally acceptable modalities, may provide adjuvant and alternatives to the more expensive conventional treatments.

Ayurveda is one of several ancient healing traditions over 3,000 years old developed in the South Asian subcontinent. Classical Ayurvedic treatment includes not only individualized medicinal plant prescriptions but also encourages diet modification, exercise, and mental balance. The Ayurvedic paradigm of healing has a long and continuous history of use, a substantial scientific literature on the efficacy of Ayurvedic medicinal plants, and is concurrent with allopathic modalities of treatment.[416]

Classical Sanskrit texts describe “prameha” (an overproduction of urine) that includes over 20 subtypes that are divided into three categories: kaphaja, pittaja, or vataja prameha. “Madhumeha”, a subtype of vataja, is a condition where one passes a large quantity of sweet urine. Based on detailed descriptions of signs and symptom, madhumeha correlates with modern definitions of DM2.[417] [418] Over the centuries Ayurvedic practitioners have developed numerous classical formulations for individual sub-types to treat madhumeha.

Clinical Research on Ayurvedic Management Therapy of DM2 patients

The six Ayurvedic madhumeha formulations (MF1-6) to be used in the study include 36 medicinal plants and one fish species: two in decoction (kashayam) and two in powder (churna) and two in capsule form. Although there does not appear to exist any open clinical studies that test Ayurvedic Management Therapy of DM2, a review of the literature of the medicinal plants to be used in the study reveals extensive scientific data available on individual plants and in some cases plant combinations.

A review of the medical literature of the thirty-six plants and one fish species demonstrates a range of medicinal effects. Seven of the plants have extensive research studies that include *in vitro*, *in vivo*, human and clinical studies: *Curcuma longa*, *Emblica officinalis*, *Terminalia arjuna, Terminalia bellirica, Terminalia chebula, Tinospora cordifolia,* and *Zingiber officinale* (Group I). Thirteen plants (with some overlap with the above) show various degrees of antidiabetic effect *in vitro, in vivo,* and in human studies: *Aerva lanata, Biophytum sensitivum, Curcuma longa, Emblica officinalis, Ficus racemosa, Mangifera indica, Pterocarpus marsupium, Salacia reticulata, Syzygium cumini, Terminalia bellirica,*

Terminalia chebula, Tinospora cordifolia, and *Zingiber officinale* (Group II). Thirteen other plants have also been researched but do not show direct anti-diabetic effect although other medicinal effects are demonstrated: *Acacia catechu, Berberis aristata, Bergenia ciliata, Butea frondosa, Cissampelos pareira, Coscinium fenestratum, Cyperus rotundus, Erythrina variegata, Ixora coccinea, Sarcocephalus missionis, Strychnos potatorum, Symplocos racemosa, Terminalia arjuna,* and *Vetiveria zizanioides* (Group III). Nine plants and one fish species had little research data as they relate to medicinal effects: *Cedrus deodara, Cephalandra indica (Coccinia grandis), Cyclea peltata, Ficus arnottiana, Ficus lacor, Ficus religiosa, Oxalis corniculata, Premna serratifolia*, *Sepia officianalis* (fish species), and *Symplocos laurina* (Group IV).

In terms of toxicity, safety, tolerability and adverse effects, *Salacia reticulata* and *Butea frondosa* demonstrated possible anti-implantation activity in pregnant rat and mice models.[419] [420] [421] [422] However, the amount of plant material required to produce this effect if extrapolated to a 60 kg human being is 6-60 grams for *Butea frondosa* and 600 grams for *Salacia reticulata*. These dosages far exceed the Ayurvedic prescriptions to be administered during this study.

Historically classical Ayurvedic preparations when administered by an Ayurvedic physician according to classically prescribed dosages are safe, tolerable, and non-toxic. The proposed study is intended primarily to evaluate the effectiveness of AMT in reducing hyperglycemia when administered to DM2 patients as assessed by a reduction in FBG over a 4 week

treatment period. In addition, the clinical safety of AMT will be assessed in this patient population.

Objectives

Primary

The primary objective is to evaluate the effectiveness of AMT on reducing hyperglycemia when administered to DM2 patients as assessed by a reduction in fasting plasma glucose (FPG) levels after 4 weeks of individualized Ayurvedic Management: diet and exercise regime and individualized administration of classical Ayurvedic formulations (any combination of 6 Madhumeha Formulations-MF).

Secondary

After 4 weeks on AMT:

To investigate the effect of AMT on $HgbA_{1c}$

To investigate the effect of AMT on serum lipids including total cholesterol, HDL-cholesterol, LDL-cholesterol, cholesterol/HDL ratio, LDL/HDL ratio, VLDL-cholesterol, triglycerides, free fatty acids and apolipoproteins A/B

To investigate the change in quality of life and well-being of the patient

To investigate the clinical safety

To investigate the tolerability

To investigate the changes in physical examination, vital signs, weight, clinical laboratory tests, and adverse experiences

Other parameters:

And to document the Ayurvedic physician's differential diagnosis of each patient including analysis of Ayurvedic patient classification (vata, pitta, kapha), relationship between pattern use of MFs, and reasoning for prescribed AMT.

Study Plan

Study Design

This is a 4-week open-label study of AMT administered to DM2 patients. The total duration will be eight weeks.

The study will consist of a Pre-Screening (1 week), Screening (1 week) and Baseline/run-in Period (1 week), a Treatment Period (4 weeks open-label treatment), and a Follow-up Period (1 week).

Patients on any oral antidiabetes medications are excluded from this study at screening.

Visit Schedule

Procedures	**Pre-screening**	**Screening**	**Baseline**	**Open Treatment Period**		**Follow-up**
Visit number	0	1	2	3	4	5
Weeks	1	2	3	5	7	8
Time relative to baseline (wks)	-2	-1	0	+2	+4	+5

Study Population

Number of Patients

It is anticipated that approximately 80 DM2 patients will be selected for this study (based on a 25% drop out rate) in order to produce 56 evaluable patients. The Foundation for the Revitilisation for Local Health Traditions will sponsor and be the center site. Only those patients able to comply with the requirements of the protocol should be included in the study.

The investigator must maintain and submit to the sponsor a log of all patients who were considered for the study and signed an informed consent. In order to exclude systematic bias in selecting patients, minimal data including the reason for study exclusion will be collected on such patients who were considered for but did not enter Screening.

Inclusion Criteria

Patients must meet all of the following criteria to be eligible for inclusion into the study:
Patients with Non-insulin Dependent *Diabetes mellitus* (DM2) defined by the criteria of the National Diabetes Data Group (Appendix J).
Women or men who are 30 to 60 years of age, inclusive at time of enrollment.
Fasting plasma glucose (FPG) of ≥ 126mg/dL and ≤ 220mg/dL at screening.
Patients with no present intake of oral hypoglycemic or insulin intake by the beginning of the study.
Patients who have signed informed consent to participate.

Exclusion Criteria

Patients will be excluded from the study if ANY of the following apply:

Pregnancy or lactation, or if one becomes pregnant.

Any clinically significant abnormality identified on the screening physical examination, laboratory tests which in the judgment of the investigator would preclude safe completion of the study.

Presence of clinically significant renal or hepatic disease.

Presence of angina/cardiac insufficiency NYHA class III/IV.

Systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg. But if patient is on optimal antihypertensive treatment, and BP is controlled then he/she is not excluded.

If patient is on concomitant medication that has to be drastically changed during the trial.

Significant anemia (hemoglobin < 11g/dL for males or < 10g/dL for females).

Symptomatic diabetic neuropathy of sufficient severity to require treatment for control of symptoms (e.g. painful peripheral neuropathy, symptomatic orthostatic hypotension, urinary retention, pedal ulcers, gastric stasis, etc.).

Body Mass Index (BMI) < 22 and > 38 kg/m^2 (Formula: BMI = Weight, kg ÷ height, m^2).

Active alcohol or drug abuse within the last 6 months.

Use of any investigational drug within 30 days of enrollment into the study.

Patients who have required chronic use of insulin for glycemic control in the past, patients with a history of ketoacidosis, or those requiring administration of insulin at present (See Appendices K and L).

Conduct of the Study

Ethics and Regulatory Considerations

This study will be conducted according to Good Clinical Practice, the Declaration of Helsinki (protocol Appendix F), and US 21 CFR Part 50 – Protection of Human Subjects, and Part 56 – Institutional Review Boards. Written informed consent for the study must be obtained from all subjects before protocol-specific procedures are carried out. Patients will be informed of their rights to withdraw from the study at any time.

Institutional Review Board

The protocol will be submitted to the City University of New York Graduate Center, Internal Review Board (CUNY IRB) (NY, NY, USA) and St John's Medical Hospital Internal Ethical Review Board (IERB) (Bangalore, Karnataka, India) for review. The unconditional written approval of the CUNY and St John's must be obtained and submitted to Sarah Khan (SK) at FRLHT prior to commencement of the study.

SK will supply relevant data for submission to the IRBs to support the review and the approval of the protocol. Verification of the IRBs' unconditional and written approval of the protocol and the written informed consent document will be transmitted to the Clinical Monitor. This approval must refer to the study by exact protocol title and number, identify the documents reviewed, and state the date of the review.

The IRBs must be informed of all subsequent protocol amendments and of serious or unexpected adverse experiences occurring during the study which are likely to affect the

safety of the subjects or the conduct of the study. Approval for such changes must be transmitted in writing to the Clinical Monitor via the investigator.

Informed Consent

The written consent document will embody the elements of consent described in the Declaration of Helsinki (Protocol Appendix F). Governmental, institutional, or IRB/Ethics Committee regulations or guidelines may require that additional elements be included in the informed consent document. The informed consent document should be implemented in each clinical study before protocol-specified procedures are carried out.

Informed consent must be obtained in writing, unless otherwise approved by the IRB. The consent form will be generated by the investigator with the assistance of FRLHT. The proposed consent form should be submitted to Clinical Monitor for review prior to submission to the IRB. The consent form must be acceptable to Clinical Monitor and must be approved by the IRB.

The consent form should be given in both oral and written form whenever possible and deemed appropriate by the IRB. Patients, their relatives, guardians or, if necessary, legal representatives must be given ample opportunity to inquire about the details of the study (a sample consent form is in Appendix H).

Consent forms must be in a language fully comprehensible to the prospective subject. Where appropriate, informed consent shall be documented by the use of a written consent form

approved by the IRB and signed by the patient or the patient's legally authorized representative.

Consent must be documented either by the patient's dated signature or by the signature of an independent witness who records the patient's assent. In either event, the signature confirms the consent is based on information that has been understood. Each patient's signed informed consent must be kept on file by the investigator for possible inspection.

General Instructions

Prohibited concomitant medications

The use of oral antidiabetic medications, are prohibited from the start of the screening period and during the study including the follow-up period.

Dose levels of all concomitant medications should, if medically appropriate, remain UNCHANGED while the patient is enrolled in the study. If dosage change of a concomitant medication is necessary, information pertaining to the change must be documented on the patient's case report form (concomitant medication pages)

Patient scheduling general information (see Appendix I)

Scheduled patient visits will occur in the morning, at a time of day that is 11 to 15 hours after their usual supper time. Patients are to be instructed to fast (i.e., refrain from eating and

drinking) from 11:00 PM on the night before their visit until after blood specimen collection for clinical laboratory evaluation has been completed. Water consumption is permitted during the fasting period.

Patients should be instructed NOT to take their morning dose of study medication on all study visit days, since they will be given this dose after all fasting laboratory specimens have been collected. Patients are to be reminded to bring their remaining study medication with them on study visit days.

Laboratory assessments must be done in the fasting condition. At any clinic visit, if the patient is not in a fasted condition, specimens for laboratory assessments are not to be collected. The patient should return to the clinic the following day in a fasted condition for the laboratory specimen collection, if possible, or skip that week of laboratory collection.

A trained medical technician will collect samples. Samples will be delivered to St John's Medical Hospital Central Laboratory. Full guidance, training, and materials for storage and transportation of materials to the laboratory will be provided to the study center. Normal methods and quality control used for tests will be provided for by St John's Medical Hospital laboratory.

Any result which falls outside the laboratory normal range will be considered abnormal. If this occurs, the investigator will indicate if this value is clinically significant. All laboratory tests with clinically abnormal values (i.e., beyond those expected within the patients age

group) occurring during the study will be repeated until the values return to normal. If this does not occur within a reasonable time, then the etiology will be identified and the sponsor informed.

At the completion of the study or at any time during the Open Treatment Period, when a patient discontinues from the study, all procedures specified under the Open Treatment Period are to be completed. When a patient terminates early from either the screening or baseline study periods, before open treatment has started, complete the appropriate Reason for Concluding Study pages in the case report form (CRF).

Pre-Screening Period (phone call enquiry, patient registration for screening)

Initial eligibility will be determined via phone call enquiry by prospective patients based on newspaper advertisements in English language newspapers of the Ayurvedic clinical study.

Procedures:

A log will be kept of phone call inquiries with first name, age, patient number, and phone number to be provided. Information on inclusion/exclusion criteria, what medical documents to bring to the screening, fasting after 11pm the night before visit, and pick-up point for transport to clinic will be provided to prepare for Visit 1.

Screening Period (Visit 1)

Patients will arrive for Visit 1 to clinic to discuss study details and review informed consent form. For those who sign informed consent, medical procedures will follow.

Procedures:

At the Screening Visit 1, the following procedures will be performed:

Prior phone contact to remind of appointment

Obtain patients' written informed consent

Complete physical exam/medical history—includes hip/weight ratio, BP, height

Qualitative questionnaire assessing quality of life and well-being

Complete Ayurvedic exam and protocol intake— Information sessions for participants on diet and exercise regime to prepare for Visit 2

Fasting blood glucose (lab)

Lipid profile (lab)

HbgA1C (lab)

Baseline Period (Visit 2)

During Baseline-Run-in Period, patients will be guided to establish a diet and mild exercise regime. Continued information sessions on healthy diet and exercise will be provided. Clinic visits will be scheduled at two-week intervals beginning with the end of week 2 to the end of week 6. Patients should be seen in the morning on visit days and are instructed not to take their study medication, since they will take their morning dose in the clinic after all fasting

laboratory specimens have been collected. At Visits 2 and 3, study medication will be dispensed. Patients should be instructed to bring all remaining study medication with them to EACH study visit.

Procedures:

Phone contact to remind of appointment (before appointment)

Complete physical exam—includes hip/weight ratio, BP, height

Qualitative questionnaire assessing quality of life and well-being

Complete Ayurvedic exam and protocol intake—Information sessions for participants on diet and exercise regime

Fasting blood glucose (lab)

Lipid profile (lab)

Dispense study medication

Treatment Period (Visits 3, 4)

The Open-Label Treatment Period begins on the same day that the Baseline Period ends (Visit 2).

Procedures:

At the Open Treatment Period Visits 3 and 4, the following procedures will be performed:

Phone contact to remind of appointment (before appointment)

Phone contact to encourage compliance to Ayurvedic diet and exercise regimen, address any questions related to diet, exercise, MF intake, document any adverse effects (in between appointments)

Complete physical exam—includes hip/weight ratio, BP, weight

Complete Ayurvedic exam and protocol intake

Qualitative questionnaire assessing physical and mental well-being (Visit 4)

Fasting blood glucose (lab) (Visits 3 and 4)

Lipid profile (lab) (Visit 4)

HbgA1C (lab) (Visit 4)

Dispense study medication (Visit 3)

Follow-up Period (Visit 5)

At the conclusion of the study or if the patient is withdrawn from the study prematurely, the patient will be asked to return after the last day of study medication for follow-up assessments.

Procedures:

Phone contact to remind of appointment (before appointment)

Complete physical exam—includes hip/weight ratio, BP, weight

Complete Ayurvedic exam and protocol intake

Qualitative questionnaire assessing quality of life and well-being

Fasting blood glucose (lab)

Lipid profile (lab)

HbgA1C (lab)

Clinical Observations and Procedures

In-clinic dosing

Patients should be scheduled to attend study visit days in the morning (AM). Each patient should be fasting and should not have taken their morning dose of study medication. After all clinical laboratory tests are completed in the fasting condition, the patient will be dosed in the clinic from the next supply of medicine.

Clinical laboratory testing for efficacy

The following **fasting** laboratory tests will be performed at the times specified in the protocol:

Efficacy

Fasting Plasma glucose

Hemoglobin A1C ($HgbA_{1c}$)

Lipid Levels-Total Cholesterol-HDL Cholesterol, LDL Cholesterol, VLDL Cholesterol, Triglycerides, Free Fatty acids, Apolipoprotein A/B

St John's Medical Hospital Central Laboratory (SJMHCL) will be used for all laboratory assessments. Samples must be clearly labeled with the patient's number, initials, protocol number, center number, visit number, and date. Full details for the preparation and shipment of samples will be provided by SJMHCL to the Investigator before the start of the study.

Normal reference ranges for all parameters will be obtained from SJMHCL prior to starting the study. The laboratory undertaking tests should not be changed unless absolutely necessary. If a change is unavoidable, the new normal range should be clearly identified in the CRFs concerned. All laboratory tests with values that become significantly abnormal after study drug administration should be repeated until the values return to normal or baseline and are to be recorded as an adverse experience if deemed appropriate by the investigator. If such values do not return to normal within a period judged reasonable by the Investigator, the etiology should be identified and the sponsor notified.

Measurement of blood pressure and heart rate

The plethysmographic method (with a mercury column sphygmomanometer) must be used to measure blood pressure throughout the study. All measurements will be made on the patient's non-dominant arm supported at heart level, using the same cuff size. If the patient's arm circumference is >32 cm, a large blood pressure cuff should be used. Diastolic blood pressure will be measured at the disappearance of Korotkoff sounds- phase V. If possible, measurement will be taken by the same staff member at each visit.

Blood pressure and heart rate will be measured as follows:

After the patient sits quietly for at least 10 minutes, blood pressure and heart rate will be measured two times at approximately 2-minute intervals. The two measurements will be recorded and averaged to obtain the mean standing systolic and diastolic blood pressure. If the patient is a smoker, a period of 30 minutes should be allowed prior to taking measurements.

Medical History, medical exam, diet and exercise

All relevant previous medical history will be documented at screening (Visit 1) and any new medical history will be documented at each subsequent visit. Standard medical terminology will be used to record all current conditions by diagnosis together with significant past conditions, operations, and therapeutic or diagnostic procedures. At each subsequent visit, the patient must be encouraged to comply with the dietary and exercise regimen.

Ayurvedic History, medical exam, differential diagnosis, and Ayurvedic Management Therapy prescription

All relevant previous medical history will be documented (Visit 1) and any new medical history will be documented at each subsequent visit. Standard Ayurvedic terminology will be used to record all current conditions by diagnosis together with significant past conditions, operations, and therapeutic or diagnostic procedures. At each subsequent visit, the patient must be encouraged to comply with the dietary and exercise regimen.

Study Medication and Administration

Dosing Schedule:

During the 4 week Treatment Period, the patient will take any combination of 0-6 Madhumeha Formulations daily : MF1 and MF2 dosage of 40-60 ml/day with an equal quantity of water; MF3 and MF4 dosage of 6-12 gms with honey as a vehicle; and MF5 and MF6 dosage of 2 capsules/500mg each in the AM and PM.

Rationale for Dosage Selection:

Ayurvedic practitioners, like Traditional Chinese Medicine practitioners, have established guidelines for dosages in the classical Sanskrit Ayurvedic texts. These formulations have been found to be safe and well tolerated in the prescribed doses. However, the Ayurvedic physician reserves the right to alter or modify an individual's regime based on on-going Ayurvedic examinations and assessments. It is anticipated that a 30 mg/dL reduction in FBG will be achieved during the 4 weeks of AMT.

Formulation, Dosage, and Administration

Regimen	AM Dose	PM Dose	Total Daily Dose
MF1	20-30 Decoction	20-30 Decoction	40-60 ml/day total
MF2	20-30 Decoction	20-30 Decoction	40-60 ml/day total
MF3	3-6 gm Powder	3-6 gm Powder	6-12 gm/day total
MF4	3-6 gm Powder	3-6 gm Powder	6-12 gm/day total
MF5	2 500mg/capsules	2 500mg/capsules	4 500mg/capsules
MF6	2 500mg/capsules	2 500mg/capsules	4 500mg/capsules

Packaging and Labeling

Formulations MF1-3 and MF5 will be supplied by Arya Vaidya Pharmacy; MF4 will be supplied by FRLHT; and MF6 will be supplied by Sudarshan. MF1 and MF2 will be supplied in clear glass 500 ml bottles. MF3 and MF4 will be in powder forms in folded packages of 3-6 grams each. MF5 and MF6 will be in capsule form in opaque bottles containing a two week supply plus four days of 72 capsules. Each patient will receive bottle(s) of medication at the appropriate clinic/office visit.

Arya Vaidya Pharmacy, FRLHT and Sudarshan will provide pre-packaged, patient specific and visit specific medications sufficient for each center to complete the open treatment period of study. Each bottle of study medication distributed will have a lot/batch number that will be copied on the case report form at the initial dispensing of each bottle of study medication. The code on the study medication bottle should be recorded on the case report form in the space provided on the study medication label record.

Patients will receive any combination of MF 1-6 based on individual differential diagnosis:

Storage Requirements

Study medication will be stored in a cool and dry secured, supervised location. A log for recording receipt of and use of study medications will be maintained by the designated personnel at the investigator site.

Drug Accountability

At the time of delivery of medication to the study site, the Investigator or his/her designate or pharmacist (where appropriate) will sign a Drug Receipt Form to confirm that the supplies for the study have been received. This will specify job or lot numbers, quantities shipped/delivered and the date of receipt. The form will also contain statements confirming that:

the investigational products will be handled and stored safely and properly;
the investigational products will only be dispensed to patients in accordance with the protocol; and any unused products will be kept by FRLHT or returned to suppliers.

The Investigator or his/her designate or pharmacist (where appropriate) will record all study medication dispensed on a Drug Accountability Form. At the end of the study, reconciliation must be made between the amount of medication supplied, dispensed, and subsequently returned. Any discrepancies must be accounted for. A certificate of return must be signed incorporating the assurance from the Investigator or Pharmacist that all used and unused investigational products have been returned, if required. Supplies will in the majority of cases, be returned to the local site for subsequent destruction. In exceptional cases and because these medications are not hazardous to handle, supplies may be destroyed at the center. Destruction should only be performed by authorized personnel who are aware of any possible hazardous effects (Dr. Gangadharan). The procedure should be documented in full, in writing.

Assessment of Compliance

The number of bottles and packages of powder dispensed at each clinic visit and compliance percent will be recorded on the CRF. Patients will be instructed to return any unused drug at the next visit. Counts of bottles and packets returned will be made at the beginning of Visits 3 and 4. If the patient takes less than 80% or more than 120% of the study medication prescribed by the Ayurvedic physician during the two visits, the patient will be considered non-compliant and will be withdrawn from the study.

Treatment of Over dosages

The dose of MF1-6 considered to be an overdose has not been defined. Treatment of suspected or confirmed overdose should be symptomatic.

Occupational Safety

Study medications are not expected to pose occupational safety risks to investigational staff under normal conditions of use and administration.

Concomitant Medication/Treatment

The use of insulin and oral antidiabetic medications, are prohibited during the study. No other medications are specifically prohibited for concomitant use.

If medically appropriate, dosage levels of all concomitant medications should, remain unchanged (especially, those medications known to significantly effect glucose control or significantly change lipid profiles, e.g., thiazide diuretics, β-blockers, oral corticosteroids, etc.) while the patient is enrolled in the study. All concomitant medication taken during the study must be recorded in the case report form with indication, daily dose and dates of administration. If dosage change of concomitant medication is necessary, information pertaining to the change must also be documented on the patient's case report form (concomitant medication pages).

Adverse Experiences

The recording of adverse experiences is an important aspect of study documentation. Detailed guidelines are set out below.

Eliciting and Documenting Adverse Experiences

It is the responsibility of the investigator to document all adverse experiences that occur during the investigation.

An adverse experience includes an noxious, pathological or unintended change in anatomical, physiological or metabolic functions as indicated by physical signs, symptoms and/or laboratory changes occurring in any phase of clinical study whether associated with the study drug, active comparator or placebo and whether or not considered drug related. This includes an exacerbation of pre-existing conditions or events, intercurrent illnesses, drug interaction or the significant worsening of the disease under investigation that is not recorded

elsewhere in the case record form under specific efficacy assessments. Anticipated day-to-day fluctuations of pre-existing conditions, including the disease under study, that do not represent a clinically significant exacerbation or worsening need not be considered adverse experiences. Discrete episode of chronic conditions occurring during a study period should be reported as adverse experiences in order to assess changes in frequency or severity.

Adverse experiences should be documented in terms of a medical diagnosis(es). When this is not possible, the adverse experience should be documented in terms of signs and/or symptoms observed by the investigator or reported by the patient at each study visit.

N.B. Any pre-existing conditions or signs and/symptoms present in a patient prior to the start of the study should be recorded on the Medical/Surgical history form within the patient's case report form (CRF).

In the case of "open" studies involving a marketed drug in an established indication, an adverse experience includes significant failure of expected pharmacological or biological action.

Adverse experiences that occur after informed consent is obtained, but prior to starting active treatment will be documented on the "Baseline signs and symptoms" report form as instructed by the clinical study monitor. All adverse experiences occurring after administration of the first dose of study medication (i.e., comparator drug, active drug, placebo) and on or before the final visit must be reported on the Adverse Experience form in

the subject's CRF. All subsequent adverse experiences, whether no drug (i.e. during reference 'run-in' or 'wash-out' period) or when active drug is being administered, must be reported REGARDLESS OF WHETHER OR NOT THEY ARE CONSIDERED DRUG RELATED.

Serious adverse experiences that occur during the clinical study or within 30 days or five half lives, whichever is the longer of receiving the last dose of study medication, whether or not related to study drug, must be reported.

Instances of death, cancer, or congenital abnormality if brought to the attention of the Investigator to be possibly related to study medication should be reported to the study monitor.

At each visit/assessment, adverse experiences will be evaluated by the Investigator. Adverse experiences not previously documented in the study will be recorded in the adverse experiences record form within the patient's CRF. The nature of each experience, date and time (where appropriate) of onset, outcome, course (i.e. intermittent or constant), maximum intensity, action taken with respect to dosage and relation ship to treatment should be established. Details of changes to the dosage schedule or any corrective treatment should be recorded on the appropriate pages of CRF.

Adverse experiences already documented in the CRF i.e. at a previous assessment and designated as 'ongoing' should be reviewed at subsequent visits as necessary. If these have

resolved, the documentation in the CRF should be completed. N.B. If an adverse experience increases in frequency or severity during a study period, a new record of the experience will be started.

For studies in which there is a delay of greater that 30 days between dosing, and during this time no protocol specific procedures required (e.g. vaccine studies), adverse experiences will be recorded for a period of 30 days only after each dosage administration (N.B. See section 8.5 below for qualification with regard to serious adverse experiences.

As a consistent method of soliciting Adverse Experiences, ask the subject a non-leading question such as:

“Have you felt different in any way since starting the new treatment/or since the last visit?”

Assessment of Intensity

Maximum intensity should be assigned to one of the following categories:

Mild: An adverse experience that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.

Moderate: An adverse experience that is sufficiently discomforting to interfere with normal everyday activities.

Severe: An adverse experience that prevents normal everyday activities.

Assessment of Causality

Every effort should be made by the investigator to explain each adverse experience and assess its relationship, if any, to study drug treatment. Causality should be assessed using the following categories: not related, unlikely, suspected (*reasonable possibility*), probable.

Not related: The adverse experience is definitely not related to the test drug.

Unlikely: There are other, more likely causes and the drug is not suspected as a cause.

Suspected (*reasonable possibility*): A direct cause and effect relationship between the drug and the adverse experience has not been demonstrated but *there is a reasonable possibility that the experience was caused by the drug.*

Probable: There *probably* is a direct cause and effect relationship between the adverse experience and the study drug.

The degree of certainty with which an adverse experience is attributed to drug treatment (or alternative causes, e.g. natural history or underlying diseases, concomitant therapy, etc.) will be determined by how well the experience can be understood in terms of one or more of the following:

Known pharmacology of the drug.

Reaction of similar nature being previously observed with this drug or class of drug.

The experience having often been reported in literature for similar drugs as related

The experience being related by time to drug ingestion terminating with drug withdrawal (dechallenge) or reproduced on rechallenge.

Following-up Adverse Experiences

Investigators should follow-up subjects with adverse experiences until the event has subsided (disappeared) or until the condition has stabilized. Reports relative to the subsequent course of an AE noted for any subject must be submitted to the clinical study monitor.

Serious Adverse Experiences

Definition of Serious Adverse Experiences

A serious adverse experience is any event that is fatal, life-threatening*, disabling/incapacitating**, or results in hospitalization***, prolongs a hospital stay or is associated with congenital abnormality, cancer or overdose (either accidental or intentional). In addition any experience that the investigator regards as serious or that would suggest any significant hazard, contraindication, side effect ot precaution that may be associated with the use of the drug will be documented as a serious event.

Definition of Life Threatening Experience:

An adverse experience is life threatening if the subject was at immediate risk of death from the event as it occurred; i.e. it does not include a reaction that if it had occurred in a more serious form might have caused death. For example, drug induced hepatitis that resolved without evidence of hepatic failure would not be considered life threatening even though drug induced hepatitis can be fatal.

***** Definition of Disability/Incapacitating Experience:***

An adverse experience is incapacitating or disabling if the experience results in a substantial and/or permanent disruption of the subject's ability to carry out normal life functions.

******Hospitalization:***

Adverse experiences requiring hospitalization+ should be considered serious. Hospitalization for elective surgery or routine clinical procedures++ that are not the result of an AE (e.g. elective surgery for a pre-existing condition) need not be considered AEs and should be recorded on the medical/surgical procedures form. If anything is reported during the procedure, that occurrence must be reported as a AE, either 'serious' or 'non-serious' according to the usual criteria.

+Definition of Hospitalization

In general, hospitalization signifies that the subject has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment

that would not have been appropriate in the physician's office or out-patient setting. When in doubt as to whether 'hospitalization' occurred or was necessary, the AE should be considered serious.

++***Definition of Routine Clinical Procedure.***

One that is defined in the protocol as a procedure that may take place during the study period and should not interfere with the study drug administration or any of the ongoing protocol specific procedures.

Reporting Serious Adverse Experiences

Any serious adverse experiences that occur at any time during the clinical study or within 30 days or five half lives, whichever is the longer of receiving the last does of study medication, whether or not related to the study drug, must be reported by the investigator to the study monitor by telephone within 24-hours.

Investigator should not wait to receive additional information to fully document the event before notifying FRLHT of a serious adverse experience. The telephone report should be followed by a full written summary utilizing the FRLHT serious Adverse Experience worksheet detailing relevant aspects of the adverse experiences in question. Where applicable, information from relevant hospital case records and autopsy reports should be obtained.

Instances of death, cancer, or congenital abnormality if brought to the attention of the Investigator AT ANY TIME after cessation of study medication AND considered by the Investigator to a previous clinical trial, should be reported to the study monitor.

Reporting of Overdosage

Any instance of overdose (suspected or confirmed and irrespective of whether or not it involved study medication) must be communicated to FRLHT within 24 hours and be fully documented as a serious adverse experience. Details of any signs or symptoms and their management should be recorded including details of any antidote(s) administered.

Pregnancy

Subjects who become pregnant during the study should discontinue the study immediately, unless the protocol states otherwise.

Subjects should be instructed to notify the investigator if it is determined after completion of the study that they become pregnant either during the treatment phase of the study or within (30 days or five half-lives after the treatment period, whichever is longer).

Whenever possible a pregnancy should be followed to term, any premature termination reported, and the status of the mother and child should be reported to FRLHT after delivery.

Patient Completion and Withdrawal

Definitions

All patients who complete the current study and the assessments and procedures scheduled at Visit 5.

Any patient, who enters the study, (i.e. gives written informed consent) but does not, for any reason, complete the study according to the definition given above, will be considered as a withdrawal, irrespective of whether they have received any study medication.

Procedures for Handling Withdrawals

Enrollment to the study will continue until 80 patients have registered or until scheduled Screening Period begins whichever comes first. At this time recruitment will cease. It is anticipated that some patients will withdraw from the study.

Patients who terminate their participation in the study due to adverse experiences should be followed up as appropriate (Section 7.4) in order to determine the final outcome.

All patients who withdraw or are withdrawn from the study prior to the Open Treatment Period should return for a follow-up visit wherever possible and all the early withdrawal assessments and procedures should be completed. All patients who withdraw or are withdrawn for the study after commencement of the Treatment Period should return for a

follow-up visit wherever possible and all the Visit 5 assessments and procedures should be completed.

Case Report Forms for all patients entered into the study must be kept and the reasons for withdrawal will be noted on the Study Conclusion page for all enrolled patients who do not complete the study. In addition, the date of last dose of study medication must be recorded on the Study Conclusion page for all patients withdrawn from the study.

Reasons for Withdrawal

Every effort must be made by the Investigator to keep patients in the study. However, a patient may be discontinued prior to completion of the study for the following reasons:

Adverse experience (see Section 7.0)

Lack of efficacy (i.e. insufficient therapeutic effect) as defined below:

Patients with a fasting plasma glucose ≥ 220mg/dL on 2 consecutive study visits during the baseline or treatment period.

Fasting plasma glucose has increased to a level that is deemed by the investigator to represent a safety risk to the patient.

Patients will be withdrawn if they require insulin or any additional agent to manage glycemic control.

Any other metabolic disorder deemed by the investigator to be a safety risk to the patient.

A protocol violation, including lack of compliance with the study medication, or visit or treatment with prohibited concomitant medications.

Patient lost to follow-up.

The patient requested an early discontinuation.

Termination of the study by FRLHT.

Other (reason to be documented in the CRF).

All adverse experiences leading to withdrawal or a patient must be fully documented and followed-up as appropriate (see Section 7.0). To ensure that all withdrawals due to Adverse Experiences are correctly identified, "Adverse Experience" should only be checked as the reason for withdrawal on the Study Conclusion page for those patients for whom an Adverse Experience was considered to be the direct cause of the patient withdrawing from the study. This is particularly important when Adverse Experiences are ongoing at the time of withdrawal but the reason for withdrawal is not related to the Adverse Experience.

Extension Studies

Following completion of all assessments and procedures at Visit 5, patients may enter an open-treatment, long-term extension protocol. **To be eligible for the long-term extension study, AMT must have been found to be safe and well tolerated throughout the current protocol by both the investigator and the patient.** Furthermore the extension study will be fully paid for by the patient under the guidance of G.G. Gangadharan.

Patients will not be eligible to enter the open treatment, long-term extension study should **any** of the following apply:

They experience any significant and/or serious Adverse Experience that, in the opinion of the investigator, could have been attributed to study medication;
A clinically significant laboratory abnormality is recorded that in the opinion of the investigator, would preclude continuation of treatment with study medication;
The patient withdraws from the study for any reason prior to completion of all assessments and procedures scheduled at Visit 5.

Data Evaluation

Criteria for Efficacy

Primary efficacy variables

The primary parameter will be change from baseline of FBG at the end of 4 weeks of treatment. Baseline will be defined as Visit 2 and, if it is missing, the screening visit will be used.

Secondary efficacy variables

Secondary efficacy and safety parameters analyzed as change from baseline after 4 weeks of treatment include:-

HgbA1C

Total cholesterol

HDL-cholesterol

LDL-cholesterol

Cholesterol/HDL ratio

LDL/HDL ratio

VLDL-cholesterol

Triglycerides

Free fatty acids

Apolipoproteins A/B

Vital signs including heart rate, systolic blood pressure and diastolic blood pressure, weight, bmi, hip/weight ratio

Qualitative questionnaire on quality of life and well-being.

And to document the Ayurvedic physician's differential diagnosis of each patient including analysis of Ayurvedic patient classification (vata, pitta, kapha), relationship between pattern use of MFs, and reasoning for prescribed AMT.

Adverse events during the study will also be recorded.

Statistical Methodology

Comparisons of Interest

The main comparison of interest in this study is for the primary endpoint FBG level after 4 weeks of AMT against baseline levels. Secondary endpoints including HgbA1C , total

cholesterol, HDL-cholesterol, LDL-cholesterol, cholesterol/HDL ratio, LDL/HDL ratio VLDL-cholesterol, Triglycerides, free fatty acids, apolipoproteins A/B, vital signs including heart rate, systolic blood pressure and diastolic blood pressure and weight will be similarly compared. Incidences of AEs will be summarized.

Sample Size Determination

Sample size for this study was based on the primary variable FBG. Sample size of 56 subjects achieves 90% power to detect a change from baseline in FBG of 20 mg/dL based on an estimated standard deviation of 45 mg/dL and with a significance level (alpha) of 0.05 using a two-sided one-sample t-test.

Interim Analysis

No interim analysis is planned.

Efficacy Analysis

Methods of Analysis

All primary and secondary variables including adverse experiences (AEs) will be summarized and plotted if appropriate. AEs will be further summarized by run-in period, treatment period and follow-up period.

All change from baseline analysis will be conducted by estimating the mean change from baseline. 95% confidence intervals will also be provided.

Repeated measures analyses will be sued for analyzing time course data for the efficacy parameters if deemed necessary. In this estimates of mean change from baseline for each time point will be provided along with its 95% confidence interval.

No statistical testing will be performed for incidences of AEs.

Subject Populations/Datasets to be evaluated

All subjects randomized into the study will be considered for evaluating the AEs. Subjects who receive at least one dose of the study medication will be considered for the analyses of all efficacy endpoints. Last observation carried forward will be used for all efficacy parameters in case of early withdrawals.

Efficacy analyses will be further carried on with per protocol population which includes all subjects who got at least one dose of the study medication and excludes everyone who is a protocol violator.

Safety Analysis

No statistical analyses of safety parameters will be performed. Statistical summaries, listings and figures will be provided for these parameters.

Administrative Matters

To comply with Good Clinical Practice, important administrative obligations relating to Investigator responsibilities, monitoring, archiving data, confidentiality, and publications must be fulfilled as given in Appendix B.

Chapter 6: Research Results in India

This chapter presents quantitative results and conclusions, as well as discussions concerning my research trips to northwest, southwest, and south central India, where I conducted medicinal plant research in three types of institutions—governmental, private, and non-governmental organizations (NGOs)—from 2001-2004 (Figure 13). The first two sections focus on data collected in Gujarat and Kerala that culminated in the the development and implementationof a protocol that was used in the pilot clinical studies in Bangalore, India and Shanghai, China (See protocol details in Chapter 5).

In the first section, I describe my experience as a student of Ayurveda at Gujarat Ayurved University (GAU) in Jamnagar, Gujarat, where I enrolled in a 4-month intensive course that focused on the eight branches of Ayurveda. While formally studying Ayurveda, I also carried out a small study to document the formulations used to treat NIDDM by two Ayurvedic practitioners. A brief discussion of this study is included in this section.

The second section presents a brief history of Arya Vaidya Sala (AVS) and describes its significance as an institution located in the southwestern Indian state of Kerala. At AVS, I experienced a specific type of Ayurvedic *Pancha Karma* Therapy (a particular Kerala Ayurvedic treatment therapy) based on my health status at the time. This participant-experience research period allowed me better to understand the practical applications rather than only the theoretical aspects of Ayurveda as I studied it at GAU.

The third section presents the data and results of a 7-week open label study of Ayurvedic management therapy for NIDDM, which was carried out in collaboration with The Foundation for Revitalization of Local Health Traditions (FRLHT) and St. Johns Medical College and Hospital (SJMCH), both based in Bangalore, Karnataka, India. This chapter ends with discussions of the data, the significance of the study results, and the study design.

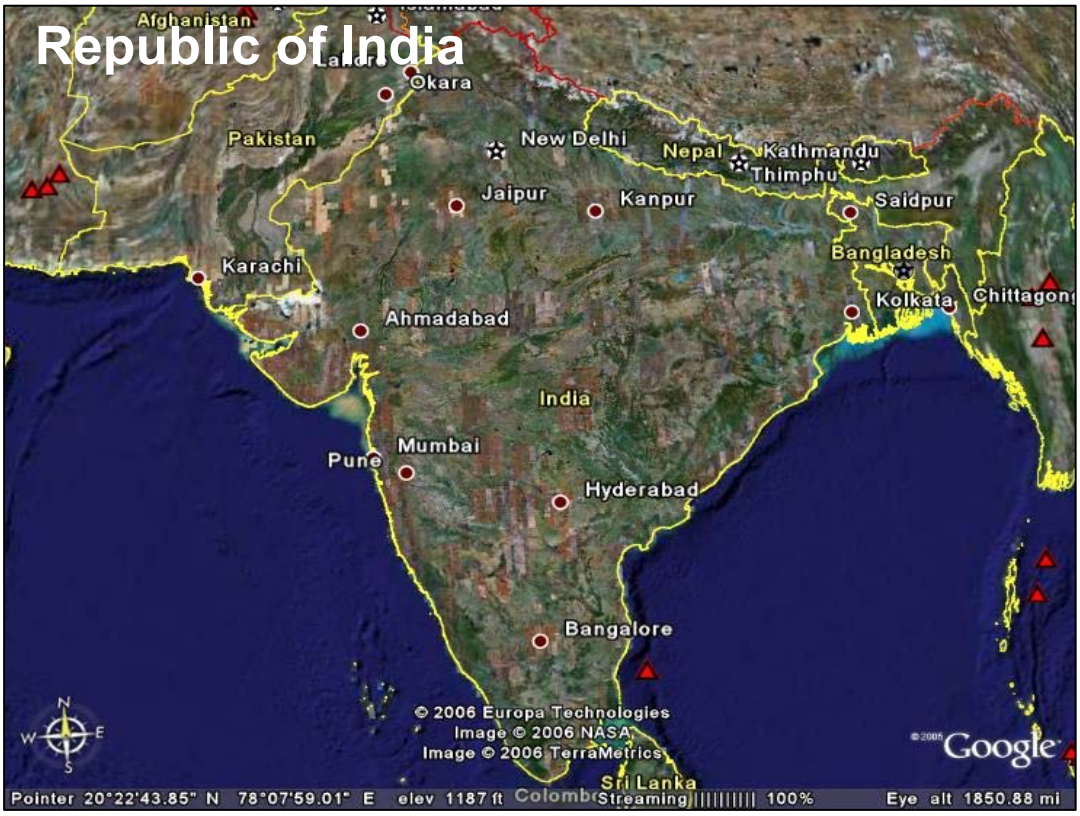


Figure 13: Map of Republic of India

Gujarat Ayurved University (Jamnagar, Gujarat—Northwest India)

Gujarat Ayurved University (GAU) is one of seven government-funded educational facilities in India that focuses solely on Ayurvedic education (with B.A., M. A., and Ph.D. programs), and it functions as a public teaching hospital. The purpose of this research period was to

learn as much as possible about the basics of Ayurveda in a university setting and thus to become better informed about the contemporary theory and practice of Ayurveda.

I chose to engage in a type of research described by Hsu (an anthropologist) as 'participant experience.' [423] By engaging in participant-experience, I was not only a researcher but also a student, follower, and a sort of disciple of my teachers at GAU. Now, the Ayurvedic doctors with whom I interacted were in a position of teacher, mentor or master. Like Hsu, I wanted to "modify the unequal relationship which prevails between informant and anthropologist." Hsu emphasized, as did I, that learning "the specifics of a practice in a foreign culture may help to encourage understanding of it in [one's] own culture."[424] The advantages to this type of approach is that the participant is immersed in the program and not a mere observer of the process. By participating in the experience, a different kind of knowledge (knowledge about social class, academic hierarchy, teaching styles, appropriate questioning techniques) is acquired that provides other insights into the research experience. For example, I noticed that one professor could describe the massage techniques quite well theoretically but was not a very good practitioner when it came to demonstrating the procedure. Would I have learned this if I just read about Ayurvedic theory or practice? The disadvantage of the participant experience apporach is that it requires a longer time commitment; and there is always the possibility, that the researcher must factor in, of being treated differently despite making efforts to level the playing field as much as possible.

The research period provided me not only with the tools to begin to undestand Ayurvedic concepts, but also provided me with the equally important social experience of interacting in

a Gujarati environment and context. Furthermore, this research period facilitated and informed the later development and implementation of a small clinical study conducted at FRLHT in Bangalore. In addition to fulfilling the course work at GAU, I researched classical texts on prameha under the guidance of classically trained Ayurvedic practitioners, researchers, and professors. After the first two months of study, along with two Ayurvedic practitioners (Drs. H.M. Chandola and D. Bhatt), I documented the plants and plant formulations they used to treat NIDDM in a clinical setting adjacent to the GAU hospital grounds. The first task of this section is to present the basic classical literature on prameha. A discussion of the results of the small study conducted to determine what plants and plant formulations were used to treat a small prospective and retrospective sample population in Jamnagar, Gujarat follows the summary of the literature.

Prospective and Retrospective Sample Studies, Jamnagar, Gujarat

Objective

The purposes of this research period were formally to study Ayurveda, to research Ayurvedic treatments for diabetes, and to document the general Ayurvedic treatment practices and plants prescribed in a small clinic in Jamnagar, Gujarat. To this end, I and two Ayurvedic practitioners, Drs. H.M. Chandola and D. Bhatt, conducted prospective and retrospective research of NIDDM case studies at Gujarat Ayurved University and Shri Gulabkunverba Ayurvedic Society (SGAS) from January-February 2002 in Jamnagar, Gujarat, India.

Methodology

Patients with established NIDDM, determined by outside laboratory post-prandial and fasting or random blood glucose tests, were interviewed upon arrival for their scheduled or non-

scheduled appointments at the SGAS clinic (December 2001- January 2002). Thirteen prospective case studies were documented, and ten retrospective case studies were analyzed. In addition to general medical data on patients, clinical data on prescribed Ayurvedic treatment protocols, allopathic medicines, blood glucose levels, 24-hour food-recall, and length of treatment were also collected when available. Ayurvedic medicines prescribed were acquired by the patient after the consultation at the SGAS clinic from the clinic dispensary. No plant voucher specimens were collected from the dispensary. Interviews with Drs. H.M. Chandola and D. Bhatt to determine what Ayurvedic plant and plant formulations were specifically prescribed to treat NIDDM were conducted after the patient visit or, in the case of retrospective patients, reviewed while assessing the patient folder.

Results

Of the 13 prospective and 10 retrospective case studies combined, the total sample size included 11 males and 12 females (n = 23). The average patient age was 53.8 years (35-64 age range) and the average weight was 65.7 kg (43.5-86 kg weight range; three data points were not available).

The treatments prescribed by the two Ayurvedic practitioners consisted predominantly of individual or medicinal plants formulations. The practitioners also provided basic dietary guidance. Of the 23 case studies, six formulations were determined to have been used in treating DM2. Based on the total 23 case studies, a detailed list of all Ayurvedic medicines prescribed to treat all conditions was compiled. On the basis of the aforementioned list, Drs. H.M. Chandola and D. Bhatt identified six plant formulations prescribed that they determined were particularly efficacious in treating DM2. Of the six formulations described

by the Ayurvedic physicians, three are classical Ayurvedic formulations, and three are classically inspired single plants or formulations. The classical formulations are *Chandraprabha guggulu vati* (CPGV), *Dhatri haridra* (DH), and *Tejapatra pushkarmula* (TP). During my interviews with Drs. H.M. Chandola and D. Bhatt about plant formulations, both concluded the CPGV was most often prescribed because of documentation in Ayurvedic texts and its efficacy with their own patients in the clinic. The three other formulations were developed using local plants and/or by applying classical Ayurvedic reasoning to develop three additional formulations. These three additional formulations are not discussed in the present dissertation. (For a visual representation of a classical preparation of a diabetes pill, see Figures 14-20. These photographs were taken during Rasashastra (science of Ayurvedic preparations) class in January 2002.)

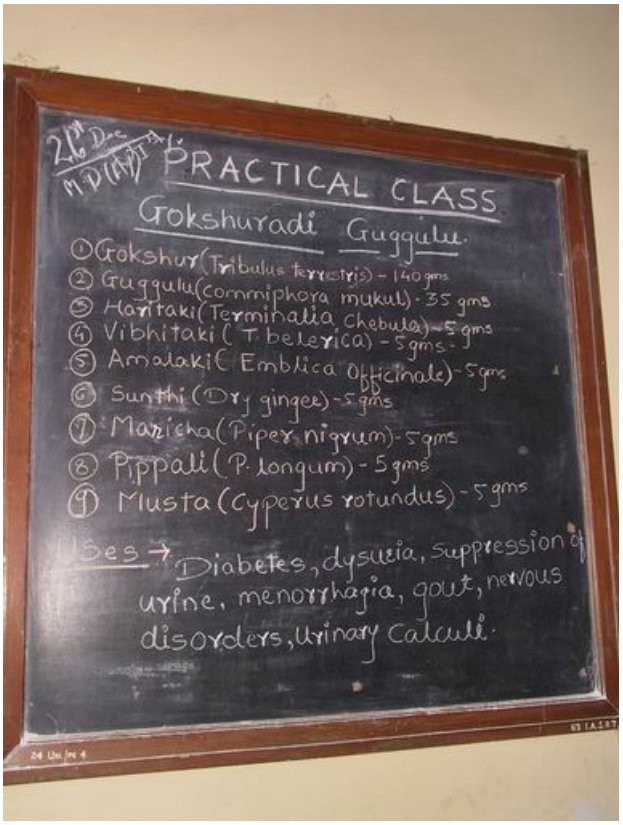


Figure 14. ***Gokshuradi Guggulu Vati*** **Preparation—Classical Formulation**

Figure 15. ***Gokshuradi Guggulu Vati*** **Preparation—Powdered plants**

Figure 16. *Gokshuradi Guggulu Vati* Preparation—Simmering plant powders in a water decoction

Figure 17. *Gokshuradi Guggulu Vati* Preparation—Mixing plants in water decoction

Figure 18. *Gokshuradi Guggulu Vati* Preparation—Reducing the water content

In the course of a patient's treatment (prospective and retrospective), classical Ayurvedic formulations were prescribed in the following order: CPGV 16/23 (70%), TP 11/23 (48%), and DH 6/23 (26.1%). In the small retrospective study of 10 patients, CPGV was prescribed

Figure 19. *Gokshuradi Guggulu Vati* Preparation—Forming pills by hand

Figure 20. *Gokshuradi Guggulu Vati* Preparation—Pills ready to dry

9/10 (90%). In both the retrospective and prospective studies on average, each patient was prescribed 10 Ayurvedic plants or plant formulations over the course of the treatment. Ayurvedic classical texts provide extensive herbal-mineral formulations, detailed regimens, and diet modification protocols to treat all types of *prameha*, including *madhumeha*. One of these formulations, Chandraprabha guggulu vati (CPGV), included up to 29 different plants depending on the classical text referenced.[425] [426] [427] The therapeutic effect of mineral compounds (*bhasmas*) included in the CPGV formula and bitumen (*shilajatu*) will not be evaluated here. CPGV was found to be the most prescribed classical formula in the small prospective and retrospective studies conducted at GAU.

Based on a review of the medical literature, a large number of the plants (93%) used in CPGV show some type of effect. Eleven categories were created to represent the effects (n = 516) of CPGV based on *in vitro*, *in vivo*, and human studies (excluding the minerals and

shilajatu from the literature review). In addition, a review of the individual plants in this classical formulation revealed multiple effects for many conditions: cardiovascular (20%), *Diabetes mellitus* (10.7%), antioxidant (9%), immunomodulating (7.6%), and anti-inflammatory and analgesic (4.5%). (Tables 14 and 15, Figure 21).

Table 14. *Chandraprabha guggulu vati*, excluding *shilajatu* and minerals [428] [429]

Aconitum heterophyllum Wall.	Ativisha
Acorus calamus Linn.	Vaca
Baliospermum montanum Muell.Arg.	Danti
Bambusa arundinacea Willd.	Vansalochana
Berberis aristata DC	Daru haridra
Cedrus deodara (Roxb. Ex Lambert) G.Don	Devadaru
Cicer arietinum L.	Chanaka
Cinnamomum camphora (L.) T.Nees & C.H.Eberm.	Karpura
Cinnamomum tamala T.Nees & Eberm.	Tamalapatra/Tejapatra
Cinnamomum zeylanicum Nees	Tvak
Commiphora mukul (Stocks) Engl.	Guggulu
Coriandrum sativum L.	Dhanyak
Curcuma longa L.	Haridra
Cyperus rotundus L.	Musta
Elettaria cardamomum (L.) Maton	Ela
Embelia ribes Burm.f.	Vidanga
Emblica officinalis Gaertn.	Amlaki
Hemidesmus indicus R.Br.	Sariva
Ipomoea turpethum (L.) R.Br.	Trivrit
Piper chaba Hunter	Cavya
Piper longum L.	Pippali/Pippali mula
Piper nigrum L.	Marichi/Marichi mula
Plumbago zeylanica L.	Citrak
Scindapsus officinalis Schott	Gaja pippali
Swertia chirata Buch.-Ham. Ex Wall	Kiratatikta/Bhunimba
Terminalia bellirica Roxb.	Bibhitaka
Terminalia chebula Retz.	Haritaki
Tinospora cordifolia Miers	Guduci
Zingiber officinale Roscoe	Sunthi

Table 15. *Chandraprabha Guggulu Vati* (CPGV); A select literature review of plants with human studies)

Latin/ Sanskrit	Study Type	Effect	References
***Cicer arietinum* L. Chanaka**	Human volunteers	Glycemic response	Panlasigui, L.N., Panlilio, L.M., Madrid, J.C. 1995. Glycaemic response in normal subjects to five different legumes commonly used in the Philippines. International Journal Food Science Nutrition 46 (2), 155-60.
C. arietinum	Healthy human subjects	Postprandial plasma glucose	Dilawari, J.B., Kamath, P.S., Batta, R.P., Mukewar, S., Raghavan, S. 1981. Reduction of postprandial plasma glucose by Bengal gram dal (*Cicer arietinum*) and rajmah (*Phaseolus vulgaris*). American Journal Clinical Nutrition 34 (11), 2450-53.
***Cinnamomum camphora* (L.) T.Nees & C.H.Eberm. Karpura**	Multicenter Human Clinical Trial	Anti-infective, Anti-inflamatory, Degenerative ophthalmic disorders improved	Biswas, N.R., Gupta, S.K., Das, G.K., Kumar, N., Mongre, P.K., Halder, D., Beri, S. 2001. Evaluation of Opthacare eye drops—a herbal formulation in the management of various ophthalmic disorders. Phytotherapy Research 15 (7), 618-20.
***Cinnamomum tamal* Tejapatra**	Human Clinical Trial	Hypoglycemic	Chandola, H.M., Tripathi, S.N., and Udupa, K.N. 1980. Hypoglycemic response of *C. tamala* in patients of maturity onset (insulin independent) Diabetes. Journal of Research in Ayurveda and Siddha 1 (2), 275-90.
***Commiphora mukul* (Stocks) Engl. Guggulu**	Human Case Study	Osteoarthritis	Singh, B.B., Mishra, L., Aquilina, N., Kohlbeck, F. 2001. Usefulness of guggul (Commiphora mukul) for osteoarthritis of the knee: An experimental case study. Altern Ther Health Med 7 (2), 120, 112-14.
C. mukul	Randomized Clinical Trial	Hypolipidemic, Cholesterol decrease, Lipid peroxide decrease (antioxidant)	Singh, R.B., Niaz, M.A., Ghosh, S. 1994. Hypolipidemic and antioxidant effects of *Commiphora mukul* as an adjunct to dietary therapy in patients with hypercholesterolemia. Cardiovascular Drugs Therapy 8 (4), 659-64.
C. mukul	Randomized Controlled Clinical Trial	Hyperlipidemia decrease	Verma, S.K., Bordia, A. 1988. Effect of *Commiphora mukul* (gum guggulu) in patients of hyperlipidemia with special reference to HDL-cholesterol. Indian Journal Medical Research 87, 356-60.
C. mukul	Humans	Antiobesity, Hypercholesterolemia, Hyperlipidemic decreases	Kuppurajan, K., Rajagopalan, S.S., Rao, T.K., Sitaraman, R. 1978. Effect of guggulu (*Commiphora mukul*--Engl.) on serum lipids in obese, hypercholesterolemic and hyperlipemic cases. Journal Association Physicians India 26 (5), 367-73.
***Curcuma longa* L. Haridra**	In vitro Human Pilot Study	LPS-induced COX-2 protein levels, PGE(2) production reduced	Plummer, S.M., Hill, K.A., Festing, M.F., Steward, W.P., Gescher, A.J., Sharma, R.A. 2001. Clinical development of leukocyte cyclooxygenase 2 activity as a systemic biomarker for cancer chemopreventive agents. Cancer Epidemiol Biomarkers Prev 10 (12), 1295-99.

C. longa	Multicenter Human Clinical Trial	Anti-infective, Anti-inflamatory Degenerative ophthalmic disorders	Biswas, N.R., Gupta, S.K., Das, G.K., Kumar, N., Mongre, P.K., Haldar, D., Beri, S. 2001. Evaluation of Ophthacare eye drops--a herbal formulation in the management of various ophthalmic disorders. Phytother Research 15 (7), 618-20.
C. longa	Healthy human subjects	ApoB/apoA ratio decrease Coantioxidant	Ramirez-Bosca, A., Soler, A., Carrion, M.A., Diaz-Alperi, J., Bernd, A., Quintanilla, C., Quintanilla Almagro, E., Miquel, J. 2000. An hydroalcoholic extract of curcuma longa lowers the apo B/apo A ratio. Implications for atherogenesis prevention. Mech Ageing Dev 119 (1-2), 41-7.
***Emblica officinalis* Gaertn. Amlaki**	Multicenter Human Clinical Trial	Anti-infective, Anti-inflamatory, Degenerative ophthalmic disorders improved	Biswas, N.R., Gupta, S.K., Das, G.K., Kumar, N., Mongre, P.K., Haldar, D., Beri, S. 2001. Evaluation of Ophthacare eye drops--a herbal formulation in the management of various ophthalmic disorders. Phytother Research 15 (7), 618-20.
E. officinalis	Randomized Controlled Trial	Postprandial glycemia decrease Blood cholesterol decrease	Manjunatha, S., Jaryal, A.K., Bijlani, R.L., Sachdeva, U., Gupta, S.K. 2001. Effect of Chyawanprash and vitamin C on glucose tolerance and lipoprotein profile. Indian J Physiol Pharmacology 45[1 #0], 71-9.
E. officinalis	Clinical Trial	Hypoglycemic	Pandey, V.N., Rajagopalan, S.S., Chowdhary, D.P. 1995. An effective Ayurvedic hypoglycemic formulation. Journal of Research in Ayurveda and Siddha XVI, 1-2, 1-14.
E. officinalis	Human Trial	Serum cholesterol decrease	Jacob, A., Pandey, M., Kapoor, S., Saroja, R. 1988. Effect of the Indian gooseberry (amla) on serum cholesterol levels in men aged 35-55 years. European Journal Clinical Nutrition 42 (11), 939-44.
E. officinalis	**Clinical Trial**	**Antidiabetic**	Sivaprakasam, K., Rao, K.K., Yasodha, R., Veluchamy. 1982. Siddha remedy for Diabetes mellitus. Journal of Research in Ayurveda and Siddha. V, 1-4, 25-32.
***Piper nigrum* L. Marichi**	**Clinical Trial**	**Antidiabetic**	Kumar, N., Kumar, A. 1995. A clinical trial of M-93 compound in the management of Madhumeha (*Diabetes mellitus*). Journal of Research in Ayurveda and Siddha XVI, 3-4, 102-07.
***Terminalia belerica* Roxb. Bibhitaki**	Clinical Trial	**Hypoglycemic**	Pandey, V.N., Rajagopalan, S.S., Chowdhary, D.P. 1995. An effective Ayurvedic hypoglycemic formulation. Journal of Research in Ayurveda and Siddha XVI, 1-2, 1-14.
T. belerica	**Clinical Trial**	**Antidiabetic**	Sivaprakasam, K., Rao, K.K., Yasodha, R., Veluchamy. 1982. Siddha remedy for *Diabetes mellitus*. Journal of Research in Ayurveda and Siddha. V, 1-4, 25-32.
***Terminalia chebula* Retz. Haritaki**	**Clinical Trial**	**Hypoglycemic**	Pandey, V.N., Rajagopalan, S.S., Chowdhary, D.P. 1995. An effective Ayurvedic hypoglycemic formulation. Journal of

			Research in Ayurveda and Siddha XVI, 1-2, 1-14.
T. chebula	**Clinical Trial**	**Antidiabetic**	Sivaprakasam, K., Rao, K.K., Yasodha, R., Veluchamy. 1982. Siddha remedy for Diabetes mellitus. Journal of Research in Ayurveda and Siddha. V, 1-4, 25-32.
***Tinospora cordifolia* Miers Guduci**	Human Clinical Trial	Immunomodulator	Bapat, R.D., Rege, N.N., Koti, R.S., Desai, N.K., Dahanukar, S.A. 1995. Can we do away with PTBD? HPB Surgery 9 [1 #0], 5-11.
T. cordifolia	Randomized Controlled Trial	Host defenses strengthened Immunomodulator	Rege, N., Bapat, R.D., Koti, R., Desai, N.K., Dahanukar, S. 1993. Immunotherapy with Tinospora cordifolia: a new lead in the management of obstructive jaundice. Indian J Gastroenterology 12 [1 #0], 5-8.
***Zingiber officinale* Roscoe Sunthi**	Multicenter Randomized Controlled Trial	Osteoarthritis	Altman, R.D., Marcussen, K.C. 2001. Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum 44(11):2531-38. Comment in: Arthritis Rheum. 2001 44(11):2461-62.

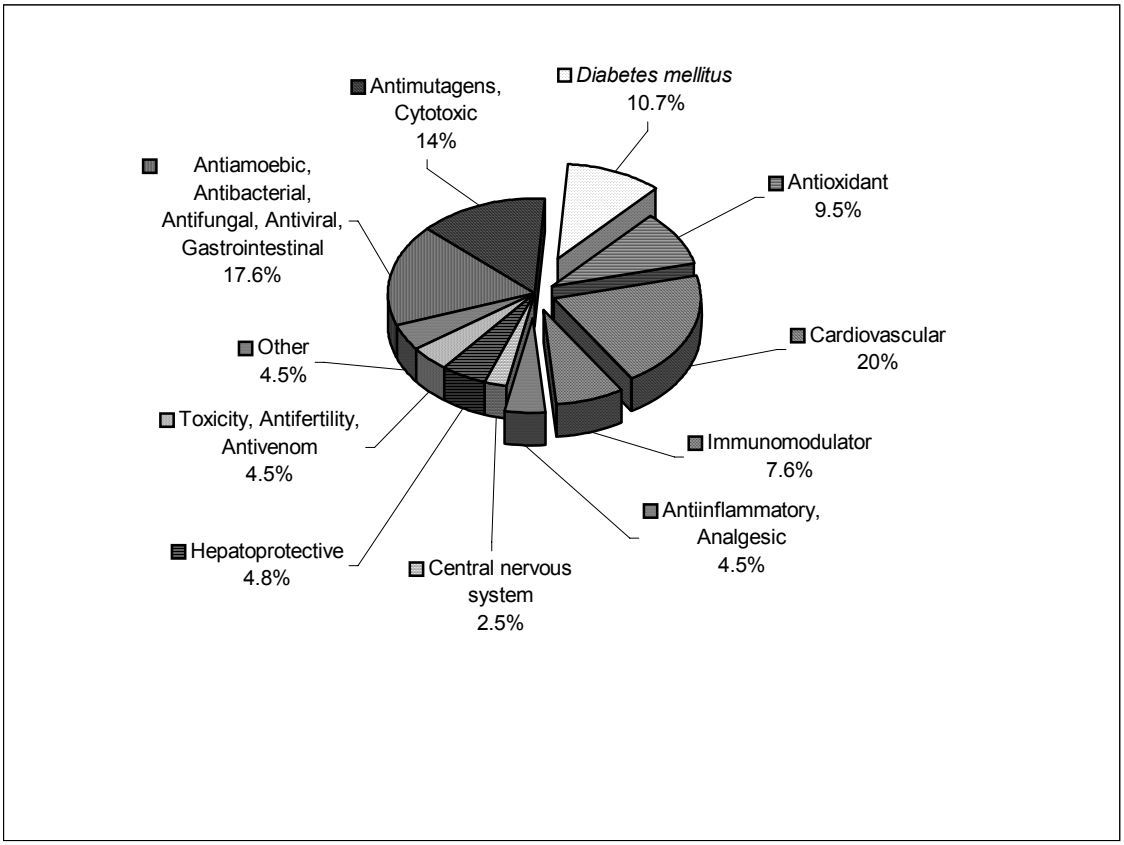


Figure 21. *Chandraprabha guggulu vati*: Summary of plant effects (n=516) based on *in vitro*, *in vivo*, and human studies.

Based on Figure 21, the list was then condensed to include only the plants used in human studies (Table 15). Based on the literature review, 11/29 CPGV plants have human studies alone (*Cicer arietinum, Cinnamomum camphora, C. tamala, Commiphora mukul, Curcuma longa, Emblica officinalis, Piper nigrum, Terminalia bellirica, T. chebula, Tinospora cordifolia, and Zingiber officinale*). On the basis of these human studies, CPGV appears to affect not only glucose levels, but also cholesterol, lipid, and triglyceride levels; CPGV also acts as an antiinflammatory, antioxidant, and immunomodulator. Comparing the review of the medical literature of common Ayurvedic plants by Khan and Balick to Table 14, *Swertia*

chirata (Wall) C.B. Clarke is the only common plant used by two Ayurvedic practitioners in Gujarat.

Conclusions

In the retrospective and prospective studies combined, Drs. H.M Chandola and D. Bhatt prescribed CPGV the most often to treat madhumeha in this small sample. Both physicians prescribed CPGV because of its use according to classical Ayurvedic texts and according to a positive response in their clinic. Based on classical Ayurvedic texts, the formulation for CPGV was provided. However, whether or not these exact plants were used could be verified only if voucher specimen samples were collected at the clinic dispensary. This posed an especially difficult challenge in relation to the three *Cinnamomum* species. For example, how were we to be sure which species were used in the CPGV formulation? The choice of plant may have had to do as much with individual efficacy, market availability, and/or season. This was an important weakness of the study design. In the future, Good Botanical Practices as described by Balick should be implemented to ensure proper identification of plant species.[430]

Despite this weakness, a review of the literature revealed CPGV to be an herbal-mineral formulation with multiple phytochemical effects. As DM2 progresses, more complications arise. Both the World Health Organization (WHO) [431] and the National Cholesterol Education Program[432] have proposed definitions for metabolic syndrome. Based on these definitions, metabolic syndrome[MS #0] has evolved to include the following: disturbed glucose and insulin metabolism, overweight and abdominal fat distribution, mild

dyslipidemia, hypertension, and the subsequent development of DM2 and cardiovascular disease.[433] In fact individuals with diabetes have increased rates of cardiovascular disease (CVD).[434] Furthermore, CVD imposes a heavy burden of both morbidity and mortality on DM2 patients.[435]

CPGV has been used in Ayurveda at least since classical times to treat what conventional medicine describes as Types 1 and 2 *Diabetes mellitus*. Ayurveda represents an ancient scientific paradigm for treating health and disease. Codified formulations from the Ayurvedic repertoire are a culmination of centuries of fine-tuning by practitioners. CPGV is one such formulation. As Ayurveda becomes more popular, research scientists may gain insight into the complexity and richness of Ayurveda as a healing art. In addition, Ayurvedic classical formulations such as CPGV should be evaluated as whole compounds with potential multiple therapeutic effects.

Arya Vaidya Sala (Kottakkal, Kerala)

History and Uniqueness of Ayurveda in Kerala

In 1902, P. S. Varier opened the Arya Vaidya Sala (AVS) a private institution located in Kottakkal, Kerala in southwest India. Along with other indigenous revitalization programs occurring throughout parts of South Asia, P. S. Varier contributed dramatically to the modernization of traditional Ayurvedic preparations with the vision of preserving and marketing them on a large scale in the southwestern region of the subcontinent. In effect, P. S. Varier implemented the standardization of Ayurvedic medicine and medical treatment.[436] In 1907 he published the *Cikitsa Samgraham*,[437] a summary of Vagbhata's work describing indications, dosage, price, etc. This publication facilitated the popularization of Ayurveda and provided patients with clear cut guidelines as to how to use basic Ayurvedic medicines at home. In 1917, The Arya Vaidya Patasala, a center of Ayurvedic study, was inaugurated adjacent to the AVS branch in Calicut. This institution acted as an effective instrument to further modernize the transmission of Ayurvedic traditional knowledge to anyone who wanted to study, and not just to the select caste elites within the tradition[438] (See Figures 22 and 23).

Figure 22. Arya Vaidya Sala entrance to temple.

Figure 23. Arya Vaidya Sala inside the temple where the founder, P. S. Varier, is venerated.

The Purpose of *Pancha Karma* Therapy

According to R.H. Singh (my Pancha Karma professor at GAU), an authority on *Pancha Karma* therapy (five actions or treatments), *Pancha Karma* is an integral and important therapy derived from Ayurvedic theories of physiology and pathogenesis.[439] The goal of *Pancha Karma* therapy is to eliminate vitiated doshas (to reduce their value or impair their quality) in order to achieve equilibrium.[440] According to Charaka, Singh summarized that *Pancha Karma* includes five practices: emesis (*vamana*), purgation (*virecana*), oily enema (*anuvasana*), non-oily enema (*niruha*), and head evacuation (*nasya* or *sirovirecana*—via nasal passages). Some other Ayurvedic texts consider the two enemas under one category and add blood-letting (*rakta mokshana*) as a fifth category. [441] [442]

Pancha Karma treatment is broadly categorized into two areas: evacuation or elimination (*shodhana*), and pacification (*shamana*). It is generally believed that in the case of cure through elimination treatment, a disease will not reoccur, whereas if pacification treatment cures a disease, the disease may reoccur.[443] Singh emphasized that most *Pancha Karma* therapy today is based on pacification therapies because these are considered conservative, and their practitioners utilize various drug therapies, with the exception of practitioners in Kerala.[444] AVS is particularly known for the Ayurvedic medicated oil massages that are now an integral part of most Ayurvedic *Pancha karma* therapies worldwide. In the next section, I describe in detail my own experience with *Pancha Karma* therapy while admitted to Arya Vaidya Sala in Kerala.

Immersion Ethnobotany

In order better to understand the practical applications as opposed to the theoretic foundations of Ayurvedic therapy, I admitted myself to the AVS for a treatment period of three weeks. According to Balick, this immersion ethnobotany experience is a relatively new approach in the broad field of ethnobotany. By reducing the distance between the subject and the observer, I was able to submit myself to a traditional healing system in order directly to experience the profound or not so profound effects of a system that I could later describe in detail.[445] Upon admittance to AVS for treatment, I fully disclosed my intentions to learn as much about AVS' Ayurvedic treatment from an experential perspective. The staff accepted my wish to learn from this non-academic perspective. In fact, the Ayurvedic practitioners appreciated my desire to learn as much about Ayurveda as possible from as many different persepctives as possible: recipient of care as opposed to caregiver or researcher, for example. Ethical problems, however, may arise with this immersion ethnobotany approach if the researcher does not fully discose her intentions or pretends to have an illness that does not exist. The moral responsibility lies with the researcher. As noted earlier, when Hsu participated in Chinese medicine field research in Kunming, China, she went one step further and chose to engage in 'participant experience' by learning specific technical knowledge and practice.[446] My previous participant experience at GAU further helped me understand the procedures I underwent while admitted at AVS.

My Immersion Ethnobotany Experience and Treatment Protocol

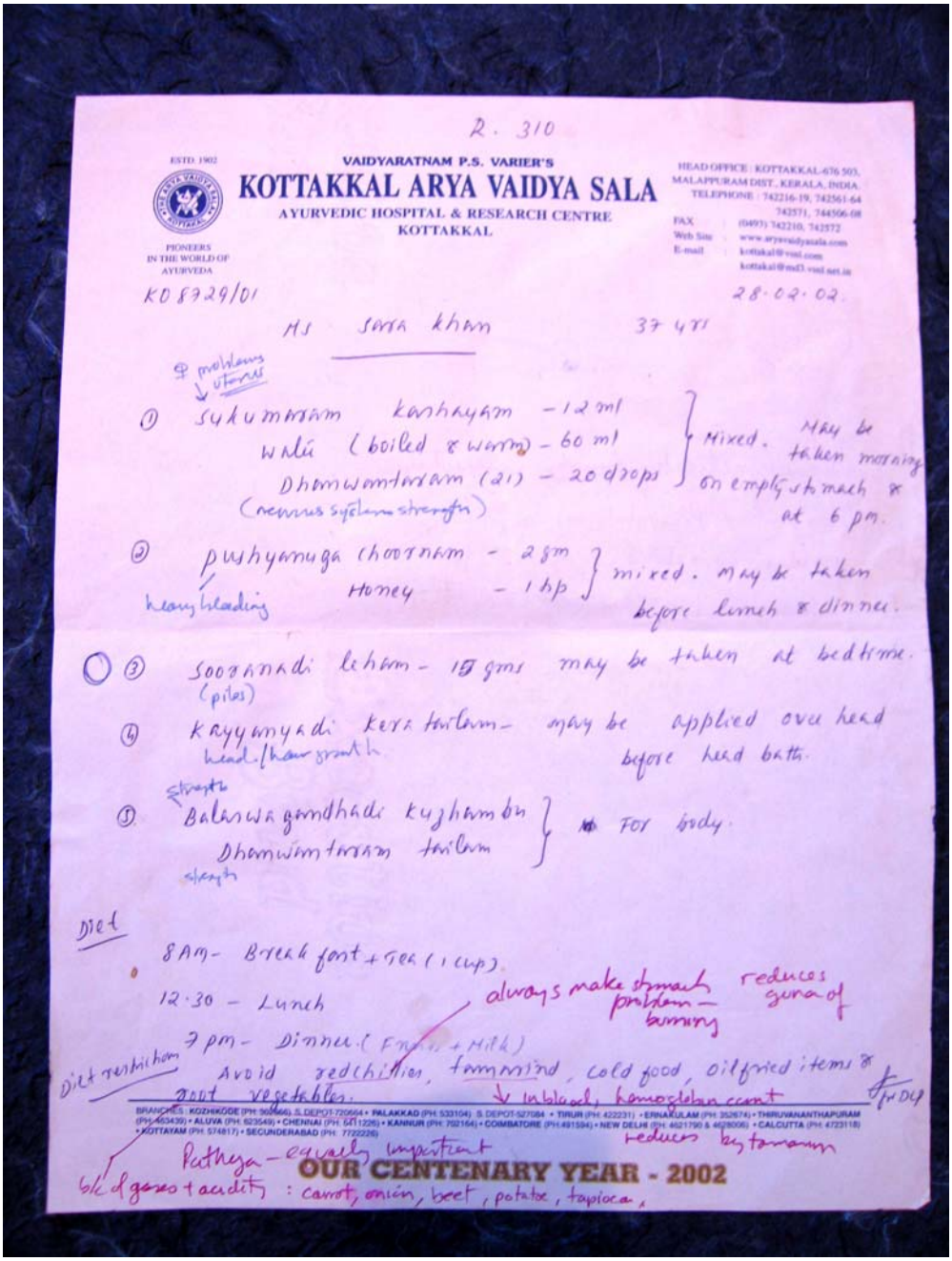
Located in the south west of India, Kerala (a subtropical climate), Arya Vaidya Sala, situated in a quiet part of the Mallapuram district, provided the perfect opportunity to

escape the demands of daily life and focus on the healing process. I had the chance to focus on my health for three weeks—a luxury that few people are allowed anywhere in the world. I was hesitant to take a break for so long, as it seemed indulgent, but I was relieved that I could focus on my body and state of health without having to take care of daily obligations such as cooking, cleaning, and traveling at the same time I partook in experiential Ayurvedic studies. The mere fact that I was supposed and encouraged to pay attention to my health for the entire time period improved my state of mind.

I had a room with cool cement floors, two single beds neatly made with white cotton sheets and draped with mosquito nettings, a bathroom with a sink and shower, a desk, and a small porch where I sat every morning and read from about 5:30 am until 8 am. Kerala, unlike other states in India, distributed land more equitably after 1947, the partition and independence, so that many residents own the land on which their houses sit. This has also deterred overbuilding, so the landscape and view from AVS and my porch were rich with waving coconut trees, small farms interspersed with water ways for irrigation, and simple dirt roads. The room was cleaned regularly (please note that AVS provided different tiers of service in terms of accommodations and amenities; for example, non-resident Indians were required to live in more expensive accommodations).

My 'immersion ethnobotany' [447] experience began with a consultation with the chief Ayurvedic doctor and two other Ayurvedic physicians. Once I was settled in my room, the doctors arrived and took a complete medical history (the physicians explained that they would follow-up every day or every other day to note progress, answer questions,

and/or change the course of treatment based on individual patient feedback). The examination included a standard allopathic assessment (with laboratory tests, if required) and an Ayurvedic assessment to determine dosha imbalance, dhatu imbalance, Prakriti, and course of treatment. My only complaints were some digestive problems from food poisoning experienced while traveling. At first the physicians were perplexed. Why did an apparently healthy individual want to undergo such a strict regimen? Based on their assessment, my medical complaints were minor. I explained that I wanted to experience, as closely as possible, AVS's treatment protocol so that I could be a better informed student, academic, and researcher of Ayurveda. Normally, if a patient presents more serious medical issues, the protocol required is a minimum of 28 days, which may or may not include Pancha Karma therapy depending on the individual case. In my case, the physicians decided to prescribe a standard course of treatment to deal with the digestive imbalance and to balance the doshas. This did not involve all the five Pancha Karma therapies. The three-week treatment period included an individualized protocol (see Figures 24-27 and Tables 16-18). The protocols noted in Figures 24 and 25 are not complete. I kept a journal of all products prescribed, and these details are listed in Tables 16-18. This protocol included herbal-mineral preparation, dietary advice, a series of medicated oil massages, and two types of enema. Any text in italics in Tables 16-18 is defined in Appendix D. AVS adheres to the protocols and prescriptions described in the *Chikitsa Samgraham* as translated by P. S. Varier. Appendix D provides a summary of those prescriptions and procedures used during the immersion ethnobotany experience. I noted that my individual experience adhered closely to the protocols described in the *Chikitsa Samgraham* for each procedure.



R. 310

ESTD. 1902

PIONEERS IN THE WORLD OF AYURVEDA

VAIDYARATNAM P.S. VARIER'S

KOTTAKKAL ARYA VAIDYA SALA

AYURVEDIC HOSPITAL & RESEARCH CENTRE
KOTTAKKAL

HEAD OFFICE : KOTTAKKAL-676 503, MALAPPURAM DIST., KERALA, INDIA.
TELEPHONE : 742216-19, 742561-64
742571, 744506-08
FAX : (0493) 742210, 742572
Web Site : www.aryavaidyasala.com
E-mail : kottakal@vsnl.com
kottakal@md3.vsnl.net.in

KO 8929/01

28.02.02.

MS Sara kham 37 yrs

problems utensil

① Sukumaram kashayam - 12 ml
Water (boiled & warm) - 60 ml
Dhanwantaram (21) - 20 drops
(nervous system strengthen)
} Mixed. May be taken morning on empty stomach & at 6 pm.

② Pushyanuga choornam - 2 gm
Honey - 1 tsp
heavy bleeding
} mixed. may be taken before lunch & dinner.

③ Soorannadi leham - 15 gms may be taken at bedtime.
(piles)

④ Kayyanyadi kera tailam - may be applied over head before head bath.
head / hair growth

⑤ Balaswagandhadi kuzhambu
Dhanwantaram tailam
} For body.
strength

Diet

8 AM - Breakfast + Tea (1 cup).

12.30 - Lunch

7 pm - Dinner (Fruits + Milk)

always make stomach problem — tamarind reduces guna of

Diet restriction

Avoid redchillies, tamarind, cold food, oil fried items & sour vegetables.

↓ in blood hemoglobin count

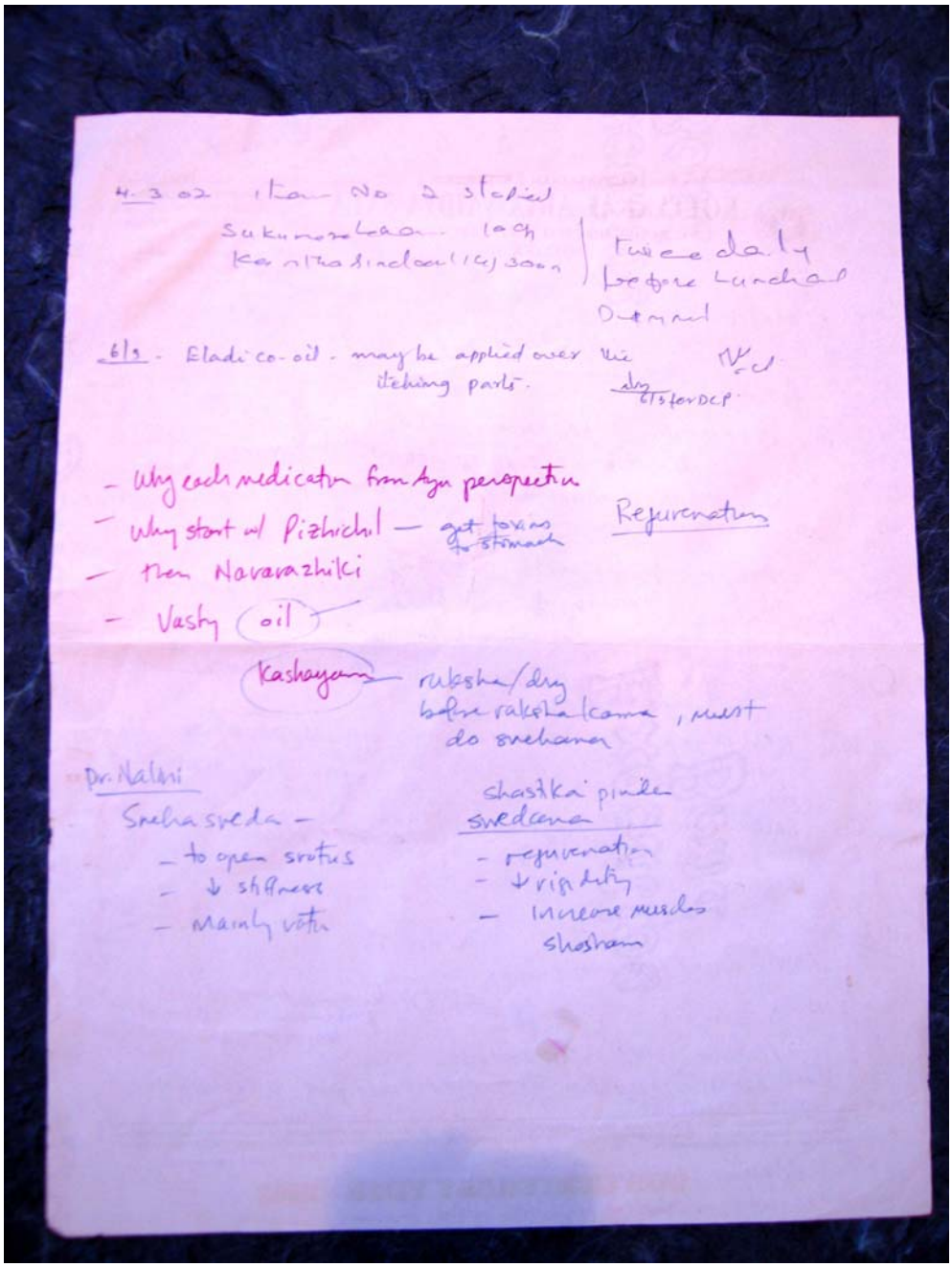
for DM

Pathya — equally important

reduces by tamarind

bl of gases + acidity : carrot, onion, beet, potato, tapioca,

Figure 24. AVS medical plant prescription, Page 1.



- Why each medication from Ayu perspective
- Why start w/ Pizhichil — get toxins to stomach — Rejuvenation
- then Navarazhilci
- Vasty (oil)

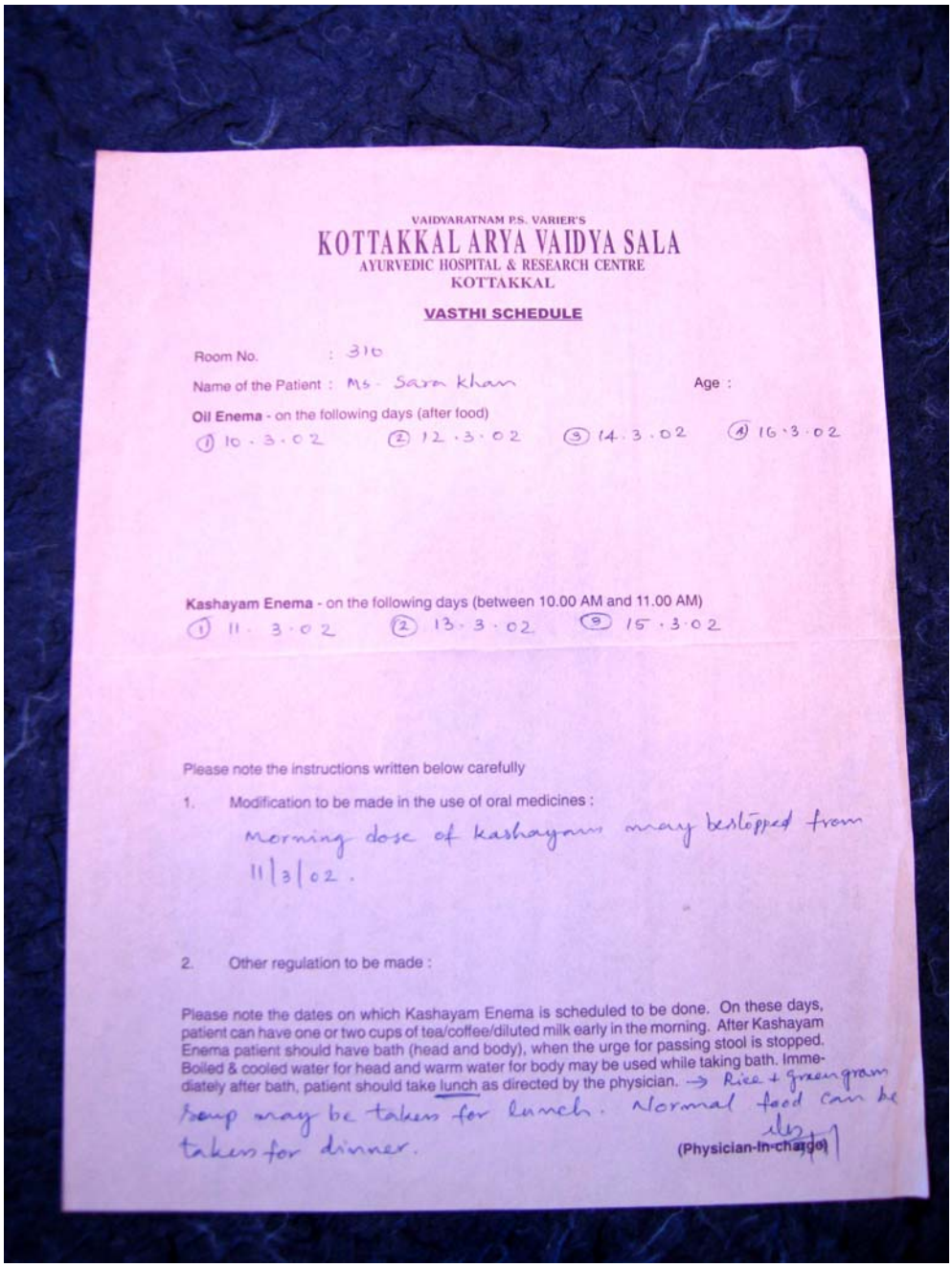
Kashayam — ruksha/dry
before rakshalcana, must
do snehana

Dr. Nalini

Sneha sveda —
- to open srotus
- ↓ stiffness
- Mainly vata

shastika pinda
sveda
- rejuvenation
- ↓ rigidity
- Increase muscles
shoshana

Figure 25. AVS medical plant prescription, Page 2.



VAIDYARATNAM P.S. VARIER'S
KOTTAKKAL ARYA VAIDYA SALA
AYURVEDIC HOSPITAL & RESEARCH CENTRE
KOTTAKKAL

VASTHI SCHEDULE

Room No. : 310

Name of the Patient : Ms. Sara Khan Age :

Oil Enema - on the following days (after food)

① 10.3.02 ② 12.3.02 ③ 14.3.02 ④ 16.3.02

Kashayam Enema - on the following days (between 10.00 AM and 11.00 AM)

① 11.3.02 ② 13.3.02 ③ 15.3.02

Please note the instructions written below carefully

1. Modification to be made in the use of oral medicines :
Morning dose of kashayam may be stopped from 11/3/02.

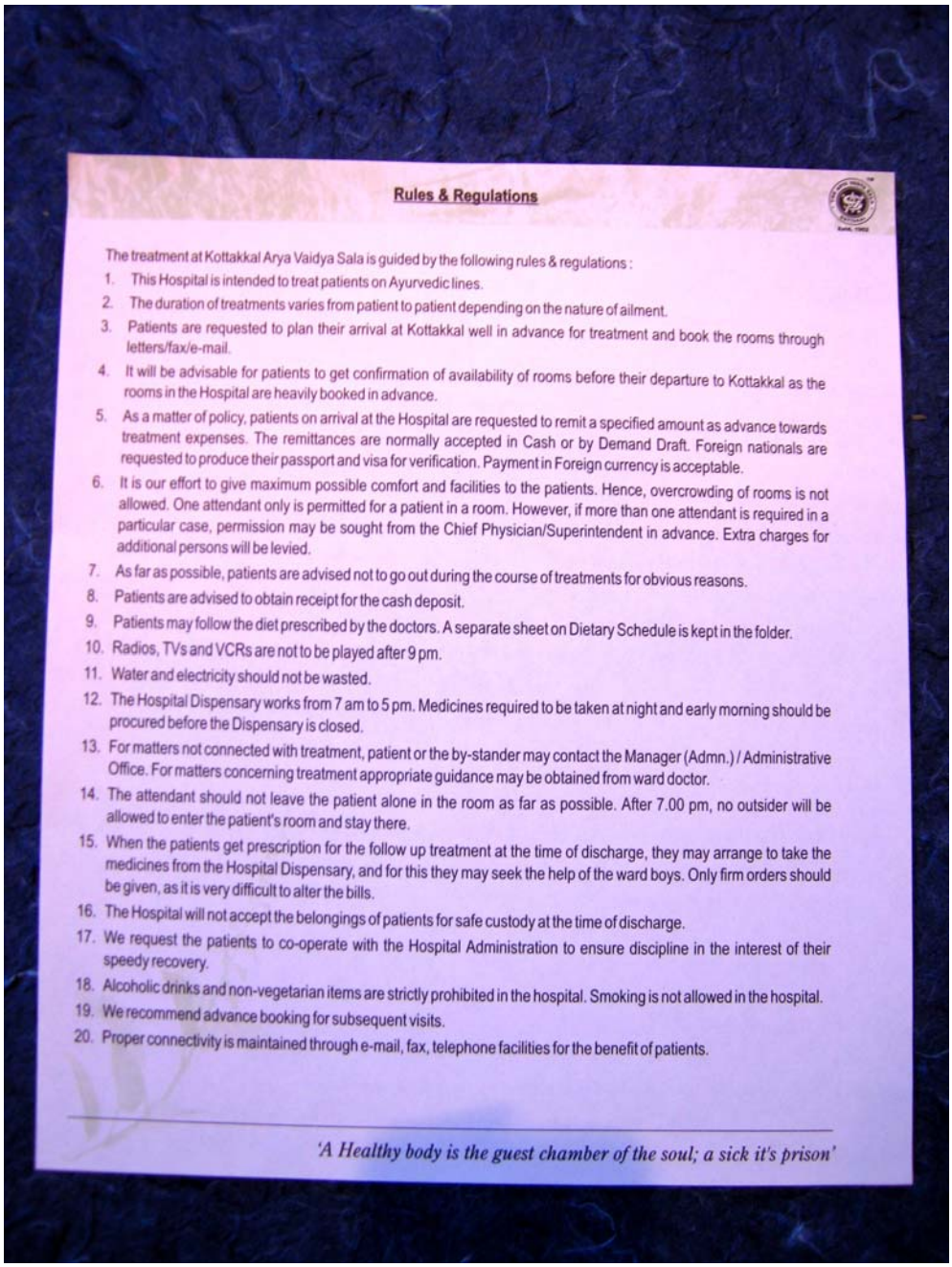
2. Other regulation to be made :

Please note the dates on which Kashayam Enema is scheduled to be done. On these days, patient can have one or two cups of tea/coffee/diluted milk early in the morning. After Kashayam Enema patient should have bath (head and body), when the urge for passing stool is stopped. Boiled & cooled water for head and warm water for body may be used while taking bath. Immediately after bath, patient should take lunch as directed by the physician. → Rice + green gram soup may be taken for lunch. Normal food can be taken for dinner.

(Physician-in-charge)

Figure 26. AVS *Vasthi* Schedule

Figure 27 presents some of the rules and regulations. For example, patients were requested to refrain from leaving AVS grounds during the course of treatment; radios, TVs, and VCRs were to be turned off after 9 pm (only a few higher priced rooms had TV and VCR, mine did not); after 7 pm, no patients were allowed to have outside guests



Rules & Regulations

The treatment at Kottakkal Arya Vaidya Sala is guided by the following rules & regulations :

1. This Hospital is intended to treat patients on Ayurvedic lines.
2. The duration of treatments varies from patient to patient depending on the nature of ailment.
3. Patients are requested to plan their arrival at Kottakkal well in advance for treatment and book the rooms through letters/fax/e-mail.
4. It will be advisable for patients to get confirmation of availability of rooms before their departure to Kottakkal as the rooms in the Hospital are heavily booked in advance.
5. As a matter of policy, patients on arrival at the Hospital are requested to remit a specified amount as advance towards treatment expenses. The remittances are normally accepted in Cash or by Demand Draft. Foreign nationals are requested to produce their passport and visa for verification. Payment in Foreign currency is acceptable.
6. It is our effort to give maximum possible comfort and facilities to the patients. Hence, overcrowding of rooms is not allowed. One attendant only is permitted for a patient in a room. However, if more than one attendant is required in a particular case, permission may be sought from the Chief Physician/Superintendent in advance. Extra charges for additional persons will be levied.
7. As far as possible, patients are advised not to go out during the course of treatments for obvious reasons.
8. Patients are advised to obtain receipt for the cash deposit.
9. Patients may follow the diet prescribed by the doctors. A separate sheet on Dietary Schedule is kept in the folder.
10. Radios, TVs and VCRs are not to be played after 9 pm.
11. Water and electricity should not be wasted.
12. The Hospital Dispensary works from 7 am to 5 pm. Medicines required to be taken at night and early morning should be procured before the Dispensary is closed.
13. For matters not connected with treatment, patient or the by-stander may contact the Manager (Admn.) / Administrative Office. For matters concerning treatment appropriate guidance may be obtained from ward doctor.
14. The attendant should not leave the patient alone in the room as far as possible. After 7.00 pm, no outsider will be allowed to enter the patient's room and stay there.
15. When the patients get prescription for the follow up treatment at the time of discharge, they may arrange to take the medicines from the Hospital Dispensary, and for this they may seek the help of the ward boys. Only firm orders should be given, as it is very difficult to alter the bills.
16. The Hospital will not accept the belongings of patients for safe custody at the time of discharge.
17. We request the patients to co-operate with the Hospital Administration to ensure discipline in the interest of their speedy recovery.
18. Alcoholic drinks and non-vegetarian items are strictly prohibited in the hospital. Smoking is not allowed in the hospital.
19. We recommend advance booking for subsequent visits.
20. Proper connectivity is maintained through e-mail, fax, telephone facilities for the benefit of patients.

'A Healthy body is the guest chamber of the soul; a sick it's prison'

Figure 27. AVS General Rules and Regulations for all Patients

enter their rooms and stay there; and alcoholic drinks and non-vegetarian items were strictly prohibited.

Table 16. Week 1: Arya Vaidya Sala regime for Sarah Khan

28 February- 4 March 2002
Daily massage treatment: 2 pm: *Pizhichil*
Ayurvedic Medicines:

1. ***Sukumaram Kashayam***-12 ml in water (boiled and warm)-60 ml
2. ***Dhanwantharam*** (21)-20 drops (mix it all together and take twice/day: morning on empty stomach and at 6pm)
3. ***Pushyanauga Choornam***-2 grams with honey-1 tsp (mix together and take twice/daily before lunch and dinner)
4. ***Vanasuranadi leham***-15 grams (may be taken at bedtime)
5. ***Kayyanyadi Kera Thailam***-may be applied over head before head bath
6. ***Balaswagandhadi Kuzhampu*** and ***Dhanwantharam Thailam*** (to be applied during ***Pizhichil*** massage for 9 days)
7. ***Rasnadi Choornam***-for head after massage

Diet: Breakfast: 8am breakfast and tea (1 cup); Lunch: 12:30pm; Dinner: 7pm
Diet Restrictions: Avoid red hot peppers, tamarind, cold food, oil-fried items, root vegetables

Table 17. Week 2: Arya Vaidya Sala regime for Sarah Khan.

4-9 March 2002
Daily massage treatment: 2 pm: Pizhichil
Ayurvedic Medicines:

1. *Sukumaram Kashayam*-12 ml in water (boiled and warm)-60 ml
2. *Dhanwantharam* (21)--20 drops (mix it all together and take twice/day: morning on empty stomach and at 6pm)
3. ***Sukumara Leham*** and ***Kantham Bhasmam*** (mix together and take twice/day before lunch and dinner)
4. *Vanasuranadi Leham*-15 grams (may be taken at bedtime)
5. *Kayyanyadi Kera Thailam*-may be applied over head before head bath
6. *Balaswagandhadi Kuzhampu* and *Dhanwantharam Thailam* (to be applied during *Pizhichil* massage for 9 days)
7. *Rasnadi Choornam*-for head after massage

Diet: Breakfast: 8am breakfast and tea (1 cup); Lunch: 12:30pm; Dinner: 7pm
Diet Restrictions: Avoid red hot peppers, tamarind, cold food, oil-fried items, root vegetables

Table 18. Week 3: Arya Vaidya Sala regime for Sarah Khan

10-16 March 2002
Ayurvedic Medicines:

1. *Sukumara Leham* and *Kantham Bhasmam* (mix together and take twice/daily before lunch and dinner)
2. *Vanasuranadi Leham*-15 grams (may be taken at bedtime)
3. ***Sathahwadi Vasthi Thailam***

Diet: Breakfast: 8am breakfast and tea (1 cup); Lunch: 12:30pm; Dinner: 7pm
Diet Restrictions: Avoid red hot peppers, tamarind, cold food, oil-fried items, root vegetables

10 March 2002
2 pm: *Pizhichil* massage, 3 pm: *Tailam Vasti*
11 March 2002
7 am: Light breakfast
7 or 9 am: ***Navarakkizhi*** massage, 10 am: ***Kashayam Vasti***
12:30 pm: Lunch rice and green gram soup; 7:00 pm: Normal dinner
12 March 2002
2 pm: *Navarakkizhi* massage, *Tailam Vasti*
13 March 2002
7 am: Light breakfast
10 am: *Navarakkizhi* massage, *Kashayam Vasti*
12:30 pm: Lunch rice and green gram soup; 7:00 pm: Normal dinner
14 March 2002
2 pm: *Navarakkizhi* massage, *Tailam Vasti*
15 March 2002
7 am: Light breakfast
10 am: *Navarakkizhi* massage*, Kashayam* Vasti
12:30 pm: Lunch rice and green gram soup; 7:00 pm: Normal dinner
16 March 2002
2 pm: *Navarakkizhi* massage, *Tailam Vasti*

For the first two weeks, the massage treatment was *Pizhichil*. According to one of my Ayurvedic physicians, Dr. Nalini, the treatment began with *Pizhichil* in order to gather toxins in the stomach for eventual elimination. The sneha sweda (oil fomentation massage) of *Pizhichil* facilitated this process by opening the srotas (passage ways or channels), decreasing stiffness, and decreasing vata.[448]

In my journal, I wrote the following to describe my first *Pizhichil* massage experience:

> I had to donate a rupee [Indian currency] for the puja/prayer/offering before the treatment began, the doctor had to come and pray, then I offered the rupee where the wicks were lit, and the doctor took some thaila [oil] and applied it to the crown of my head, rubbed it in, once he left the room [the offering occurred only at the first treatment], I could take off my clothes but I could not get up off the dhroni [massage table—blue color in Figures 28-36—the traditional hand-made wooden dhronis are no longer made available to the patients, unless on request], I had to stay seated; the [four] women … all sat around the dhroni and each worked on a quadrant of my body. First I lay on my back and they took cotton cloth and they soaked them in the heated [medicated] oil and washed my body in about ½ liter of thaila…the feeling was smooth, slippery, warm, unctuous and strange,… and at times it felt like one big hand rhythmically kneading…after a while, I flipped over, twisting and turning my neck periodically and never finding a comfortable position…I flipped back over, at one point also, the women changed their seats and focused on a different quadrant…[449]

At a later date I noted in my journal that "…what is so wonderful is that I have nowhere to go and nowhere to be, so there is no anxiety about being up and about"… [450]

As my treatment progressed, different types of massages were prescribed. Figures 21-29 represent the *Navarakkizhi* massage that I experienced during the last week of treatment. *Navarakkizhi* (or *shastika pinde swedana*—rice bundle fomentation) was prescribed after *Pizhichil* because it helped in rejuvenation after the concentration and removal of toxins via the digestive organs.[451] I "started the massage quite alert, awake, perhaps a little wired, by the end of the hour, I felt relaxed, mellow, sleepy and tired." [452]

Figure 28. *Navarakkizhi* massage preparation—Kerala *shashtika* rice cooked near dry in 3 liters of milk and *Bala* (*Sida rhombifolia*) decoction.

Figure 29. *Navarakkizhi* massage preparation—Kerala *shastika* rice placed in cloth to make four equal-sized bundles.

Figure 30. *Navarakkizhi* massage preparation—Kerala *shastika* rice bundles being tied.

Figure 31. *Navarakkizhi* massage preparation—Kerala *shastika* rice bundles being tied.

Figure 32. *Navarakkizhi* massage preparation—Kerala *shastika* rice bundles heated in the milk decoction mixture.

Figure 33. *Navarakkizhi* massage preparation—Kerala *shastika* rice bundles heated in the milk decoction mixture.

Figure 34. *Navarakkizhi* massage preparation—Kerala *shastika* rice bundles heated in the milk decoction mixture.

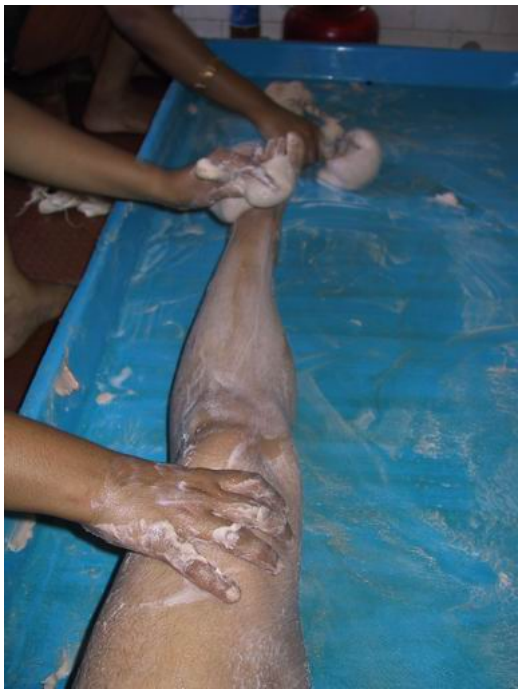


Figure 35. *Navarakkizhi* massage—Kerala *shastika* rice bundles applied to leg for massage.

Figure 36. *Navarakkizhi* massage—Kerala *shastika* rice bundles after completed massage.

During this time, two types of enemas were also administered: oil and decoction. The oil decoctions were intended to aid the concentration and extraction of the toxins into the

eliminatory organs. The decoction assisted in decreasing the dampness created by the oil decoction.[453] During the last week of treatment, I felt more tired and drained. In my journal I wrote "…luckily no more enemas, after lunch I fell asleep till about 2pm, felt beat and exhausted…"

The following is a summary description I wrote to describe my experience at AVS:

> My rejuvenation treatment involved 10 days of warmed medicated oils massaged for over an hour by four women (that's right, four pairs of hands). Through this process both oleation and sweating are accomplished. This helps concentrate the toxins in the fat and also brings them to the digestive system. Following the treatment, I had a series of medicated enemas: first day oil, then the next day a decoction. This went on for 6 days and I also underwent a different type of massage where boiled rice (only grown in Kerala) is put in poultices, warmed in a decoction of herbs and milk, and rubbed all over the body also for an hour. The point of the enemas is to now dispel the built up toxins. The rice massage also facilitated this process. I finished with a few days of *shirodhara*. This is where medicated oil is poured over your forehead in a continuous stream for an hour while you receive a light oil massage. I spent my days quietly, often speaking little except when meeting fellow patients at meals…[454]

From Participant-Experience (GAU), Participant-Observer (AVS) to Clinical Research Manager (FRLHT)

These two research experiences in India provided me with different windows from which to experience Ayurveda: those of student-researcher and patient. Each experience, as described in each section, allowed me to understand Ayurveda from a unique perspective. My student and research time at GAU grounded me in Ayurveda basics, so that I could ask more informed questions. While at AVS, I was able to communicate with my Ayurvedic physicians using Ayurvedic terminology and could process their responses in the same terminology.

Results and Conclusions

The digestive problems that I experienced prior to arriving at AVS appeared to have diminished. I experienced less bloating and less discomfort upon eating certain previously problematic foods. Once I stopped ingesting the prescribed formulations, the irregularities returned over time (2-3 months), but the intensity of the irregularities had diminished. Unexpected results included dramatically increased flexibility, minor weight loss, increased energy, and improved complexion. A continuation of the protocol while I was traveling or back home, however, was a challenge. Furthermore, ingesting a large number of prescribed formulas in different forms (powder, pill, decoction, and paste) was a deterrent, a problem in terms of transport, and costly.

From a research perspective, I gained insight into the practical applications of the Kerala Ayurvedic treatment protocols. By experiencing the treatment myself, I was no longer a

mere observer but a participant-observer, thereby increasing my understanding of the theory by engaging in the process and documenting my own experience.

In the next section, I present the data on my experience as a clinical research manager. When I designed, developed, and implemented a small clinical study at FRLHT, I was no longer a recipient of Ayurvedic treatments but was, in fact, instrumental in providing those services to the patients in our study. Running and overseeing any type of clinical study required that I employ my skills in public health and clinical study design while relying on the expertise of my colleagues to take care of the Ayurvedic treatments.

A 4-Week Open Label Study to Evaluate Ayurvedic Management Therapy (AMT) of Diabetes mellitus Type 2 (DM2), Bangalore, Karnataka

Study Design

This pilot clinical protocol is based on the protocol presented in Chapter 5. The only change noted is that the Ayurvedic practitioner decided to use only four of the Madhumeha Formulations (MF), instead of the initially anticipated six.

Indication

This study evaluated the use of Ayurvedic Management Therapy (AMT) for the reduction of hyperglycemia in patients with DM2. Ayurvedic Management Therapy is defined as complete Ayurvedic evaluation of disease etiology, individualized differential diagnosis,

and prescriptions of formulations, diet, and exercise regimens. (*Pancha Karma* therapies were not prescribed due to logistical, time, and financial constraints). For complete protocol details, please refer to Chapter 5.

Please note that the original plan to include 6 Madhumeha formulations (MF) was reduced to 4 MF formulations. This decreased the original number of total plants used in the protocol. In order to provide a complete chapter, however, I have included the objectives, study population, sample and study design, dosing schedule and rationale, and recent medical literature review of plants and one fish species used in the clinical study.

Objectives

Primary: The primary objective was to evaluate the effectiveness of AMT in reducing hyperglycemia when administered to NIDDM patients as assessed by a reduction in fasting plasma glucose (FPG) levels after 4 weeks of individualized AMT—diet and exercise regime and individualized administration of classical Ayurvedic formulations (any combination of 4 Madhumeha Formulations-MF).

Secondary: After 4 weeks of AMT, the objectives were to investigate: the effect of AMT on $HgbA_{1c}$; serum lipids including total cholesterol, HDL, LDL, triglycerides; the change in quality of life and well-being of the patient; clinical safety; tolerability; and the changes in physical examination, vital signs, weight, clinical laboratory tests, and adverse experiences.

Other parameters: Another goal was to document the Ayurvedic physician's differential diagnosis of each patient including analysis of Ayurvedic patient classification (*vata*, *pitta*, and *kapha*), relationship between patterns use of MFs, and reasoning for prescribed AMT.

Study Population, Sample Size and Study Design

Males and females of non-childbearing potential, 30 to 60 years of age, with a diagnosis of NIDDM defined by the criteria of the National Diabetes Data Group (see Appendix E), and fasting plasma glucose (FPG) of ≥ 126mg/dL and ≤ 220mg/dL at screening, with no present intake of oral hypoglycemic or insulin by the beginning of the study. It was anticipated that approximately 80 NIDDM patients would be selected for this study (based on a 25% drop-out rate) in order to produce 56 evaluable patients. The Foundation for the Revitalization for Local Health Traditions sponsored the study and was the center site. The study consisted of a Pre-screening period (first contact via phone registration), Screening period (1 week), Baseline Period (1 week—diet and exercise regimen), Treatment Period (4 weeks Open-Label Study), and Follow-up Period (1 week). Fasting Blood Glucose levels were evaluated over the course of treatment.

Dosing Schedule and Rationale

During the 4-week Treatment Period, the patient took any combination of 0-4 Madhumeha Formulations (MF1-4) daily: an MF1 (liquid) dosage of 40-60 ml/day with an equal quantity of water; an MF2 (powder) dosage of 6-12 g with honey as a vehicle; and MF3 and MF4 dosages of 2 capsules/500mg each in the AM and PM. Ayurvedic practitioners, like Chinese Medicine practitioners, have established guidelines for

dosages in the classical Sanskrit Ayurvedic texts. These formulations have been found to be safe and well tolerated in the prescribed doses. However, the Ayurvedic physician has always reserved the right to alter or modify an individual's regime based on ongoing Ayurvedic examinations and assessments. It is anticipated that a 20 mg/dL reduction in FBG would be achieved during the 4 weeks of AMT.

Recent Medical Research on 32 Plants and one Fish species from the Four Madhumeha Formulations (MF1-4)

Many studies exist on individual Ayurvedic plants and formulations for the treatment of diabetes.[455] In the mainstream allopathic literature (i.e., Medline), however, there are few studies that concomitantly document the Ayurvedic diagnosis, prescription, and treatment protocol. Clinical trials that assess allopathic and traditional healing systems parameters in conjunction (in this case Ayurveda) do not appear to exist in non-Ayurvedic-based literature. The four Ayurvedic madhumeha formulations (MF1-4) used in the study included a total of 32 medicinal plants and one fish species: one in decoction (kashayam), one in powder (churnam), and two in capsule form (Table 19).

Table 19. MF1-MF4 medicinal plants and one fish species.

Acacia catechu Brandis Leguminosae
Berberis aristata DC Berberidaceae
Biophytum sensitivum (L.) DC Oxalidaceae
Butea frondosa Roxb. Ex Willd. Fabaceae
Cedrus deodara Loud. Pinaceae
Cephalandra indica Naudin Cucurbitaceae
Cissampelos pareira L. Menispermaceae
Coccinia grandis Voigt Cucurbitaceae
Coscinium fenestratum Colebr. Menispermaceae
Curcuma longa L. Zingiberaceae
Cyclea peltata Hook.f. & Thomson Menispermaceae
Cyperus rotundus L. Cyperaceae
Emblica officinalis Gaertn. Euphorbiaceae
Erythrina variegata L. Fabaceae
Ficus arnottiana Miq. Moraceae
Ficus lacor Buch.-Ham. Moraceae
Ficus racemosa L. Moraceae
Ficus religiosa L. Moraceae
Mangifera indica L. Anacardiaceae
Oxalis corniculata L. Oxalidaceae
Premna serratifolia L. Lamiaceae
Pterocarpus marsupium Roxb. Leguminosae
Salacia reticulata Wight Celastraceae
Sarcocephalus missionis Havil. Rubiaceae
Strychnos potatorum L.f. Loganiaceae
Symplocos laurina Wall. Symplocaceae
Syzygium cumini (L.) Skeels Myrtaceae
Terminalia arjuna Wight & Arn. Combretaceae
Terminalia bellirica (Gaertn.) Roxb. Combretaceae
Terminalia chebula Retz. Combretaceae
Tinospora cordifolia Miers Menispermaceae
Zingiber officinale Rosc. Zingiberaceae

Sepia officinalis L. Sepiidae (Mollusk) Os Sepiae (internal shell—cuttle bone)

A review of the medical literature of the thirty-two plants and one fish species demonstrated a range of medicinal effects. As seen in the Group I table of Appendix C, twelve of the 32 plants showed various degrees of effect on several antidiabetic parameters *in vitro, in vivo,* and in human studies; these were *Biophytum sensitivum, Curcuma longa, Emblica officinalis, Ficus racemosa, Mangifera indica, Pterocarpus marsupium, Salacia reticulata, Syzygium cumini, Terminalia bellirica, Terminalia chebula, Tinospora cordifolia,* and *Zingiber officinale* (Group I). Appendix C is not exhaustive, but merely representative of the type of antidiabetic studies that exist on these 12 plants. I tried to include only those studies published since 2000 in the cases of plants that have had extensive research trials. In the event that there were not many research studies, I included studies that were published before 2000.

The review of the medical literature also revealed that ten other plants did not demonstrate a direct antidiabetic effect although other medicinal effects are shown. These ten plants included *Acacia catechu, Berberis aristata, Butea frondosa, Cissampelos pareira, Coscinium fenestratum, Cyperus rotundus, Erythrina variegate, Sarcocephalus missionis, Strychnos potatorum,* and *Terminalia arjuna* (Group II). Finally, the literature review showed that the remaining ten plants and one fish species had little research data on medicinal effects. These included *Cedrus deodara, Cephalandra indica, Coccinia grandis, Cyclea peltata, Ficus arnottiana, Ficus lacor, Ficus religiosa, Oxalis corniculata, Premna serratifolia*, *Symplocos laurina* and *Sepia officianalis* (fish species) (Group III). Neither Group II nor III is represented in table format. The Group II literature review is too large and that for Group III is too small.

In terms of toxicity, safety, tolerability, and adverse effects, two plants, *Salacia reticulata* and *Butea frondosa*, demonstrated possible anti-implantation activity in pregnant rat and mouse models.[456] [457] [458] [459] However, the amount of plant material required to produce this effect, if extrapolated to a 60 kg human being, would be 6-60 grams for *Butea frondosa* and 600 grams for *Salacia reticulata*. The dosages used in the animal studies exceeded the Ayurvedic prescriptions administered during this small clinical study.

Historically, classical Ayurvedic preparations when administered by an Ayurvedic physician according to classically prescribed dosages are safe, tolerable, and non-toxic. The proposed study was intended primarily to evaluate the effectiveness of AMT in reducing hyperglycemia when administered to NIDDM patients as assessed by a reduction in FBG over a 4-week treatment period. In addition, the clinical safety of AMT was assessed in this patient population.

Study Results

Statistical Methods

To evaluate the change from baseline, paired t-tests were performed for each efficacy variable. Since diet and exercise can usually reduce the fasting blood glucose level by around 20 mg/dL, we tested whether Ayurvedic Management Therapy resulted in more than a 20 mg/dL of reduction in fasting blood glucose level. For the secondary efficacy variables, we tested if there was significant change from baseline. 95% confidence intervals for the mean change from baseline were also provided.

In spite of explicit inclusion and exclusion criteria, these requirements were not well enforced during the study. Some patients that should not have been included were still admitted into the study (details provided in discussion section). Therefore, we divided the data analysis into two parts. In the first section, all patients were included in the data analysis, while in the second section; only the patients that met the criteria were included.

Data Analysis—Quantitative

Entire Sample

Thirty-one patients were enrolled in the study. Only 22 completed the study. Fifty-six evaluable patients were required to achieve statistical power. Based on the 22 patients who completed the study, however, the result showed that AMT did not have a significant effect on reducing fasting blood glucose levels. However, the secondary parameters—HDL-cholesterol, LDL-cholesterol, and weight—decreased significantly with p-values .0454, .0161, and .0005, respectively. Table 20 summarizes the 95% confidence intervals for the mean change from baseline of each variable.

Table 20. 95% confidence intervals for the mean change from baseline of each variable. The p-value is provided if the mean change from baseline is significant.

Variable	95% Confidence Interval		*p*-value
Fasting blood glucose mg/dL	-21.848	13.848	-
HgbA1C %	-0.116	0.498	-
Total cholesterol mg/dL	-34.387	9.296	-
HDL-cholesterol mg/dL	-10.338	-0.117	.0454
LDL-cholesterol mg/dL	-33.988	-3.917	.0161
Cholesterol/HDL ratio	-0.348	0.765	-
HDL/LDL ratio	-0.052	0.063	-
Triglycerides mg/dL	-44.010	78.191	-
Weight kg	-0.673	-0.218	.0005
Systolic blood pressure mm/Hg	-9.122	6.577	-
Diastolic blood pressure mm/Hg	-10.480	6.935	-
Heart rate beats/min	-3.396	4.487	-

Representing the data visually in box plots, Figure 37 shows the changes in HDL-cholesterol, LDL-cholesterol, and weight from Week 2 to Week 6. For patient number 15, the LDL-cholesterol at Week 6 is 34, which is suspected to be an outlier. This patient will be excluded in the second part of the data analysis in the next section. Hence, no further analysis is conducted here.

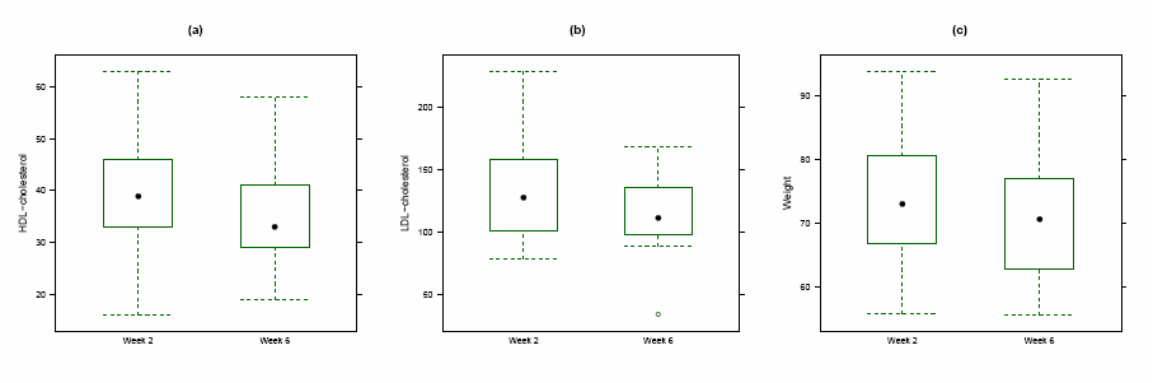


Figure 37. Box plots of (a) HDL-cholesterol; (b) LDL-cholesterol; and (c) Weight.

Sub-Sample that met the Inclusion-Exclusion Criteria

In another analysis of the data, patients that did not stop medications a minimum of two weeks before the screening period were excluded. These patients were excluded because some of the hypoglycemic medications prescribed required at least a two-week wash out period for the blood glucose levels to normalize. Only 13 patients were included in this

part of data analysis. Although Ayurvedic Management Therapy reduced the fasting blood glucose level, it did not result in more than 20 mg/dL of reduction in fasting blood glucose, which would have been significant, in this sub-sample. Similar to the data from the entire sample, HDL-cholesterol, LDL-cholesterol, and weight decrease significantly during the 4-week Treatment Period, with p-values of .0482, .0301, and .0082, respectively. Table 21 summarizes the 95% confidence intervals for the mean change from baseline of each variable.

Table 21. 95% confidence intervals for the mean change from baseline of each variable. The p-value is provided if the mean change from baseline is significant.

Variable	95% Confidence Interval		*p*-value
Fasting blood glucose mg/dL	-33.288	-2.866	-
HgbA1C %	-0.068	0.314	-
Total cholesterol mg/dL	-46.209	5.747	-
HDL-cholesterol mg/dL	-14.394	-0.067	.0482
LDL-cholesterol mg/dL	-38.162	-2.299	.0301
Cholesterol/HDL ratio	-0.220	1.106	-
HDL/LDL ratio	-0.093	0.074	-
Triglycerides mg/dL	-12.055	85.439	-
Weight kg	-0.754	-0.138	.0082
Systolic blood pressure mm/Hg	-6.848	15.771	-
Diastolic blood pressure mm/Hg	-7.114	13.268	-
Heart rate beats/min	-4.852	6.390	-

Figure 38 shows the changes of HDL-cholesterol, LDL-cholesterol, and weight from Week 2 to Week 6.

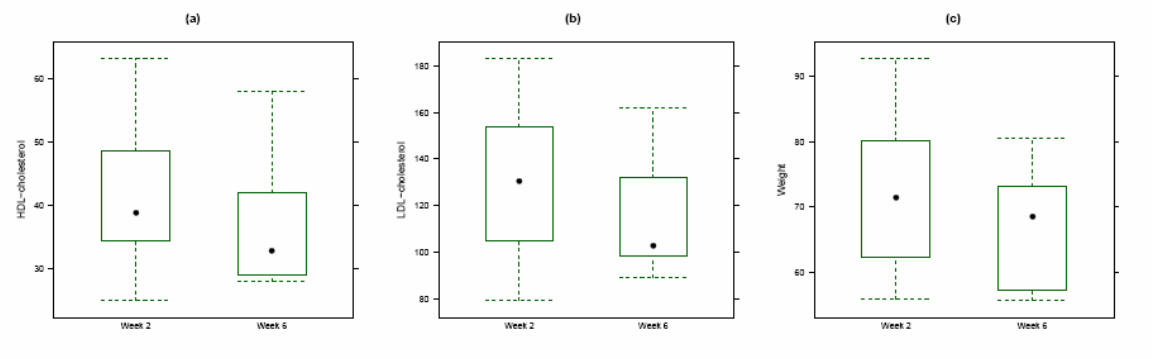


Figure 38. Box plots of (a) HDL-cholesterol; (b) LDL-cholesterol; and (c) Weight.

HDL-cholesterol, LDL-cholesterol, and Weight

The Scatter Plot Matrix represented in Figure 39 shows that the changes in HDL-cholesterol and LDL-cholesterol were positively correlated. This is apparent in the scatter plot matrix shown in Figure 39 between HDL and LDL. This implies that HDL and LDL may influence one another. Due to the correlation between these two variables and a small sample size, a Hotelling's T^2 test was performed to test whether the changes in HDL-cholesterol and LDL-cholesterol were different from zero simultaneously as opposed to independently.

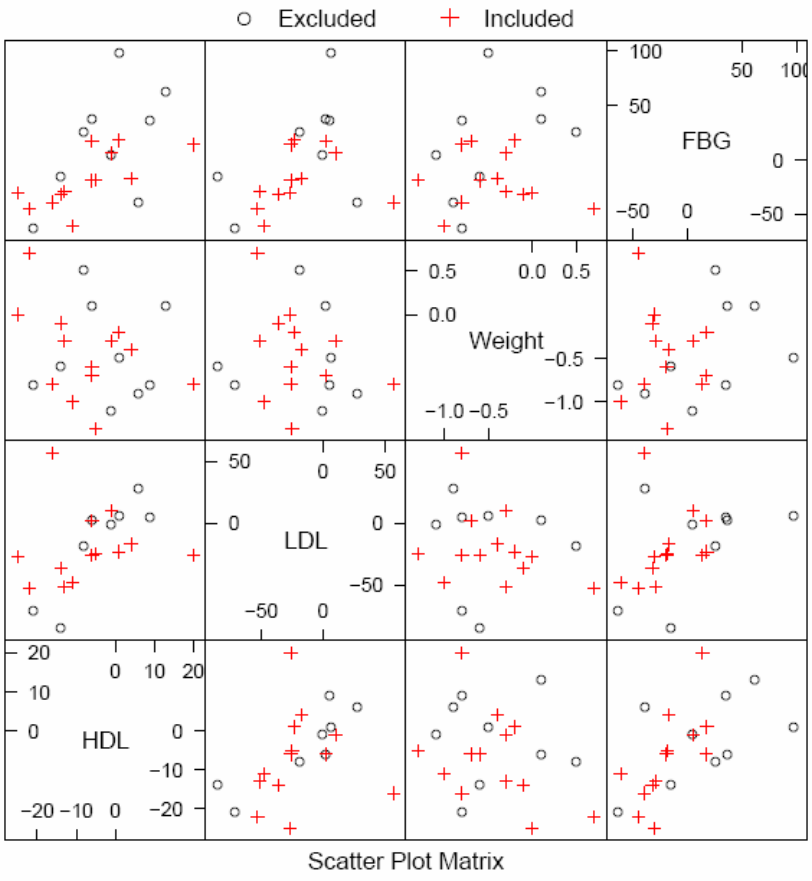


Figure 39. Scatter plot matrix of FBG, HDL-cholesterol, LDL-cholesterol, and Weight. HDL and LDL changes are positively correlated. "Included" indicates the observations included in the analysis, and "Excluded" indicates those not in the analysis.

When all 22 patients were considered, the results showed that the changes in HDL-cholesterol and LDL-cholesterol were different from zero simultaneously, with p-value .033. When only the 13 patients that meet the criteria were considered, the result remained the same with p-value .024. Figure 39 also suggests that there is no difference in the changes of these four variables (FBG, HDL, LDL, weight) between the entire sample (n = 22) and those that meet the inclusion-exclusion criteria (n = 13) excluded. This is supported by two-sample t-tests.

Data Analysis—Qualitative

Twenty-two patients successfully completed the study, and only 13 adhered to the protocol. Among this group of 13, 10 had data on basic Ayurvedic differential diagnoses such as *Prakriti* analysis (inherited, natural body constitution); *Vikara* analysis (current constitution) that included *dosha*, *dhatu* (tissue), *agni* (fire, digestive capacity) and *kostha* (bowel function) imbalances; and the Ayurvedic diagnosis.

The *Prakriti* analysis revealed 4 patients categorized as *vata-pitta*, 3 as *pitta-vata*, 1 as *pitta-kapha*, 1 as *kapha-vata*, and 1 as *pitta-vata-kapha*. The *Vikara* analysis showed that in the doshas there were 4 *vata-pitta*, 2 *pitta-vata*, 1 *vata-pitta-kapha*, 1 *kapha-vata*, 1 *pitta-kapha*, and 1 *vata* that were vitiated. In the dhatus (tissues), imbalance was noted with 7 *rasa* (plasma) imbalance, 1 *rasa* and *rakta* (blood) imbalance, and 2 being normal. Eight *agnis* proved normal, while 1 *jatharagni* and 1 *trishnagni* were imbalanced. The *kostha* level was defined as 7 *madhya* (moderate), 2 *ksura* (hard), and 1 normal. The Ayurvedic diagnosis consisted of 2 *pramehas*, and 8 remaining were defined as

individual types of *Prameha*: *Vata-prameha*, *pitta-prameha*, *kapha-prameha*, *vata-pitta-prameha*, *vata-kapha-prameha*, *pitta-vata-prameha*, and *kapha-pitta-prameha*.

Because this sample is so small, clear conclusions or generalizations would be misleading. However, one can note that the *Prakriti* analysis might be able to show trends if a larger sample size were obtained. For example, *vata-prameha* often includes patients who are of normal body weight, whereas a large sample of patients with *kapha-prameha* tends to be obese. These two groups, both with NIDDM, may require dramatically or slightly different Ayurvedic treatment protocols. The *Vikara* analysis revealed that in 9 of the 10 cases, *vata* was imbalanced. In terms of tissues, the most frequent imbalances were seen at the level of the *rasa* (plasma), and 8 of the 10 patients had moderate *kostha* (bowel) imbalances. Once again, one cannot generalize, but if a future study included a larger sample, trends might be notable. These data trends would be useful both to modern Ayurvedic practitioners and to those who integrate Ayurveda into their treatment programs.

Conclusions

Primary and Secondary Variables

In the entire sample and the sub-sample of this small-scale pilot study, AMT did not have a significant effect on reducing FBG by more than 20 mg/dL, which suggests that AMT is not better than good control of diet and exercise. AMT did not affect other secondary efficacy variables according to the 95% confidence intervals in Tables 21 and 22. However, AMT did significantly reduce HDL-cholesterol, LDL-cholesterol, and weight

in the entire sample and sub-sample patient populations. Although lower HDL-cholesterol is not desirable, reductions of LDL-cholesterol and weight are considered beneficial for DM2 patients.

Comparing the results of the entire sample and the sub-sample, there was not much difference between them, except the 95% confidence interval for the mean change from baseline of FBG. This means that the sub-sample of patients that met the criteria showed a change in FBG that was greater than that in the entire sample. However, as described above, the AMT effect on FBG is not significantly better than that of good control of diet and exercise, even though the patients that stopped medications relatively late were excluded from the analysis.

It is difficult to conclude what the causes are of the lowered weight and cholesterol levels. The study was confounded by several variables, so whether these effects are due to some aspect of AMT therapy, diet modification, or exercise remains to be proven in a larger more comprehensive study.

Multivariate Analysis

The analysis provided on the sub-sample was valid to evaluate the mean changes of HDL-cholesterol and LDL-cholesterol together, because these two variables were correlated. The result implied that AMT had a significant effect on reducing HDL-cholesterol and LDL-cholesterol simultaneously. The p-values from the Hotelling's T^2 test were more accurate than those from paired t-tests.

Power

On the basis of the protocol, the required minimum sample size required in order to achieve statistical power was 56 patients. This sample size was too small and resulted in a low power for the statistical tests performed. With limited time and budget, it was understood that no more patients could be recruited. Thus, we were not able to improve the power of the statistical tests or achieve the desired power. In order to improve this study, there must be more patients and a control group. This would also make the analysis more reliable for comparing the effect of AMT to the effect of diet and exercise only.

Study Discussions

Significant reduction in FBG did not occur in the patient population and the sub-sample. However, significant decrease did occur in the HDL, LDL, and weight secondary parameters. Although a decrease in HDL is not desirable, a decrease in LDL and weight is especially beneficial for those suffering from DM2 to avoid later complications associated with long-term DM2.

Challenges

The challenges to this study included the following: the recruitment time of three weeks was too short, resulting in a small sample; inclusion and exclusion criteria were not adhered to rigorously, and this resulted in admittance of patients who did not stop medication according to protocol, or who had DM2 that was too advanced; when patients were identified, some MDs did not keep a list of contact information for follow-up; the inconvenient location of the study (one hour to one and a half hours drive from Bangalore

to the study site) deterred patient travel; the treatment period was too short; free laboratory results attracted participants who merely wanted the benefit of free tests and did not necessarily adhere to protocol; multiple formulations, and diet and exercise regimes confounded results (although this was expected); and our team could see patients only on weekdays during regular business hours, and this limited the diversity of our patient population. In addition, the four MF plant formulations utilized in the study were manufactured by Indian companies that did not provide voucher specimens.

Improvements

How to improve the study in the future? To begin with, patients should be recruited over a longer period of time from within a medical setting to ensure inclusion of only recently diagnosed patients. Once a patient is recruited, she should be treated immediately and for a longer period of time. Inclusion and exclusion criteria must be strictly adhered to, and this may be better controlled within a hospital setting and with proper pre-clinical trial training. The problem of hypoglycemic medication intake would be resolved by limiting recruitment to only recently diagnosed patients with no history of prescription intake. A hospital setting would also resolve the problem of travel time to the site and provide the needed sample population and control. When patients are recruited, one should ensure that they are neither too eager to join because of excess remuneration nor dissatisfied with the arrangement. A discussion and training sessions with the collaborative team, especially those individuals involved with clinical study design, would be required. Weekend and evening availability for full-time working patients would be required to obtain a more representative cross-section of the patient population. Finally, Ayurvedic medicinal plant formulations would be manufactured in small batches for the study. This

would ensure obtaining proper voucher specimens and adherence to good manufacturing practices. Otherwise the team should work only with those manufacturers who adhere to good manufacturing practices, good botanical practice standards, and provide voucher specimens.[460]

Accomplishments

The positive aspects of this study are several-fold. First, FRLHT was able to carry out a small clinical study. This process helped introduce and train certain members of the staff concerning the challenges involved in conducting a rigorous clinical study. Second, the clinical study sought to develop Ayurveda at the same time it tested AMT using western biomedical parameters. FRLHT Ayurvedic practitioners are in the process of analyzing the qualitative data gathered from the study to begin documenting treatments for DM2. The qualitative data is also being assessed, by FRLHT Ayurvedic practitioners, for its adherence to classical Ayurveda theory in addition to documenting the Ayurvedic practitioner's innovations.

An important future goal is to develop clinical tools whereby a traditional healing system such as Ayurveda, TCM, or any other non-allopathic healing system, may be tested for efficacy using allopathic parameters that retain for the practitioner the ability to treat his or her patients individually with minimal constraints. Developing a paradigm that allows the Ayurvedic practitioner, in this case, to treat the entire patient with multiple modalities (i.e., diet, exercise, and multiple formulations) is a formidable challenge. By carrying out and presenting this small study, I hope that better, more rigorous studies may follow.

Chapter 7: TCM Management Therapy for DM2 Patients, Department of Integrative and Traditional Chinese Medicine, Hua Shan Hospital, Fudan University, Shanghai, China

> There is sufficient evidence of Western Medicine's effectiveness to expand its use into Traditional Chinese Medicine (TCM) and to encourage further studies of its physiology and clinical value…In particular Western Medicine shows promise as adjunctive treatment to TCM. As a stand-alone medicine, however, its efficacy is mainly in the areas of acute and catastrophic care that comprise a relatively minor percentage of total patient complaints.
>
> *Summary of a report from Sin Hua, China News Agency, April 1, 2001.*
> China Gives Limited Approval to Western Medicine: At the conclusion of a 3-day meeting held in the Great Hall of the People in Beijing, March 28-30, an elite panel of 12 TCM practitioners declared the above.

Introduction

Since 2001, I have spent a total of over two years in India studying, researching, and collaborating with Ayurvedic practitioners, academics, and physicians in three regions of India: Northwest, Southwest, and South central. On the other hand, I spent a mere seven weeks at Hua Shan Hospital, a private institution, working with the director, Wenjian Wang MD, and Chunyan He, a PhD candidate, both at the Traditional Chinese Medicine Department of Hua Shan Hospital, Shanghai, China.

The purpose of the research period in China was to compare how another ancient healing system in Asia but not in South Asia treated patients with diabetes. As I had in India, I relied on the expertise of my collaborators and gathered data on patients with diabetes. Unlike the data I obtained in India, the data I gathered in China pertained only to what TCM practitioners prescribed to newly diagnosed patients with diabetes at the initial consultations, as opposed to a small pilot study conducted in Bangalore, India. The purpose of this analysis was to compare plants prescribed by a TCM practitioner to those prescribed in India—GAU and FRLHT—and to document the qualitative data on TCM symptoms, diagnoses, and actions. Independent of my own dissertation research, my TCM colleagues decided to carry out a two-month pilot study of their individualized TCM treatment for the 20 patients we initially documented. (Based on my academic training and clinical research experience in India, I contributed to the development and design of this pilot study. Once we evaluate the results, this pilot study will be the basis for a grant proposal to conduct a larger clinical research trial.)

In the following chapter, I present and discuss the data my colleagues and I gathered on 20 recently diagnosed patients with diabetes. I chose not to review TCM diagnostic techniques because it is outside of the realm of my training.

Historical Background: Spice, Silk, and Spiritual Routes between South Asia and China

Exchanges of religious and material culture have existed for millennia between South Asia and China. Beginning as far back as the second century B. C. E., documentation

exists that Chinese envoys and monks (i.e., Zhang Qian, Ban Chao, Fa Xian, and Xuan Zhang) traveled the northern and southern silk routes to expand political territories, to trade in silks, spices, and other luxury items, or to seek Buddhist mentors, texts, and relics.[461] [462]

In 644 C. E. the Buddhist monk, Xuan Zhang, traveling home to China after a 16-year pilgrimage to India, crossed the one-mile wide Indus River at Hund in boats "piled high with scriptures, relics, statues, and rare flower seeds he had gathered from the four corners of India".[463] Although a storm arose, and all the manuscripts and seeds fell into the water, both these accounts attest to the exchange of botanical material and information between South Asia and China from an early period. Material exchange between the two civilizations has continued over the centuries to the present even though sea routes, train routes, and air travel have replaced the ancient silk and spice routes. While India and China share a history of exchange of material and religious culture, they independently gave rise to two of the oldest and most continuous documented healing paradigms: Ayurveda and Chinese Medicine. (Refer to Chapter 2 for a brief history of Ayurveda, and to Chapter 3 for Ayurveda Basics.)

Chinese Medicine as a Science

Kaptchuk argued that Chinese medicine is a coherent system of thought that does not require validation by the Western biomedical paradigm as an intellectual construct. He emphasized that the way to approach Chinese concepts intellectually is to see whether they are internally logical and consistent, not to disguise them as Western concepts or dismiss them because they do not conform to the Western biomedical paradigm. Like

Ayurveda, the Chinese medical corpus is internally consistent—it is an organization of all the observable manifestations of the body into an integrated set of functions and relationships. Understanding of these functions and relationships enables the practitioner to identify and treat a disharmony among them.[464]

In the same way Shankar described Ayurvedic medicine (See Chapter 1), Kaptchuk asserted that Chinese medicine is a coherent and independent system of thought and practice that has evolved over two millennia. Based on ancient texts, Chinese medicine emerges from a continuous process of critical thinking, as well as extensive clinical observation and testing. It represents a formulation and continual reformulation of material by respected clinicians and theoreticians over millennia. At the same time Chinese medicine is rooted in the philosophy, logic, sensibility, and habits of a particular civilization (like South Asia, China possesses a rich population with multiple ethnicities) within the area we call China today. Chinese medicine has therefore developed its own unique perception of the body and of health and disease.[465]

Chinese Medicine and Traditional Chinese Medicine (TCM)

Hsu has elegantly outlined and explained the emergence of Traditional Chinese Medicine out of the more general field of Chinese medicine. Hsu explained that the context of learning Chinese medicine that deserves particular attention, not least because it is the most discussed in the Western literature, is the traditional Chinese medicine that is promoted on a nationwide scale in colleges, hospitals, and clinics. In the late 1950s and early 1960s, its legitimation in the People's Republic of China (PRC) led to a reforging and renewal that was and continues to be driven by several factors such as "nationalism,

Confucian values, humanitarian ideals, reformist and 'Enlightenment' movements, the pragmatic politics of a party in pursuit of power, and economic considerations of how to allocate manpower and scarce resources." [466] This medicine is called 'Traditional Chinese medicine' and is abbreviated as TCM. Hsu carefully noted that TCM, when used by Chinese authors in translation, implicitly refers to Chinese medicine in general. For the purposes of this dissertation, however, TCM will refer only to the more narrowly defined and government-promoted medicine and the more general term, 'Chinese medicine' (inclusive of TCM), will refer to the myriad of healing arts practiced all over China, including non-codified and codified traditions.[467]

Based on extensive research on different aspects of Chinese medicine, Hsu elaborated that TCM, despite being called 'traditional' is generally referred to as the 'modernized', 'scientific', 'systematic', and 'standardized' Chinese medicine. In short, she explained that TCM, like professionalized Ayurvedic medicine in India, or Kanpo in Japan, can be regarded as the professionalized Chinese Medicine.[468] Considering how intertwined Chinese medical practice is with shamanic, temple-based, divinatory, fortune-telling, home-based herbal drug, and other practices, Hsu concluded it is unlikely that before 1949 TCM was a separate discipline for the majority of practitioners. [469]

Chinese Medicine History

According to Bensky and Gamble, Traditional Chinese Medicine is based on the *Yellow Emperor's Inner Classic* (Qin Shi Huang Di) compiled by unknown authors between 200 BC and 100 AD. It is the oldest major Chinese medical text extant, and is the theoretical and philosophical foundation of contemporary Traditional Chinese Medicine.[470]

Unschuld also considered the *Inner Classic* as the great foundation from which Chinese medical theory departed. In addition, he argued that the corpus was composed of textual fragments written by various authors at different times.[471] Ni added that the *Inner Classic* is undoubtedly the most important work representing a major achievement of the Chinese prior to the unification of the country by Emperor Qin Shi in 221 B. C. E.. Huang Di, the Yellow Emperor, is the symbol of the vital spirit of the Chinese civilization. It should also be noted that the *Inner Classic* is actually made up of two works: the *Su wen*, "*Questions of Organic and Fundamental Nature*," and the *Ling shu*, "*Classic Acupuncture*," a technical book on acupuncture and moxibustion.[472]

Before the unification of the empire, Unschuld remarked that during the period of the "Warring States," the theoretical foundations of a medicine in China were laid down and formed during the subsequent three centuries.[473] Svoboda and Lade added that during the Han dynasty (206 B. C. E.-C. E. 220) subsequent works laid the groundwork for much of modern Chinese medicine and for the government-sanctioned TCM of today. The authors highlighted three texts in particular:

1. *Classic of Difficult Issues* elaborated and clarified topics in the *Inner Classic* with emphases on the correspondences and uses of Five Element doctrine and on the use of the wrist pulse diagnosis;
2. *Discussion of Cold Induced Disorders* summarized the prevention and treatment of infectious and febrile diseases with a list of 370 prescriptions; and

3. *Shen Nong's Materia Medica* recorded 365 different types of medicinal substances describing their properties and effects.[474]

From a constructively critical perspective, Unschuld astutely stated that the authorities of the PRC and the ideologues of the Communist Party have at no time vouched for the safety of historical Chinese medicine. Instead, from a more political perspective, authorities have recognized the important role of traditional medicine in the public health policy of the PRC. Unschuld argued that traditional Chinese medicine has always been connected to the social and scientific conditions of the Modern Age. He further asserted that the traditional Chinese medicine which is officially supported by the PRC is only a small remnant of the complex and multi-faceted medicine of the Imperial Age. All aspects of the tradition that refer to religious or otherwise metaphysical notions of the past that may appear absurd in light of current science (and that go back terminologically to the feudal hierarchy of the Imperial Age) have been deleted from textbooks. Unschuld concluded that the significance of the remaining medicine is to a large extent based on the interest of European and American visitors to China who have invested a great deal of money and time since the 1980s into knowledge that has gained respect in the West to the same degree to which it has fallen into secondary status in China.[475] These comments are profound in that they show how any science can be influenced by individuals, institutional, and/or government interests.

Based on her more recent experience in the field (specifically in Kunming, China—one of the most ethnically diverse states of China), Hsu concluded that TCM teachers

considered Chinese medical concepts to be coarse and to be based on more primitive understandings. From a political perspective, and following Mao's slogan that "The new supersedes the old," these concepts had to be rendered more fashionable. To be improved, they had to be modernized. The foremost goal was therefore to standardize and make Chinese medicine systematic in order to render it more scientific.[476] (Please note that on many occasions my TCM colleagues quoted Mao's slogan: "The new supersedes the old". This was often said in the context of debates around collaboration and integrating aspects of TCM into the Western biomedical paradigm. Upon further discussion, my colleagues also voiced a concern that they wanted TCM to be understood on its own merits, too. But these discussions emerged later, perhaps as my colleagues became more comfortable with me.)

Traditional Chinese Medicine Basics

In this section, I present an overview of Traditional Chinese Medicine. I provide basic information on yin and yang philosophy, the five phases and organs, the essential substances, the bowels and viscera, and disease causation. I have not presented any more detailed information on TCM theory and practice, since this is not my area of expertise. (In the following section, I have relied on the translation by Wiseman and Ellis entitled: *Fundamentals of Chinese Medicine: Zhong Yi Xue Ji Chu*. This is a basic text used throughout modern China to teach TCM foundational basics. I have also relied upon Kaptchuk's classic book on Chinese medicine which many Western students read entitled *The Web that has No Weaver*.)

Yin-Yang, Five Phases

> Huang Di said, The law of yin and yang is the natural order of the universe, the foundation of all things, mother of all changes, the root of life and death. In healing, one must grasp the root of the disharmony, which is always subject to the law of yin and yang.
>
> In the universe, the pure yang qi ascends to converge and form heaven, while the turbid yin qi descends and condenses to form the earth. Yin is passive and quiet, while the nature of yang is active and noisy. Yang is responsible for expanding and yin is responsible for contracting, becoming astringent, and consolidating. Yang is the energy, the vital force, the potential, while yin is the substance, the foundation, the mother that gives rise to all this potential.[477]

Unschuld explained that the *yin* and *yang* theory represents a dualistic world view of obscure origins. These two, opposite yet complementary poles are constantly passing into, and emerging out of, each other.[478] According to Wiseman and Ellis, the theory of *yin* and *yang* describes the way phenomena naturally group into pairs of opposites that are also mutual complements: heaven and earth, sun and moon, night and day, winter and summer, male and female, up and down, inside and outside, movement and stasis.[479]

Another philosophy that appeared to be distinct from the *yin-yang* philosophy was based on the *Five Phases*. This philosophy involved categorizing everything into five equal groupings.[480] This five phase theory describes all phenomena in the universe as the products of the movement and mutation of five qualities: wood, fire, earth, metal, and water. This theory has considerably influenced Chinese medicine in terms of physiology, pathology, diagnosis, treatment, and pharmacology.[481]

Wiseman and Ellis summarized the five qualities in the following fashion:

- Wood represents bending and straightening. It has the characteristics of growth, up bearing, and effusion.
- Fire represents the ability to flame upwards. It possesses the quality of heat and upward motion.
- Earth represents sowing and reaping. It represents the planting and harvesting of crops and the ability to bring forth phenomena.
- Metal represents change. It has the qualities of purification, elimination, and reform.
- Water represents moistness and the ability to descend to low places. It has the qualities of moistness, downward movement, and coldness.[482]

> Qi Bo replied, The Principles of the five elements would help you understand all transformations in the universe. For example, metal can cut down wood; water can put out fire;

> wood can penetrate earth; fire can melt metal; earth can contain water. These transformations can be applied to the myriad of things in the universe. In acupuncture one applies the same principles. In this way, one can bestow benevolence upon all people.[483]

Unschuld elaborated that these two philosophical systems merged into a complex system of ideas during the early Han period. This natural-law foundation of Chinese medicine is called the *Medicine of Systematic Correspondences* because the body, with its anatomical components and physiological processes, was included in the *yin-yang Five Phases* system, just like the entire social and natural environment surrounding it. In this system, all individual appearances were viewed as parts of a greater whole whose internal transformations were never to be considered in isolation but only in relationship with each other.[484]

Essential Substances

Qi, blood, essence, and fluids are the basic elements of all physiologic activity, according to Wiseman and Ellis. *Qi* has the ability to vitalize, propel, and warm the body, and is yang in nature. Blood and fluids are the sustenance of the body, nourishing and moistening the entire organism, and are yin in nature. Essence is the basis of physical development and reproduction. Essence is the surplus potential of the human body, and the basis of blood and fluid production.[485] It is interesting to note that the Wiseman and Ellis translation of a textbook for first-year Chinese medical students in China's Colleges

of Chinese Medicine in Beijing, Nanjing, and Shanghai does not include spirit as one of the essential substances.

Kaptchuk, using the *Inner Classic* as his main source, summarized the five essential substances, including spirit, in the following manner:

- *Qi* is fundamental to Chinese medical thinking. But *qi* is neither an immutable material nor a merely vital energy. Kaptchuk described *qi* as matter on the verge of becoming energy, or energy at the point of materializing.[486]
- Blood is not the same as what western science calls blood. The major activity of blood is to circulate continuously through the body while nourishing, maintaining, and to a lesser degree moistening various parts. Blood moves through vessels and meridians. It is considered a yin substance because of its liquid qualities.[487]
- Essence is the substance that underlies all organic life and is the source of change. It has the qualities of fluidity, support, and nutrition. Essence is also the basis of reproduction and development.[488]
- Fluids are bodily liquids other than blood, such as sweat, saliva, gastric juices, and urine. The fluids function to moisten and partly nourish the hair, skin, membranes, orifices, flesh, muscles, inner organs, joints, brain, marrow, and bones. Although the fluids are considered essential substances they are understood as being less essential than qi, blood, essence, and spirit.[489]

- Spirit is the substance unique to human life, added Kaptchuk. Spirit represents the vitality behind essence and qi. It indicates the presence of human consciousness. Spirit also possesses a material quality.[490]

The Bowels and Viscera

> …In terms of zang fu[491] organs, the heart, liver, spleen, lungs, and kidneys are the zang organs, since they are yin in nature and their function is transformation and storage. The gallbladder, stomach, large intestine, small intestine, bladder, and sanjiao (the three viscera cavities responsible for fluid metabolism) are six fu or hollow organs, and they are considered yang. Their function is reception and passage…[492]

According to Wiseman and Ellis, *The Visceral Manifestation Theory* includes all the knowledge related to the organs. This includes anatomy, physiology, pathology, identification of disease patterns and their treatment. Visceral manifestation ascribes function to the organs and categorizes organs according to function. The major categories are the bowels and viscera. The five viscera (*yin* organs) include the heart, lung, spleen, liver, and kidney. These viscera produce and handle *qi*, bones, and sense organs. The six bowels (*yang* organs) are the stomach, small intestine, large intestine, bladder, gallbladder, and triple burner (Table 22). These handle food and discharge waste. The

extraordinary organs also exist. These include the following: the brain, bones, marrow, blood vessels, uterus, and gallbladder (the gall bladder is also a bowel). Both the bowels and the extraordinary organs are subordinate to the viscera.[493]

Organs	*Yin* Organs	*Yang* Organs
Wood	Liver	Gallbladder
Fire	Heart	Small intestine
Earth	Spleen	Stomach
Metal	Lung	Large intestine
Water	Kidney	Bladder
(Pericardium)	Triple burner	

Table 22. Yin and Yang Organs

Chinese medicine seeks to understand the functional activity rather than to search for a fixed somatic structure that performs a particular activity, Kaptchuk reminded the student of Chinese medicine. For this reason, the Chinese do not have a system comparable to an anatomical system found in the Western biomedical tradition.[494] Wiseman and Ellis supported Kaptchuk's observation. The visceral manifestation theory places considerable emphasis on the relationship among bowels and viscera instead of focusing solely on the functional characteristics of each bowel and viscus in isolation.[495]

An as example, Kaptchuk described the organ known as the liver. The Chinese liver is defined first by the functions associated with it, whereas the Western biomedical liver is defined by its physical structure. In addition, the Chinese have identified organs not recognized by Western biomedicine, such as the triple burner (san jiao), while organs such as the pancreas and adrenal glands are not recognized by Chinese medicine.[496]

Disease Causation [497]

> Every individual's life is intimately connected with nature. How people accommodate and adapt to the seasons and the laws of nature will determine how well they draw from the origin or spring of their lives. When one understands the usefulness of the ten thousand things in the universe, one will be able to effectively utilize them for the preservation of health. The universe is comprised of yin and yang. The human being has the twelve channels. Nature exhibits hot and cold seasons; the human being has deficiency and excess. When one can manage the polarity changes of the universe, assimilate the knowledge of the twelve channels, and obey the rhythms of the four seasons, one will have clarity and not be confused by any disorder. Grasping the shifts of the eight winds and the transformation of the five elements, and understanding these in the context of a patient's health, you will gain insight into the truth.[498]

When conditions are balanced among *yin* and *yang*, and blood and *qi*, and the organs and channels complement, support, and counterbalance each other, then a harmonious state is achieved among all these elements, stated Wiseman and Ellis.[499] Furthermore, the authors asserted that in a normal state of balance, there is a constant interaction between the

human body and the environment. Disease ensues when there is a disruption of this physiological-environmental balance.[500]

The three causes of imbalance are internal, external, and neutral; Kaptchuk described the three causes of imbalance as emotion, environment, and way of life, respectively.[501]

- Internal factors: joy, anger, sadness, grief, pensiveness, fear, and fright
- External factors: wind, cold, heat or fire, dampness, dryness, and summer heat
- Neutral factors: diet, sexual activity, and other physical activity

All of these factors, argued Kaptchuk, would be considered causes according to the western biomedical paradigm. But he stressed that what is important in TCM practice is not the cause but the relationship of these many factors within a particular disease pattern. Ultimately, causality in TCM terms is merely a way to identify and qualify the more important relationships among environment, emotion, life style, health and illness.[502] The skilled TCM practitioner's art lies in her ability to identify and diagnose patterns of disease and then to treat accordingly.

Like all concepts and ideas discussed in this section, TCM philosophy is situated within a historical and political context that should be acknowledged. Hsu is acutely aware of this context and has noted that the standardized transmission of Chinese medical knowledge has gone hand in hand with a nationalistic reinterpretation of philosophical concepts such as yin-yang. This more body-centered focus on the body ecologic has led to a shift in

emphasis from the *Five Phases* to the *Five Organs*. This reinterpretation of prescriptive maxims has resulted in a more (and historically unknown) descriptive precision inspired by Western physiology, and a materialist reinterpretation of 'substance-forces' constituting and permeating the universe. Hsu has reasoned that this particular reinterpretation (and there have been many over the millennia) has led to a static view of processes, a disregard of the body's resilience, and a neglect of the Spiritual.[503]

TCM Management Therapy for Diabetes mellitus Type 2: An Initial Overview

Shanghai Research Experience

One of the underlying goals of my research at FRLHT in Bangalore, India was to contribute to the development of FRLHT as a scientific institution capable of carrying out its own clinical studies. The pilot study I developed, and that we carried out as a collaborative team, was the first step in training some of the instiution's staff in basic clinical study research design. At the same time, the experience taught me, as the outsider, the challenges involved in carrying out a rigorous scientific study on the unique issues surrounding Ayurvedic practice. On the other hand, the TCM Department at Hua Shan Hospital (affiliated with Fudan University of Shanghai) provided me the space to take this training to another level. Hua Shan is a private hospital affiliated with Harvard University. This affiliation, combined with the faculty's training in both TCM and the Western biomedical paradigm, allowed the study to progress relatively smoothly. The goal in Shanghai was not to train TCM practitioners about how to carry out an effective study (they are already excellently trained) but was to enhance my limited knowledge of

TCM practice; to allow me to witness how TCM and the Western biomedical paradigm are integrated in a unique Shanghai setting; and to offer me the opportunity to contribute to the development of a pilot study on TCM and diabetes for further future collaboration (Figures 40 and 41).

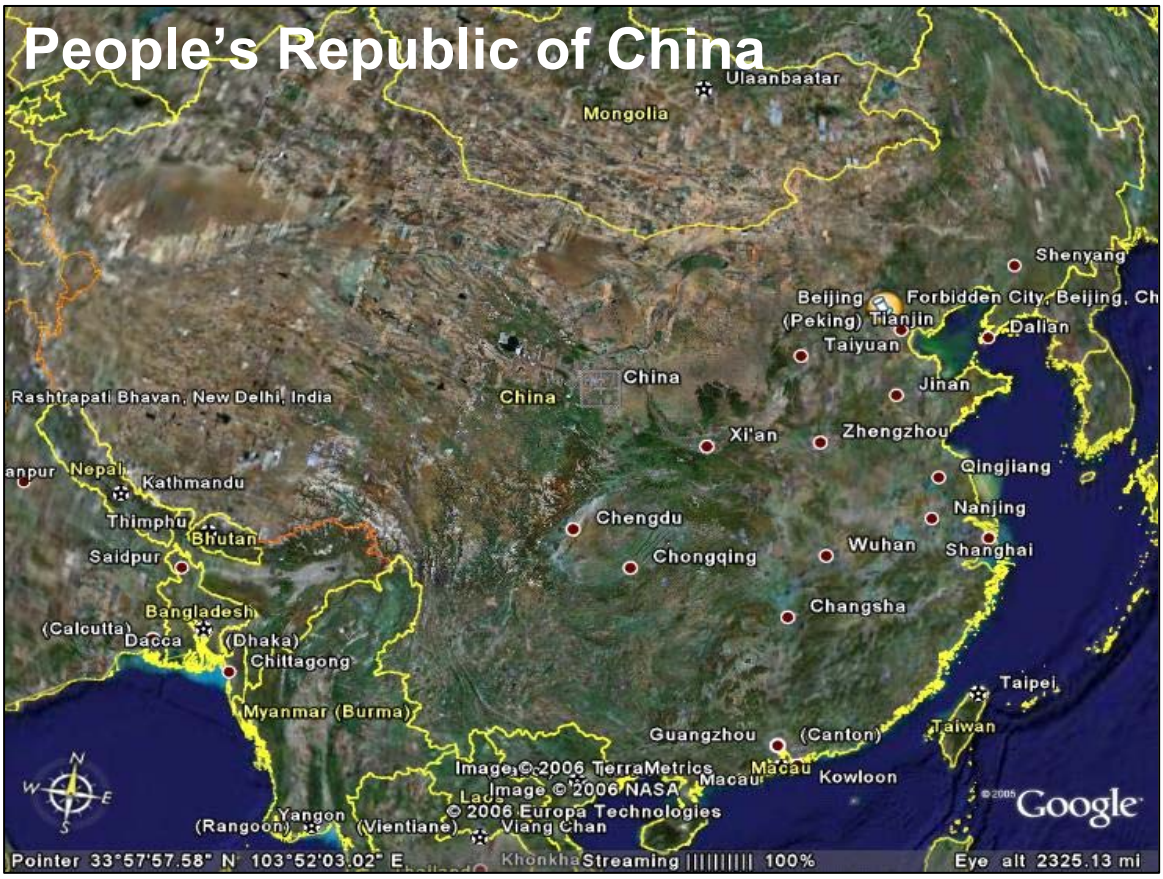


Figure 40. Map of People's Republic of China

Objectives

The purpose of this research was to collect data on how TCM practitioners treat a newly diagnosed patient with DM2 during the first appointment. The primary objective was to document the plants prescribed to patients with newly diagnosed DM2. In addition, I

documented the TCM practitioners' differential diagnoses. Each evaluation included the TCM evaluation of symptoms, diagnosis, action, and plant prescriptions. TCM Management Therapy (TCM-MT) is defined as complete TCM evaluation of disease etiology, individualized differential diagnosis, prescriptions of formulations, diet, and exercise regimens. (Acupuncture therapy was not prescribed due to logistical, time, and financial constraints).

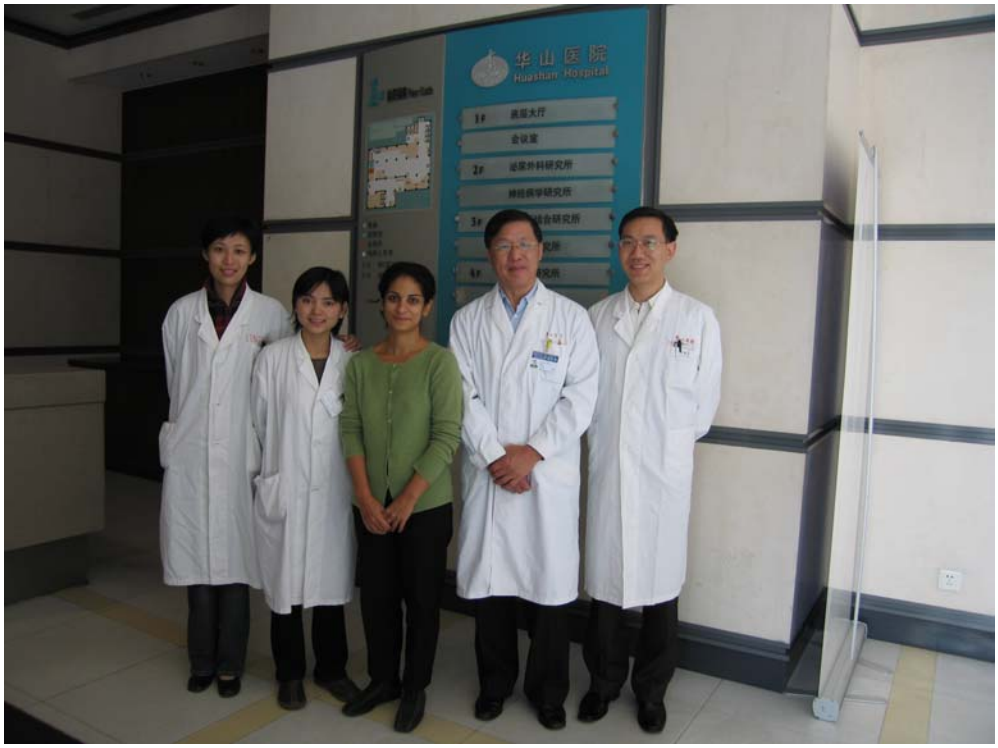


Figure 41. Hua Shan Hospital Collaborative Team for TCM-Diabetes Pilot Study (from the left: Yanming He, Chunyan He, Sarah Khan, Dr. Wenjian Wang, and Yi Liu)

Population and Sample Size

In order to access newly diagnosed patients with diabetes, the TCM department of Hua Shan Hospital in Shanghai decided to carry out a pilot study. The TCM department chose a community in Shanghai and invited the members to attend a free health check-up. The

community is known as the Longba Street community. It is affiliated with the Minghang District and lies in the west of Shanghai, adjacent to the Rainbow Bridge Airport. The area is 4.54 square kilometers. There are 110,000 residents and a floating population of 30,000. Longba is one of the biggest streets in Shanghai. The Longba Community Center welcomed the Hua Shan Hospital TCM Department to carry out the initial pilot study (Figures 42-45). This allowed the team to evaluate a community and identify new patients with diabetes.

Figure 42. Entrance to Longba Street Community Center

Figure 43. Early morning Tai qi exercises at Longba Community Center

Figure 44. View of Longba Community Center early morning classes

Figure 45. Hua Shan Hosptial TCM department staff taking blood samples of Longba Community members

Quantitative Results

From the Longba Street Community Center, 20 newly-diagnosed patients with DM2 (11 females and 9 males) were detected based on fasting blood glucose levels. The average patient age was 52.1 years (43-68 range years), the average weight was 72.8 kg (56.5-92.5 kg range), the average fasting blood glucose was 7.94 mmol/L, and the average glycated Hb was .

Plants prescribed

A total of 27 individual plants were prescribed (Table 23). The TCM team decided to prescribe a base formulation (TCM classically inspired and also based on western biomedical research data) that included plants numbered 1-6. The plants numbered 7-27 were auxiliary plants chosen to complement treatment depending on the differential

diagnoses. These additional plant products were understood to have complementary properties (assist the function of the main base formulation) or were aimed at treating a specific manifestation of a disease. As in Ayurvedic medicine, plant substitutes exist if a particular plant is not available. Often, these substitutes are from the same family. In Table 24, plant substitutes are listed based on *A Practical Chinese-English Dictionary of Traditional Chinese Medicine* (a reference book my TCM colleagues suggested I utilize). A breakdown of plants 1-27, and the number of patients who received each one, is represented in the pie-chart of Figure 46.

Table 23. Plants utilized in Hua Shan Hospital TCM-Diabetes Study: Base formula 1-6; and auxiliary plants 7-27

1. ***Alisma orientalis*** (Sam.) Juzep (Alismataceae)
2. ***Astragalus membranaceus*** Bunge, ***A. membranaceus mongholicus*** Bunge (Leguminosae)
3. ***Coptis chinensis*** Franch., ***C. deltoidea*** C.Y. Cheng. & Hsiao., ***C. teetoides*** C.Y. Cheng (Ranunculaceae)
4. ***Morus alba*** L. (Moraceae)
5. ***Polygonatum odoratum*** L. (Liliaceae)
6. ***Typha angustifolia*** L., ***Typha orientalis*** C.Presl (Typhaceae)
7. *Artemisia capillaries* Thunb., *A. scoparia* Waldst. & Kit. (Compositae)
8. *Atractylodes macrocephala* Koidz. (Compositae)
9. *Coix lacryma-jobi* L. (Gramineae)
10. *Curcuma aromatica* Salisb., *C. kwangsiensis* S.G. Lee & C.F. Liang, *C. longa* L., *C. zedoaria* Roxb. (synonym for *C. aromatica*) (Zingiberaceae)
11. *Cyperus rotundus* L. (Cyperaceae)
12. *Epimedium brevicornum* Maxim., *E. koreanum* Nakai, *E. sagittatum* Maxim. (Berberidaceae)
13. *Gardenia jasminoides* J. Ellis (Rubiaceae)
14. *Gastrodia elata* Blume. (Orchidaceae)
15. *Gypsum fibrosum* (calcium sulfate)
16. *Lonicera japonica* Thunb., *L. hypoglauca* Miq., L. confusa DC*, L. dasystyla* Rehder (Caprifoliaceae)
17. *Lycium barbarum* L. (Solanaceae)
18. *Lysimachia christinae* Hance (Primulaceae)
19. *Ophiopogon japonicus* (Thunb.) Ker-Gawl. (Liliaceae)
20. *Phellodendron chinense* Schneid, P. amurense Rupr. (Rutaceae)
21. *Pinellia ternata* (Thunb.) Makino. (Araceae)
22. *Pleione bulbocodioides* (Franch.) Rolfe (Orchidaceae) or related species
23. *Polygonum multiflorum* Thunb. (Polygonaceae)
24. *Poria cocos* (Schw.) Wolf (Polyporaceae)
25. *Pueraria lobata* (Willd.) Ohwi, *P. thomsonii* Benth. (Fabaceae)
26. *Scrophularia ningpoensis* Hemsl. (Scrophulariaceae)
27. *Zizyphus spinosa* (Rhamnaceae)

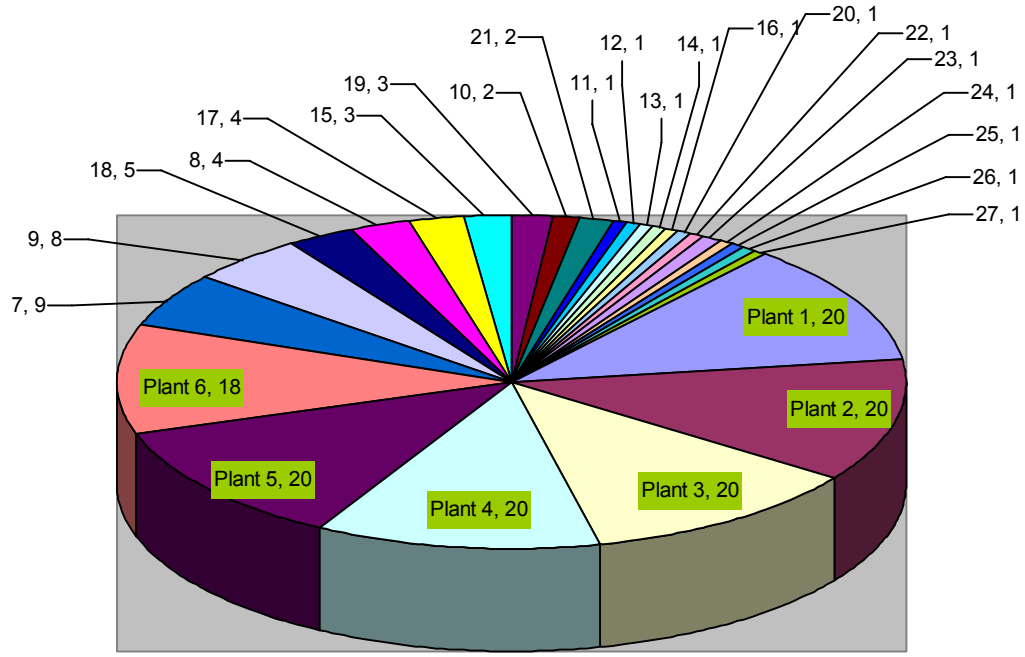


Figure 46. Breakdown of Plants 1-27 and the Number of Patients (ie., Plant 1, 20 patients)

The 6 plants used in the base formula, and their respective TCM actions, are presented in Table 24. As stated earlier, TCM (and Ayurvedic) practitioners are able to substitute plants in formulations when one is not available, in some cases. The 6 base formula plants actually included a total of 10 plants, and these are included in Table 24. In order to search Medline, I used the Latin binomial name and also the Pinyin-Chinese name for each plant in the search engine separately. On several occasions few or no study articles emerged. Once the Chinese name was put into the search engine, additional studies were located. Of the 31 articles cited in Table 24, 15 were in Chinese, and an additional 3 were published in the *American Journal of Chinese Medicine*.

Of the 10 plants searched, only 3 plants (*Atragalus membranaceus, Morus alba,* and *Polygonatum odoratum*) had studies related to diabetes. The number of studies related to

diabetes was 8 (these are highlighted in the grey scale in Table 24). Four were randomized controlled trials (RCT), and one was a case report with all testing *A. membranaceus*. The other 3 studies included two on *M. alba* and one on *P. odoratum*.

Table 24. Recent Medical Research on 6 plants of the base formulation; Studies pertaining to diabetes treatments are highlighted

Latin binomial	Medical Literature References
1. ***Alisma orientalis***	Shen AY, Wang TS, Huang MH, Liao CH, Chen SJ, Lin CC. 2005. Antioxidant and antiplatelet effects of dang-gui-shao-yao-san on human blood cells. Am J Chin Med. 33 (5): 747-58.
	Cao ZG, Liu JH, Radman AM, Wu JZ, Ying CP, Zhou SW. 2003. [An experimental study of effect of different extracts of Alisma orientalis on urinary calcium oxalate stones formation in rats]. [Chinese] Zhongguo Zhong Yao Za Zhi. 28 (11): 1072-5.
	Cao ZG, Liu JH, Zhou SW, Wu W, Yin CP, Wu JZ. 2004. [The effects of the active constituents of Alisma orientalis on renal stone formation and bikunin expression in rat urolithiasis model]. [Chinese] Zhonghua Yi Xue Za Zhi. 84 (15): 1276-9.
	Zhou L, Chen ZX, Chen JY. 1995. [Effect of wu lin powder and its ingredients on atrial natriuretic factor level in mice]. [Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 15 (1): 36-7.
2. ***Astragalus membranaceus A. membranaceus mongholicus***	Liu KZ, Li JB, Lu HL, Wen JK, Han M. 2004. [Effects of Astragalus and saponins of Panax notoginseng on MMP-9 in patients with type 2 diabetic macroangiopathy]. [Chinese] Zhongguo Zhong Yao Za Zhi. 29 (3): 264-6. Randomized Controlled Trial (RCT)
	Wang HY, Chen YP. 2004. [Clinical observation on treatment of diabetic nephro-pathy with compound fructus arctii mixture]. [Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 24 (7): 589-92. RCT
	Huang CL, Lu YP. 2003. [Effect of Astragalus injection on insulin resistance in auxiliary treating patients with diabetes mellitus type 2]. [Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 23(10):779-80. RCT
	Liu ZQ, Li QZ, Qin GJ. 2001. [Effect of Astragalus injection on platelet function and plasma endothelin in patients with early stage diabetic nephropathy]. [Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 21(4):274-6. RCT
	Wang F. 2002. Twenty-eight cases of diabetic foot ulcer and gangrene treated with the Chinese herbal medicine combined with injection of ahylsantinfarctase. J Tradit Chin Med. 22 (1): 3-4. Case Report
3. ***Coptis chinensis***, ***C. deltoidea***, ***C. teetoides***	Lin CC, Ng LT, Hsu FF, Shieh DE, Chiang LC. 2004. Cytotoxic effects of Coptis chinensis and Epimedium sagittatum extracts and their major constituents (berber-ine, coptisine and icariin) on hepatoma and leukaemia cell growth. Clin Exp Pharmacol Physiol. 31(1-2):65-9.
	Wang S, Fan M, Bian Z. 2001. [Experimental study of bacteriostatic activity of Chinese herbal medicines on primary cariogenic bacteria in vitro]. [Chinese] Zhonghua Kou Qiang Yi Xue Za Zhi. 36 (5): 385-7.
	Wang J, Wang Z, Tang G. 2003. TCM treatment of extrasystole with huanglian shengmai yin--a report of 357 cases. J Trad Chin Med. 23 (1): 35-7. RCT
	Kong XT, Fang HT, Jiang GQ, Zhai SZ, O'Connell DL, Brewster DR. 1993. Treatment of acute bronchiolitis with Chinese herbs. Arch Dis Child. 68 (4): 468-71. RCT
	Wang JR. 1989. A clinical observation of huang lian sheng mai yin in treatment of 86 patients with premature beat. J Tradit Chin Med. 9 (3): 157-8.
4. ***Morus alba***	Wattanapitayakul SK, Chularojmontri L, Herunsalee A, Charuchongkolwongse S, Niumsakul S, Bauer JA. 2005. Screening of antioxidants from medicinal plants for cardioprotective effect against doxorubicin toxicity. Basic Clin Pharmacol Toxicol. 96 (1): 80-7.

	Sohn HY, Son KH, Kwon CS, Kwon GS, Kang SS. 2004. Antimicrobial and cytotoxic activity of 18 prenylated flavonoids isolated from medicinal plants: Morus alba L., Morus mongolica Schneider, Broussnetia papyrifera (L.) Vent, Sophora flavescens Ait and Echinosophora koreensis Nakai. Phytomedicine. 11 (7-8): 666-72.
	Kusum M, Klinbuayaem V, Bunjob M, Sangkitporn S. 2004. CT Preliminary efficacy and safety of oral suspension SH, combination of five chinese medicinal herbs, in people living with HIV/AIDS ; the phase I/II study. J Med Assoc Thai. 87 (9): 1065-70.
	Hussain Z, Waheed A, Qureshi RA, Burdi DK, Verspohl EJ, Khan N, Hasan M. 2004. The effect of medicinal plants of Islamabad and Murree region of Pakistan on insulin secretion from INS-1 cells. Phytother Res. 18 (1): 73-7.
	Oh H, Ko EK, Jun JY, Oh MH, Park SU, Kang KH, Lee HS, Kim YC. 2002. Hepa-toprotective and free radical scavenging activities of prenylflavonoids, coumarin, and stilbene from Morus alba. Planta Med. 68 (10): 932-4.
	Lee SH, Choi SY, Kim H, Hwang JS, Lee BG, Gao JJ, Kim SY. 2002. Mulberro-side F isolated from the leaves of Morus alba inhibits melanin biosynthesis. Biol Pharm Bull. 25 (8): 1045-8.
	Nam SY, Yi HK, Lee JC, Kim JC, Song CH, Park JW, Lee DY, Kim JS, Hwang PH. 2002. Cortex mori extract induces cancer cell apoptosis through inhibition of microtubule assembly. Arch Pharm Res. 25 (2): 191-6.
	Kim SY, Gao JJ, Kang HK. 2000. Two flavonoids from the leaves of Morus alba induce differentiation of the human promyelocytic leukemia (HL-60) cell line. Biol Pharm Bull. 23 (4): 451-5.
	Ionescu-Tirgoviste C, Popa E, Mirodon Z, Simionescu M, Mincu I. 1989. [The effect of a plant mixture on the metabolic equilibrium in patients with type-2 dia-betes mellitus]. [Article in Romanian] Rev Med Interna Neurol Psihiatr Neurochir Dermatovenerol Med Interna. 41 (2): 185-92.
5. ***Polygonatum odoratum***	Choi SB, Park S. 2002. A steroidal glycoside from Polygonatum odoratum (Mill.) Druce. improves insulin resistance but does not alter insulin secretion in 90% pancreatectomized rats. Biosci Biotechnol Biochem. 66 (10): 2036-43.
	Lin HW, Han GY, Liao SX. 1994. [Studies on the active constituents of the Chinese traditional medicine Polygonatum odoratum (Mill.) Druce]. [Chinese] Yao Xue Xue Bao. 29 (3): 215-22.
	Xiao J, Cui F, Ning T, Zhao W. 1990. [Effects of alcohol extract from Polygona-tum odoratum (Mill.) Druce and Cuscuta australis R. Br. on immunological func-tion of mice injured by burns]. [Chinese] Zhongguo Zhong Yao Za Zhi. 15 (9): 557-9, 578.
6. ***Typha angustifolia, T. orientalis***	Xi XR, Li SX. 2000. [Analysis on contents of flavonoids and polysaccharides in pollen of Typha angustifolia L. and its different processed products]. [Chinese] Zhongguo Zhong Yao Za Zhi. 25 (1): 25-8.
	Gao G, Liao M, Feng Y. 1998. [Determination of flavonoids and quality evaluation of Chinese traditional drug "puhuang"]. [Chinese] Yao Xue Xue Bao. 33 (4): 300-3.
	Zheng RX, Fang SM, Li ZM, Zhang XM. 1993. [Prevention of arrhythmia in rats by puhuang]. [Chinese] Zhongguo Zhong Yao Za Zhi. 18 (2): 108-10, 127.
	Luo JA, Peng YM, Xia YC, Lei Y. 1993. [Therapeutic effects of Chinese drugs on early renal damage of rats caused by fish bile]. [Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 13 (2): 98-9, 70.
	Yang YH. 1986. [Chemical constituents of Typha angustata and Typha angustifolia]. [Chinese] Zhong Yao Tong Bao. 11 (12): 39-42.

TCM symptoms

A total of thirty-two symptoms were documented. They were either self-reported by the patient or noted by the TCM practitioner during the patient-intake period (Figure 47). These symptoms were broken down into the following general categories: appetite, sleep, bowel movement and urination, pulse diagnosis, and tongue diagnosis. The patients also reported the following symptoms: chest feels tight, trembling fingers, cold feeling, dizziness, face is red, heavy feeling, overweight, sweaty, sweating all over, fatigue, hungry, overeats, and thirsty.

Figure 47. Dr. Wenjian Wang during patient recruitment with his graduate students

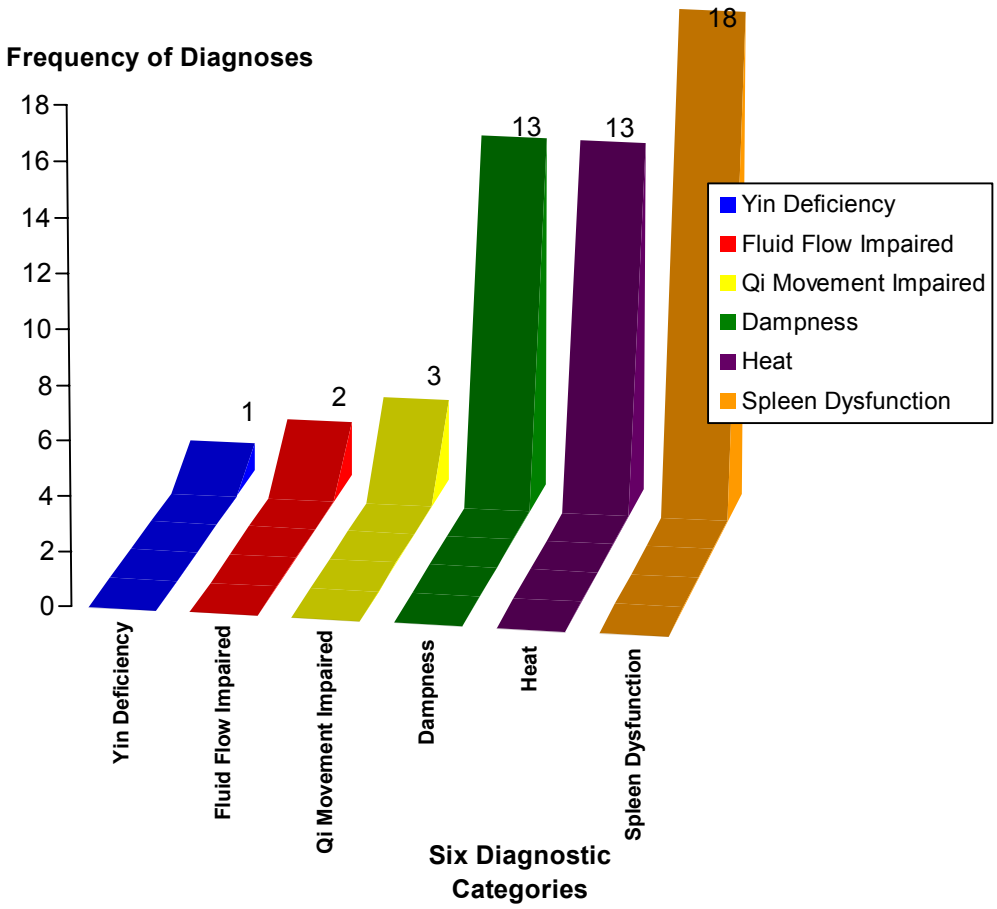


Figure 48. Breakdown of TCM Diagnoses

TCM diagnosis

In terms of TCM diagnosis, fifty diagnoses were documented. These diagnoses were broken down into the following six categories in descending order of frequency: spleen (18), heat (13), dampness (13), *qi* movement impaired (3), fluid flow impaired (2), and *yin* deficiency (1) (Figure 48).

TCM action

The TCM practitioners documented 39 actions which included the following categories in descending order of frequency: invigorate spleen (14), eliminate heat (10), nourish *yin* (9), remove dampness (4), and promote fluid production (2) (Figure 49).

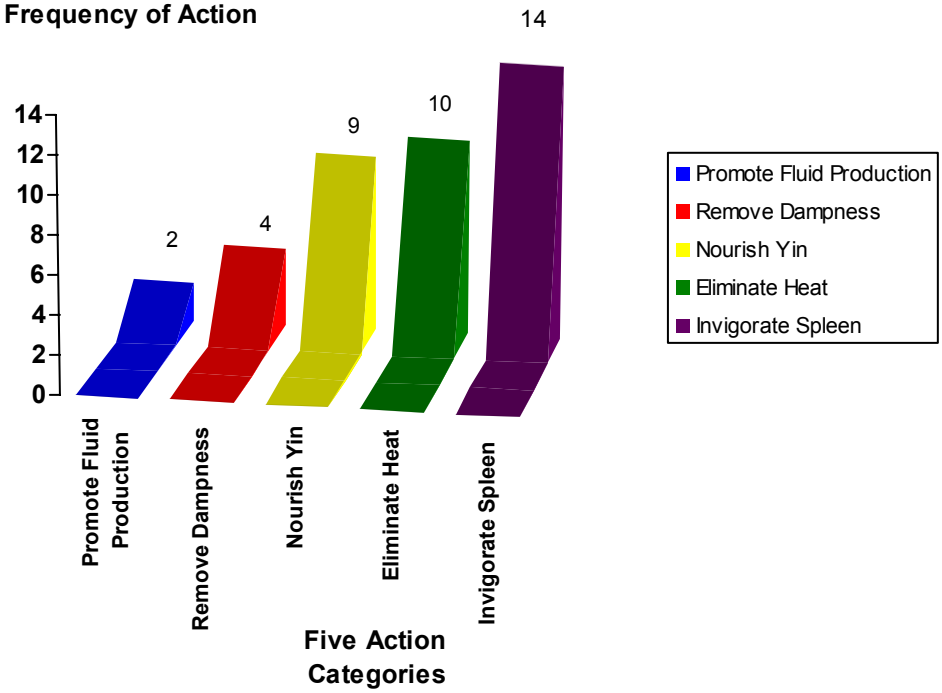


Figure 49. Breakdown of TCM Actions

Table 25 displays the 6 base plants formula (including the 4 substitutes) and the TCM action as defined by *A Practical Chinese-English Dictionary of Traditional Chinese Medicine*.

Table 25. Base Formula of 6 plants and their TCM actions

Latin binomial and Chinese Pinyin	Actions	Properties
Alisma orientalis (Sam.) Juzep (Alismataceae), Zé xiè	To cause diuresis and remove damp-heat [504]	Dried tuber, 15 g
Astragalus membranaceus Bunge, ***A. membranaceus mongholicus*** Bunge (Leguminosae), Huáng qí	To reinforce qi and strengthen the superficial resistance, and promote pus discharge and growth of new tissue [505]	Dried root, 30 g
Coptis chinensis Franch., ***C. deltoidea*** C.Y. Cheng. & Hsiao., ***C. teetoides*** C.Y. Cheng (Ranunculaceae), Huáng lián	To remove damp heat, quench fire, and counteract toxicity [506]	Dried rhizome, 10 g
Morus alba L. (Moraceae), Sāng yè	To expel wind-heat, clear away heat from the lungs, subdue hyperactivity of the liver, and improve eyesight [507]	Dried leaf, 15 or 20 g
Polygonatum odoratum L. (Liliaceae), Yù zhú	To tonify yin and moisten the lungs, promote the production of body fluid, and nourish the stomach [508]	Dried rhizome, 20 g
Typha angustifolia L., ***Typha orientalis*** C.Presl (Typhaceae), Pú huāng	To activate blood flow and remove blood stasis, and arrest bleeding and promote healing up of wounds [509]	Pollen, 15 g

Conclusions

The TCM base formulation consisted of six plants (plus four substitutes). An additional 21 auxiliary plants were part of the practitioner's repertoire. Of the base formulation plants, three (*Atragalus membranaceus, Morus alba,* and *Polygonatum odoratum*) demonstrated some type of anti-diabetic effect in studies documented on Medline. Nearly half of the studies were available only in Chinese, although abstracts were available in English for most. Thirty-two symptoms were documented along with 50 diagnoses broken down into six categories. The TCM practitioners prescribed 39 actions and these actions were grouped into five categories.

The purpose of TCM research in Shanghai was to compare Ayurvedic and TCM treatments for DM2, specifically to assess the plants used. (A comparison and contrast of Ayurveda and TCM theory and practice will have to be the subject of another dissertation). Northern and Southern India differ dramatically from linguistic, cultural, historical, and ethnic perspectives. The plants utilized at GAU in the northwest of India perhaps reflected the fact that the practitioners and professors had been trained predominantly in north Indian institutions. Furthermore, the student population consisted predominantly of Gujarati residents and/or from northern India, in general. The Ayurvedic practitioners from FRLHT in the southern city of Bangalore were all from southern India and had been trained in Ayurveda with an emphasis on South Indian Ayurvedic traditions and texts. A comparison reveals that the 29 plants utilized in *Chandraprabha guggulu vati* (CPGV—Chapter 5, GAU section) and the 32 plants utilized in the FRLHT Ayurvedic Management Therapy study had the following ten plants in common: *Berberis aristata* DC Berberidaceae, *Cedrus deodara* Loud. Pinaceae, *Curcuma longa* L. Zingiberaceae, *Cyperus rotundus* L. Cyperaceae, *Emblica officinalis* Gaertn. Euphorbiaceae, *Terminalia arjuna* Wight & Arn. Combretaceae, *Terminalia bellirica* (Gaertn.) Roxb. Combretaceae, *Terminalia chebula* Retz. Combretaceae, *Tinospora cordifolia* Miers Menispermaceae, and *Zingiber officinale* Rosc. Zingiberaceae. A comparison between the aforementioned Ayurvedic plants with the 27 TCM-Shanghai plants demonstrated two in common: *Curcuma longa* L. and *Cyperus rotundus* L. Both these plants were part of the auxiliary/complementary TCM formulation and were not included in the base formula.

Curcuma longa has been researched extensively and has demonstrated a multitude of effects in *in vitro*, animal, and human studies.[510] Although *C. longa* and some of its isolated compounds demonstrated their main effects as an antimicrobial, potentially cytotoxic, and immunomodulating agents, it has shown effect also in relation to the treatment of diabetes in animal models (see Appendix F). On the other hand, *Cyperus rotundus* has demonstrated effect based on a review of the literature but to a much lesser extent when compared to *C. longa*.[511] There does not appear to be any *Cyperus rotundus* studies showing any type of antidiabetic effect in *in vitro*, animal or human studies.

In addition to the medical literature review of all the plants used in the three studies conducted at GAU, FRLHT, and Shanghai, the data on these plants can be evaluated and assessed from multiple Ayurvedic and TCM perspectives. For example, I have compiled two simple tables from basic Ayurvedic and TCM plant classification descriptions (Tables 27 and 28) of *Curcuma longa* and *Cyperus rotundus*.

Table 26. Ayurvedic *Dravyaguna* Classification of *Haridra* and *Musta*

Latin binomial, Family, Sanskrit name, Part used	***Guna***	***Rasa***	***Vipaka***	***Virya***
Curcuma longa L. Zingiberaceae, Haridra, Rhizome	Dry, Light	Bitter, Pungent	Pungent	Hot
Cyperus rotundus L. Cyperaceae, Musta, Rhizome	Light, Dry	Pungent, Bitter, Astringent	Pungent	Cold

Table 27. TCM Classification of *Yu jin* and *Xian fu zi*

Latin binomial, Chinese Pinyin name, Part used	**Temperature and Tastes**	**Channels**	**Actions**
Curcuma aromatica Salisb., *C. kwangsiensis* S.G. Lee & C.F. Liang, *C. longa* L., *C. zedoaria* Roxb. Yù jīn Dried tuberous root	Cool, Acrid, and Bitter [512] [513]	Heart, Lung, and Liver [514] [515]	Promote the flow of qi [516] [517] [518] Eliminate blood stasis [519] [520] [521] Calm the nerves [522] [523] Ease the mind [524] Reduces jaundice [525] [526] Cools blood [527] [528]
Cyperus rotundus L. Xiāng fù zǐ Dried tuber	Slightly warm [529] Acrid [530] [531] [532] Bitter [533] [534] [535] Slightly sweet [536] [537] Neutral [538] [539]	Liver Three burners [540] [541] and Stomach [542]	Remove stagnation of qi [543] Spreads and regulates liver qi [544] [545] Regulates menstruation and relieves pain [546] [547] [548]

The two tables are just one example of how plant information may be organized and classified. The representation of plant information in this format provides researchers another opportunity to asses, evaluate, and understand medicinal plants from a non-Western biomedical paradigm. Information could be evaluated based on Ayurvedic and TCM differential diagnosis. As another example, vataja prameha patients tend to be lean, whereas kaphaja prameha patients tend towards obesity. Would we find this affirmed if a larger sample is tested? Furthermore, would we be able to then document patterns based on diabetic biomarkers and/or inflammatory markers associated with the disease process? These exercises alone could reveal new patterns, insights, formulations and/or treatment protocols not imagined when limited to one medical paradigm. In Bangalore and Shanghai, where I worked with collaborative teams to execute the studies, the Ayurvedic and TCM practitioners were engaged in continually evaluating, comparing, and improving their respective medical traditions. By engaging in this type of research, I hope to engender this collaborative effort where both scientific traditions are rigorously challenged, and potentially improved by the process.

Chapter 8: Final Dissertation Conclusions

Introduction

In Chapter 1, I presented perspectives on the discipline of ethnobotany and the particular challenges ethnobotanists encounter when conducting medicinal plant research. In order to advance the ethnobotanical discipline, Alexiades challenged researchers to develop a sound methodology by defining the research problem, selecting a conceptual model, operationalizing the chosen variables, and choosing adequate field techniques.[549] Furthermore, Farnsworth reminded the ethnobotanical researcher to include more detailed information when collecting data, particularly, the method of preparation of the medicine; the dosage; the source of information; the route of administration; and the specific medical use and/or symptomatology of the disease.[550] Balick, Farnsworth, and Lewis and Elvin-Lewis challenged research scientists to consider the effects of plant preparation, entire plants, and plant formulations as opposed to isolated single bioactive ingredients. Lewis and Elvin-Lewis, in particular, encouraged researchers to pay attention to the multiple compounds in a single plant and the synergistic roles these, often disregarded, secondary compounds may demonstrate. [551] [552] [553] [554] Cox emphasized the limitations of the ethnobotanical methodology in that many indigenous cultures have amply demonstrated knowledge of bioactivity of substances without the tools of modern Western biomedicine.[555] Finally, Anderson asserted that, in fact, all science is "ethnoscience" including the Western biomedical paradigm. By acknowledging this fact, Anderson proposed that any approach may be classified as a science as long as it

generates principles that systematize and extend beyond observations. Anderson proposed the term "empirical, practice-based knowledge of the world."[556]

In Chapter 2, Ayurveda and TCM, two empirical, practice-based knowledge systems of the world, were presented in terms of their historical treatment of madhumeha and xiao ke, respectively. In Chapters 3 and 4, I focused exclusively on the history of Ayurveda, and its philosophy, and a review of Ayurvedic basic theories. I then introduced the basic principles of pathology, treatment, and Dravyaguna, that branch of Ayurveda that deals with pharmacology. I discussed how practitioners classify plants in order to treat madhumeha. In Chapter 5, I presented the detailed pilot clinical research protocol approved by the Internal Review Boards of City University of New York (CUNY) Graduate Center, New York; St. John's Medical College and Hospital, Bangalore, India; and Hua Shan Hospital, Fudan University, Shanghai, China. The creation of this clinical research tool was key in developing a rigorous methodology for research both in India and China. In Chapters 6 and 7, I presented the research findings of my fieldwork in India and China with an emphasis on the pilot clinical studies conducted in Bangalore and Shanghai.

Research Results Summary

In this section, a research summary from study sites in Gujarat, Kerala, Bangalore, and Shanghai is presented. In Gujarat, the treatments prescribed by the two Ayurvedic practitioners consisted predominantly of individual or medicinal plants formulations. Of the six formulations described by the Ayurvedic physicians, three are classical Ayurvedic formulations, and three are classically inspired single plants or formulations. During my

interviews with Drs. H.M. Chandola and D. Bhatt about plant formulations, both concluded the *Chandraprabha guggulu vati* (CPGV) was most often prescribed because of documentation in Ayurvedic texts and its efficacy with their own patients in the clinic. Ayurvedic classical texts provide extensive herbal-mineral formulations, detailed regimens, and diet modification protocols to treat all types of *prameha*, including *madhumeha*. Chandraprabha guggulu vati (CPGV), included up to 29 different plants depending on the classical text referenced.[557] [558] [559] CPGV was found to be the most prescribed classical formula in the small prospective and retrospective studies conducted at GAU. Furthermore based on a review of the medical literature, a large number of the plants (93%) used in CPGV show some type of effect. In addition, a review of the individual plants in this classical formulation revealed multiple effects for many conditions: cardiovascular (20%), *Diabetes mellitus* (10.7%), antioxidant (9%), immunomodulating (7.6%), and anti-inflammatory and analgesic (4.5%).

While in Kerela at AVS, I gained insight into the practical applications of the Kerala Ayurvedic treatment protocols. By experiencing the treatment myself, I was no longer a mere observer but a participant-observer, thereby increasing my understanding of the theory by engaging in the process and documenting my own experience.

The results of the pilot clinical research study conducted in Bangalore demonstrated that in the entire sample and the sub-sample of this small-scale pilot study, AMT did not have a significant effect on reducing FBG by more than 20 mg/dL, which suggests that AMT is not better than good control of diet and exercise. AMT did not affect other secondary

efficacy variables according to the 95% confidence intervals in Tables 21 and 22. However, AMT did significantly reduce HDL-cholesterol, LDL-cholesterol, and weight in the entire sample and sub-sample patient populations. Although lower HDL-cholesterol is not desirable, reductions of LDL-cholesterol and weight are considered beneficial for DM2 patients.

In the pilot clinical research study in Shanghai, the TCM base formulation consisted of six plants (plus four substitutes). An additional 21 auxiliary plants were part of the practitioner's repertoire. Of the base formulation plants, three (*Atragalus membranaceus, Morus alba,* and *Polygonatum odoratum*) demonstrated some type of anti-diabetic effect in studies documented on Medline. Nearly half of the studies were available only in Chinese, although abstracts were available in English for most. Thirty-two symptoms were documented along with 50 diagnoses broken down into six categories. The TCM practitioners prescribed 39 actions and these actions were grouped into five categories.

The purpose of TCM research in Shanghai was to compare Ayurvedic and TCM treatments for DM2, specifically to assess the plants used. A comparison reveals that the 29 plants utilized in *Chandraprabha guggulu vati* (CPGV—Chapter 5, GAU section) and the 32 plants utilized in the FRLHT Ayurvedic Management Therapy study had the following ten plants in common: *Berberis aristata* DC Berberidaceae, *Cedrus deodara* Loud. Pinaceae, *Curcuma longa* L. Zingiberaceae, *Cyperus rotundus* L. Cyperaceae, *Emblica officinalis* Gaertn. Euphorbiaceae, *Terminalia arjuna* Wight & Arn. Combretaceae, *Terminalia bellirica* (Gaertn.) Roxb. Combretaceae, *Terminalia chebula*

Retz. Combretaceae, *Tinospora cordifolia* Miers Menispermaceae, and *Zingiber officinale* Rosc. Zingiberaceae. A comparison between the aforementioned Ayurvedic plants with the 27 TCM-Shanghai plants demonstrated two in common: *Curcuma longa* L. and *Cyperus rotundus* L. Both these plants were part of the auxiliary/complementary TCM formulation and were not included in the base formula.

In addition to the medical literature review of all the plants used in the three studies conducted at GAU, FRLHT, and Shanghai, the data on these plants can be evaluated and assessed from multiple Ayurvedic and TCM perspectives. The representation of plant information from an Ayurvedic or TCM pharmacological perspective, for example, provides researchers another opportunity to asses, evaluate, and understand medicinal plants from a non-Western biomedical paradigm. Information could be evaluated based on Ayurvedic and TCM differential diagnosis. For example, vataja prameha patients tend to be lean, whereas kaphaja prameha patients tend towards obesity. Would we find this affirmed if a larger sample is tested? Furthermore, would we be able to then document patterns based on diabetic biomarkers and/or inflammatory markers associated with the disease process? These exercises alone could reveal new patterns, insights, formulations and/or treatment protocols not imagined when limited to one medical paradigm. In Bangalore and Shanghai, where I worked with collaborative teams to execute the studies, the Ayurvedic and TCM practitioners were engaged in continually evaluating, comparing, and improving their respective medical traditions.

The original motivation to do research on DM2 was based on the Khan and Balick review of the literature where it was found that 25/166 commonly used Ayurvedic plants demonstrated some type of glucose altering effect in *in vitro*, *in vivo* or in human studies.[560] In the Gujarat study where 29 plants were used to treat patients with DM2, three plants (*Corandrum sativum, Swertia chirata,* and *Tinospora cordifolia*) were common to the Khan and Balick literature review. In the Bangalore pilot clinical research study, the four Madhumeha formulations included two plants found in Khan and Balick paper: *Ficus religiosa* and *Tinospora cordifolia*.[561] In the Shanghai study, no plants from the initial literature review were common. Why was there not more of an overlap in terms of the plants demonstrating potentially antidiabetic effects based on the literature review and those plants prescribed in the field in India? Perhaps an approach that includes formulations, and the possibility that these plant mixtures act synergistically or additively in some capacity, in their entirety needs assessment.

In order to shift away from the research paradigm that searches for a single, isolated compound, I chose to test Ayurvedic Management Therapy for DM2. Testing patient outcomes involving traditional plant formulations and treatment protocols may be the first step in identifying effective treatment protocols. A move away from identifying bioactive ingredients and towards identifying effective formulations, management treatments, or protocol strategies may be one way to help patients who are suffering from disease. However, in order to introduce those plants, plant formulations, or treatment protocols from the more empirical, practice-based knowledge systems into collaboration with the Western biomedical paradigm, an approach that respects the parameters of both

traditions should be developed. By engaging in this type of research, I hope to engender this collaborative effort where both scientific traditions are rigorously challenged, and potentially improved by the process.

Research Achievements

In my research in India and China, I attempted to incorporate the many aforementioned guidelines on several levels. I worked to advance the discipline of ethnobotany; to contribute concurrently to the development of Ayurvedic and TCM research disciplines; to provide integrative medical researchers with an example of one methodology to improve collaborative efforts; and to contribute research data to public health officials about alternative treatments to a diabetes epidemic. Below I go into more details as to how I reached these goals.

- Advance the field of ethnobotany.

  In the research protocols, I utilized a clinical study research methodology where I documented the following: (a) the method of preparation of the medicine; (b) dosing (amount and frequency of use); (c) source of information; (d) route of administration; and (e) specific medical use and/or symptomatology of the disease. (See the next section, “Beyond the Box”)
- Contribute to the development of Ayurvedic and TCM research disciplines.

  In the Ayurvedic and TCM protocols, the basic Ayurveda and TCM differential diagnoses were documented according to their respective terminology.

- Provide integrative medical researchers with a methodology to improve their collaborative efforts with non-Western biomedical paradigms.

  A framework/model was provided whereby integrative medical researchers and practitioners may collaborate to treat different diseases while both or more than two paradigms accrue data.

- Contribute research data to public health officials in the United States, India and China about alternative treatments to the growing world diabetes epidemic.

  Diabetes is a world-wide epidemic. In the developing world approximately 80% of the people rely on some form of medicinal plants. Instead of eliminating and replacing these already existing health care systems, why not utilize these already intact infrastructures to promote the best of both the western biomedical and non-western biomedical models?

Future Research

Based on the research findings and challenges in Bangalore, I advise another pilot clinical study that closely adheres to inclusion/exclusion criteria and addresses the many other challenges described in Chapter 6. A lack of significant effect in the Bangalore study does not mean there was no effect. In this case, the study design was weak and needs to be improved before conclusions about the efficacy of these four madhumeha formulations can be established within this particular biomedical construct. The preliminary results on the Shanghai-TCM data demonstrate a significant reduction in both fasting blood glucose and glycated Hb (not reported in Chapter 7). Once these results are published, justification for a larger, more comprehensive clinical study is

warranted. One of several approaches may include *in vitro* or cell culture studies based on antidiabetic models where those plants in the formulation are systematically eliminated to assess where and when a synergistic or additive effect is apparent or not.

Beyond the Box: Evolving Ethnobotanical Research Paradigms

In order to advance the discipline of ethnobotany, Alexiades challenged researchers to develop rigorous theoretical frameworks.[562] The discipline has evolved so much that interdisciplinarity is essential for any successful research endeavor. As an ethnobotanist with training in and focus on clinical research, I sought to create a collaborative environment where representatives of multiple disciplines would exchange and develop a clinical research protocol that satisfied and benefited Western biomedical, Ayurvedic, and TCM research paradigms.

But in preparation for the clinical research, I sought out training that was experiential as much as academic. Rosaldo argues that "social scientists should explore their subjects [and subject matter] from a number of positions, rather than being locked into any particular one."[563] Like Hsu,[564] I chose to go beyond the traditional participant-observer role as a distanced academic. Instead, my training began by engaging in a form of participant-*experience*. I enrolled in an Ayurvedic College to study Ayurvedic basics in an Indian setting among local students and professors. This exercise was not purely academic; in fact, I became better informed about the culture of Ayurvedic Colleges in the north-west of India from the students and professors perspectives. Next, I engaged in what Balick described as immersion ethnobotany.[565] In this environment, I allowed myself to gain bodily knowledge about Ayurvedic treatment protocols. This type of

methodology provided me with a multi-sensorial research experience. As an anthropologist and ethnographer of the arts, Drewal described this approach as "body-mind work."[566] In fact during the course of my three research trips to India (2001-2004), I evolved into a better observant-*participant* in all aspects of the research projects. This shift away from the traditional anthropological paradigm of participant-*observation* towards the more bodily/sensorial engagement of an observant-*participant* resulted in my ability to run a clinical research trial more effectively in an environment and among a culture directly removed from my own.

In addition to integrating this experiential training, I also relied heavily on the tools that are used in contemporary clinical research. This rigorous clinical research protocol was developed and utilized in both Bangalore and Shanghai. The multi-faceted clinical research tool improved, complemented, enhanced, and informed all aspects of the final project.

Appendices A—M

Appendix A: IRB Exemption for Gujarat Ayurved University

Office of the Vice President for Research and Sponsored Programs

Committee on the Protection of Human Subjects

The Graduate School and University Center
The City University of New York
365 Fifth Avenue
New York, NY 10016-4309
TEL 212.817.7523 FAX 212.817.1629

To: Khan, Sarah (Biology/Plant Sciences)

From: Richard Schwartz, Ph.D.
Chairperson

Date: January 23, 2002

Subject: IRB 6-16-11-01 • "Comparative Ethnobotanical Treatments for Type II Diabetes Mellitus

I have reviewed your application for IRB consideration for the above-referenced project. This project is judged to be exempt from IRB review under *45CFR46.101.b(2).*

No further IRB review is necessary unless modifications are made to the protocol related to human research subjects.

If you have any questions, please feel free to contact me through the IRB Office at 817-7523.

c: Michael Balick

Appendix B: IRB for FRLHT-SJMCH

Office of the Vice President for Research and Sponsored Programs

Committee on the Protection of Human Subjects

The Graduate School and University Center
The City University of New York
365 Fifth Avenue
New York, NY 10016-4309
Tel 212.817.7523 Fax 212.817.1629

Date: Wednesday, May 12, 2004

To: Khan, Sarah (Biology)

Study: 04-04-0554 "A 4-Week Open Label Study to Evaluate Ayurvedic Management Therapy (AMT) of Non-Insulin Dependent Diabetes Mellitas (NIDDM)"

The Institutional Review Board (IRB) of The Graduate Center of the City University of New York has approved the above study involving humans as research subjects. This study was approved through expedited review based on 45CFR46.110.(a) 7.

IRB Number *(IRB #04-04-0554)* This number is an IRB number at the Graduate Center which should be used on all consent forms and correspondence.

Approval Date: *5/12/2004* **Expiration Date:** *5/11/2005*

This approval is for a one-year period. You should receive a courtesy renewal notice approximately four weeks before the expiration of this project's approval. However, it is your responsibility to insure that an application for continuing review approval has been submitted by the required time. RESEARCH MUST BE SUSPENDED IF YOUR APPROVAL HAS EXPIRED. In addition, you are required to submit a final report of findings at the completion of the project.

Consent Form: The approved and stamped consent form must be used by all subjects. You are responsible for maintaining signed consent forms for a period of at least three years after study completion.

Reporting: The principal investigator must report to the IRB any serious problem, adverse effect, or outcome that occurs with frequency or degree of severity greater than that anticipated. In addition the principal investigator must report any event or series of events that prompt the temporary or permanent suspension of a research project involving human subjects.

Modifications: All modifications of protocols involving subjects must have prior approval except those involving the prevention of immediate harm to a subject which need to be reported within 24 hours to the IRB.

If you have any questions, please do not hesitate to contact me through the IRB Office at 817-7525.

Sincerely,

Richard G. Schwartz, Ph.D.
Chair, Institutional Review Board

c: Michael Balick

[redacted]

Verification: By signing below, I acknowledge that I have received this letter and am aware of and agree to abide by all of its stipulations in order to maintain active approval status, including prompt reporting of adverse events/serious problems and annual continuing review. I am aware that it is my responsibility to be knowledgeable of all federal and state regulations including CUNY's Multiple Project Assurance (MPA) with the Department of Health and Human Services.

Sarah Khan 12 July 2004

Signature of P[redacted] Date

Appendix C: IRB for Fudan University, Hua Shan Hospital

Office of the Vice President for Research and Sponsored Programs

Committee on the Protection of Human Subjects

The Graduate School and University Center
The City University of New York
365 Fifth Avenue
New York, NY 10016-4309
TEL 212.817.7523 FAX 212.817.1629

Date: Wednesday, September 07, 2005

To: Khan, Sarah (Ethnobotany)

Study: 05-08-0843 "Traditional Chinese Medicine and Diabetes Mellitus, Type 2"

The Institutional Review Board (IRB) of The Graduate Center of the City University of New York has approved the above study involving humans as research subjects. This study was approved through expedited review based on 45CFR46.110.(a) 7.

IRB Number *(IRB #05-08-0843)* This number is an IRB number at the Graduate Center which should be used on all consent forms and correspondence.

Approval Date: *9/7/2005* **Expiration Date:** *9/6/2006*

This approval is for a one-year period. You should receive a courtesy renewal notice approximately four weeks before the expiration of this project's approval. However, it is your responsibility to insure that an application for continuing review approval has been submitted by the required time. RESEARCH MUST BE SUSPENDED IF YOUR APPROVAL HAS EXPIRED. In addition, you are required to submit a final report of findings at the completion of the project.

Consent Form: The approved and stamped consent form must be used by all subjects. You are responsible for maintaining signed consent forms for a period of at least three years after study completion.

Reporting: The principal investigator must report to the IRB any serious problem, adverse effect, or outcome that occurs with frequency or degree of severity greater than that anticipated. In addition the principal investigator must report any event or series of events that prompt the temporary or permanent suspension of a research project involving human subjects.

Modifications: All modifications of protocols involving subjects must have prior approval except those involving the prevention of immediate harm to a subject which need to be reported within 24 hours to the IRB.

If you have any questions, please do not hesitate to contact me through the IRB Office at 817-7525.

Sincerely,

Richard G. Schwartz, Ph.D.
Chair, Institutional Review Board

c: Michael Balick

[redacted]

Verification: By signing below, I acknowledge that I have received this letter and am aware of and agree to abide by all of its stipulations in order to maintain active approval status, including prompt reporting of adverse events/serious problems and annual continuing review. I am aware that it is my responsibility to be knowledgeable of all federal and state regulations including CUNY's Multiple Project Assurance (MPA) with the Department of Health and Human Services.

[redacted]

Appendix D: AVS Product Terminology

Definitions and description of AVS products used during Immersion Ethnobotany

Thailam	an oil mixture
Kashayam	a decoction
Churnam	a powder
Bhasmam	an ash produced from processed minerals, gems, shells
Leh(y)am	semisolid or thickened extract

Balaswagandhadi kuzhampu thailam is reputed for its ability to nourish and strengthen the body. Good for vata disorders, chronic fever, insanity, consumption, coughs, and many other ailments. Not used on the head.[567]

Dhanwantharam thailam is especially effective for vata and allied ailments. These ailments are inevitable during pregnancy and after delivery. It can also be used for snehapana, nasya and vasti. Dhanwantharam kashayam also demonstrates similar benefits. Prepared in 3, 7, 14, 21, 41 and 101 repetitions. Dose as for Ksheerabala.[568]

Kayyanyadi kera thailam is suitable for those with headaches, heat and eye ailments. Gives almost all the benefits of Bhringamalakadi, but's not so cold.[569]

Sukumaram kashayam demonstrates fast results in cases of hernia, gulma, stomach ache, indigestion and constipation, and is especially suited for menstrual disorders. Women

generally fail to conceive due to raktagulma and vaginal disorders. If taken regularly, it promotes conception. Additive: Kant bhasmam, rocksalt, asafetida or Sukumara ghritam. Pathya: Light. Dose 5 to 15 ml in fourfold water boiled and cooled.[570]

Sukumara leham has all the properties of sukumaram kashayam and ghritam. It improves digestion and alleviates stomach aches. Is good for hernia and corrects bowel movements. Dose: 5 to 15 grams.[571]

Pushyanauga choornam is good in cases of diarrhea, dysentery, bleeding piles, grahani, and raktapitta. Dose: 5 to 10 g to be taken in rice washings or honey or both.[572]

Rasnadi choornam is used for rubbing over the crown in catarrh, cold, heaviness and ache of the head and sanni; this may also be cooked in equal quantities of adatoda juice and breastmilk with castor or other oils, and applied over the crown. This is essential in rheumatism.[573]

Kantham bhasmam (powder) and ***Vanasuranadi leham*** (paste) descriptions were not available.

Pizhichil

This is a modified form of sarvangadhara, but only unctuous liquids are used. Since it is not possible to ingest such a huge quantity of oil daily, this method was devised by our

old physicians to get the same effect with a reduced quantity. Usually the quantity is four measures (one measure = 480 ml).

As in the case of dhara of the body, pizhichil is performed by four attendants, each managing the part allotted to him or her. Each attendant uses folded cloths that are as broad and thick as their palms. The fifth attendant heats the oil and supplies it to the others. As in the case of dhara of the head, after anointing the head with the prescribed oil, the warm kuzhampu is applied all over the body. After being massaged for a while in a sitting position, the patient is laid in the dhroni and the whole body is massaged with the kuzhampu. Repeatedly, the attendants dip the cloths in the kuzhampu and then squeeze them over the body, massaging the body with their hands all the time. The patient turns periodically so that the attendants may reach all the body parts. The massage is to be very slow, without much exertion of pressure and with the attendants careful not to miss any part. The kuzhampu is reheated periodically. When it accumulates in the dhroni, the attendants move it to another pot by dipping the clothes and squeezing them out. Flowing out through the hole of the dhroni is not allowed. If it is allowed to flow out, it will lead to waste. The kuzhampu oil is to be changed on each day. But in cases where there are no wounds, skin diseases, or diseases involving dirty discharges, the usual practice in Kerala allows taking the clear part of the Kuzhampu of the previous day and adding fresh oil to bring it to the required amount. This is repeated for three consecutive days, and on the fourth day, a new and fresh kuzhampu is required. The time limitations are exactly as prescribed for the dhara to the head. One cannot emphasize enough the

need for experienced and well-trained attendants so that no part of the body is left untouched by their hands.[574]

At least five minutes before completion of dhara, all attendants should be particularly vigilant. Everything necessary for the next step, such as the bath towel, should be available. Quit refilling the dhara before the exact stopping time. For dhara of the head, stop the dhara by drawing the vessel back, then wipe the head with a towel. This is not to be done by the patients themselves. After wiping well, same oil that was applied earlier is smeared. In Sarvangadhara the body is to be wiped, and oil applied.

Next, the patient may take a bath as usual. Amalaka water for the head and warm water for the body are indispensable. For some people warm water may not be agreeable. For them cold water for the body may not be harmful. To remove the oil from the body, pasted green gram and/or horse gram are utilized. For the head, shampoos of leaves life vellila (*Mussaenda frondosa*), which are neither too cold nor too hot in potency, are used. For men of pitta temperament, the residue of the amalaka water prepared as a paste can be used.

After the bath, wipe the head without delay. This has to be done carefully so that no moisture is retained. After wiping well with a wet towel wipe again with a dry one. After wiping, part the hair and rub the scalp with medicated powder. As said earlier, rasnadi powder is what is usually applied. This prevents cold. Powders like kachoradi also can be used as per the disease. After the bath, enter the room slowly, and then, facing the east,

take in the prescribed medicine. Then lie down for a while on the left. Care should be taken to have the bed arranged in advance. But this rest is brief, from a minimum of five minutes to a maximum of thirty minutes. Afterword, take food with the prescribed restrictions.[575]

Navarakkizhi—Pindaswedam—This is the most important Sweda method that is used in cases of hemiplegia, opisthotonus, emprosthotonus, wasting paralysis, and other chronic vata diseases. This is most effective in gulma and colic and very efficacious wherever sweating is prescribed.

Equipment:

Shashtika rice made raw from grains over a year old. About ¾ kg. of this is cooked near dry in 3 litres of milk and Bala (*Sida rhombifolia*) decoction and tied up in 8 equal cloth bundles. They bundles should not be very tight. The other items are undiluted milk Bala (*Sida rhombifolia*) and decoction (the roots are cut fine, crushed, and cooked in water 16 times the medicine, until only a fourth is left and then strained). All other items such as oil, kuzhampu, head band (Vartti), Dhara droni, pillow, lamp, and others are useful for bath as in Dhara. A stove (kept at a distance to avoid smoke), a pan to heat the bundles, spoons and ladles, underwear cloth, and string to tie it are required. There must be 5 attendants and a physician (see Figures 21-29 in Chapter 4).

Procedure:

During seasons prescribed for Dhara, in the morning when the previous night's food is digested, and severe hunger has not set in, attend to natural calls and other routines, and enter the room free of drafts of air and cold. Do the prayers. Apply oil on the head as for Dhara, tie the Vartti, and keep massaging the body mildly with warm Kuzhampu. Four attendants now take their places as for Sarvangadhara. The fifth fetches 4 of the Shastika bundles heated in the milk decoction mixture. After checking with their palms that the bundles are agreeably hot, the four attendants start massaging with them. They must touch the patient's body with the bundles and then remove them once or twice and start fomentation gradually. If too hot, it may scald, and if not hot enough it will be less effective. The movement must always be downwards. Often press the body with the bundles. In the affected areas, this should be done with special care. Massage will have to be done gently and cautiously. Massage will have to be across and upwards, sometimes according to the direction of the nerves. First the patient must lie on his back, then on his sides and belly for the massage, many times over, during the course of the procedure. The attendants' hands must not leave any area untouched. Excessive massage in some areas, less in other places, and none at all elsewhere may do harm later. Massage must cover all parts of the body and face, except the areas covered by hair. Massaging in this area, too, may be useful in Vata of the upper body. The first 4 bundles will have lost heat by now. It is the duty of the fifth attendant to supply the four warm bundles and take the cold ones and heat them in the boiling fluid for the next change. The physician is responsible to see that the heat is maintained uniformly throughout by changing the bundles, and that the massage covers all parts of the body. Some believe that the attendants must rotate their positions daily, for fomentation to be uniform throughout the body. If they are uniformly

experienced, this rotation is not essential. If some attendants are more experienced and some less, the rotation may be unnecessary after half of the duration of the course. Duration as for Dhara may be adopted for this also. After this, the patient is to be made to sit up in the dhroni, and the paste removed slowly with the palm leaf scraps. He must then apply oil and kuzhampu, bathe, and take the medicine prescribed as in the case of Dhara.[576]

Enemas:

Enema therapy is of three kinds: Asthapana (decoction of drugs being used); Anuvasana (oil or other fatty materials); and Uttara basti (enema into the urinary bladder or uterus).

Decoction enema is prepared from a combination of different drugs appropriate to the doshas involved. Vagbhata mentioned many types. The practitioners chose to use ***Kashayam vasthi.***[577]

Oil enema is where any of four fatty materials from the oleation chapter are processed with appropriate drugs intended to produce lubrication. The practitioners chose to use ***Sathahwadi vasthi thailam***.[578]

Appendix E: Ayurvedic Management Therapy for NIDDM

Protocol # AMT-NIDDM Type II
St John's Medical Hospital & College IERB Approval # 1/110/04 13 May 2004
City University of New York IRB Approval # 04-04-0554 12 May 2004

Protocol Title

A 4-week Open Label Study to Evaluate Ayurvedic Management Therapy (AMT) of Non-Insulin Dependent *Diabetes mellitus* (NIDDM).

Protocol number: AMT-NIDDM Type II

Principal Investigator: Sarah K. Khan MS, MPH (CUNY-NYBG[1])
Co-Investigators: Padmavathy Venkatasubramanian PhD (FRLHT[2])
G.G. Gangadharan (Ayurvedacharya)) (FRLHT)
Drs. Ganapathi B. and Jyothi Idiculla (SJMCH[3])

Study Center: FRLHT, Bangalore, India

FRLHT Medical Monitor: A. Gulshanara Begum, MBBS

Foundation for the Revitilisation of Local Health Traditions (FRLHT)
Ayurvedic Clinic
No. 74/2, Jarakbande Kaval
Post: Attur, Via Yelahanka
Bangalore 560-5873
Phone: 91 080 856 8000--Fax: 91 80 856 5873

We, the undersigned, have reviewed this protocol, including Appendices, and we will conduct the study as described and will adhere to the Ethical and Regulatory Considerations stated. We have read and understood the contents of the Investigator Brochure.

_____ _____
Principal Investigator Signature Date

_____
Print Name

[1] City University of New York, Graduate Center, NY, NY and New York Botanical Garden, Bronx NY, USA
[2] Foundation for the Revitilsation of Local Health Traditions, Bangalore, India
[3] St. John's Medical Hospital and College, Bangalore, India

Appendix F: WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Recommendations guiding physicians in biomedical research involving human subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000
Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002

INTRODUCTION

The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the etiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.
Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.
The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
The subjects must be volunteers and informed participants in the research project.
The right of research subjects to safeguard their integrity must always be respected.
Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not

exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.
At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.
In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.
Footnote: **Note of clarification on paragraph 29 of the WMA Declaration of Helsinki**
The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:
- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or
- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Somerset-West, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.

Appendix G: ADMINISTRATIVE MATTERS

ADMINISTRATIVE MATTERS

RESPONSIBILITES OF THE INVESTIGATOR

To ensure that he/she has sufficient time to conduct and complete the study, and has adequate staff and appropriate facilities that are available for the duration of the study, and to ensure that other studies do not divert essential subject/patients or facilities away from the study at hand.

To submit an up-to-date curriculum vitae and other credentials to the sponsor and-where required-to relevant authorities.

To acquire the reference ranges for laboratory tests performed locally and, if required by local regulations, obtain Laboratory License or Certification.

To prepare and maintain adequate case histories designed to record observations and other data pertinent to the study.

PROTOCOL AMENDMENTS

No changes to the study protocol will be allowed unless discussed in detail with the FRLHT Medical Monitor and filed as an amendment/modification to this protocol.

Any amendment/modification to the protocol will be adhered to by the participating center and will apply to all subjects following approval as appropriate by the Institutional Review Board.

SPONSOR'S TERMINATION OF STUDY

FRLHT reserves the right to discontinue the clinical study at any time for medical or administrative reasons. When a feasible, a 30-day written notification will be tendered.

CASE REPORT FORM INSTRUCTIONS

Prior to screening the first potential participant, the investigator will provide a list showing the signature and hand-written initials of all individuals authorized to make or change entries on case report forms (CRFs). If the authorized individuals should change during the study, the investigator is to inform FRLHT.

CRFs will be supplied by FRLHT for recording all data. It is the responsibility of the investigator or co-investigator to ensure that CRFs are legible and completely filled in with a black ink ballpoint pen. The subject's identification (2-3 alphabetic letters representing initials or first letter of subject's name) the patient identification (PID) if not already pre-printed and the visit date, will be entered on the CRF Header Pages as required.

Errors must be corrected by drawing a single line through the incorrect entry and writing in the new value/data positioned as close to the original as possible. The correction must

then be initialed, dated, and justified by the authorized individual making the change. Do not obliterate, write over, or erase the original entry when making a correction.

When a subject completes a visit, it is anticipated that relevant sections of the CRF will be completed by the investigator (or designated staff) within 24 hours of the last data becoming available, but in no case later than 5 days. Similarly, when a subject completes a study, it is anticipated that all relevant CRF pages will be completed within 24 hours of the last data becoming available, but in no case later than 5 days. This also applies to forms for potential study participants who were no randomized to a treatment group.

As soon as the subject had completed/withdrawn from the study and the CRF is completed the principal investigator or designated physician(s) under his/her supervision will sign the adverse experience page(s) as well as study conclusion page of the CRF to confirm that they have reviewed the data and that the data are completed and accurate. If sections of a CRF are to be brought into FRLHT prior to study conclusion, a section conclusion signature is required.

An original (top copy) CRF must be submitted for all subjects who have undergone protocol specific procedures, whether or not the subject completed the study.

While completed CRFs will be reviewed by an FRLHT professional monitor at study site, errors detected by subsequent in-house CRF review may necessitate clarification or correction of errors and documentation and approval by the investigator.

Any questions of comments related to the CRF should be directed to the assigned study monitor.

MONITORING

A monitoring visit by a professional representative of the sponsor (St John's Medical Hospital representative) will be scheduled to take place during the study. A review of the protocol (and questionnaires) prior to commencing the study by a St. John's representative will occur. And a review of completeness and exactness of data entered on the CRF forms during and after the study will occur.

These visits are for the purpose of verifying adherence to the protocol and the completeness and exactness of data entered on the CRF and Drug Inventory Forms. The monitor will verify CRF entries by comparing them with the hospital/clinic/office records, if available. Adequate time and space for these visits must be made available by the investigator.

ARCHIVING OF DATA

The investigator must retain subject records and CRFs as well as drug disposition records in an easily retrievable form until disposal has been agreed in writing with FRLHT. The investigator must have a 'key' linking the subject's study identification number (i.e. treatment number) to the subject's clinical file. If the investigator moves or retires, he/she must nominate someone in writing to be responsible for record keeping. Archived data

may be held on microfiche or electronic record, provided that a back-up exists and a hard copy can be obtained from it if required.

FRLHT agrees to retain a copy of the protocol, documentation, approvals and all other documents related to the study, including certificates that satisfactory audit and inspection procedures have been carried out.

CONFIDENTIALITY AND PUBLICATION

You agree that all information communicated to you by FRLHT is the exclusive property of FRLHT and you will ensure that the same shall be kept strictly confidential by you or any other person connected with the work and shall not be disclosed by you or such person to any third party without the prior written consent of FRLHT. You shall communicate the results of the work promptly to FRLHT.

We agree that you shall have the right to publish or permit the publication of any information or material or material relating to or arising out of the work after prior submission to us provided that if we shall so request you will delay publication for a maximum of six months to enable us to protect our rights in such information or material. Any proposed publication or presentation (e.g. manuscript, abstract, or poster) for submission to a journal or scientific meeting should be sent to the study monitor prior to submission. FRLHT will undertake to comment on such documents within four weeks.

All rights and interests world-wide in any inventions, know-how, or other intellectual or industrial property rights that arise during the course of and/or as a result of the clinical study that is the subject of the Protocol or that otherwise arise from the information or materials supplied under this agreement, shall be assigned to, vest in, and remain the property of The Foundation for the Revitilisation of Local Health Traditions.

Appendix H: SAMPLE INFORMED CONSENT STATEMENT

Doctoral Program in Biology

The Graduate Center
The City University of New York
365 Fifth Avenue
New York City, New York 10016-4309

CONSENT FORM

My name is Sarah Khan and I am a student in the Biology Program at the CUNY Graduate Center at the City University of New York. I also have a Masters in Public Health and a Masters in Clinical Nutrition. I am the Principal Investigator and Drs. Padmavathy Venkatasubramanian and G.G. Gangadharan both at the Foundation for the Revitalization of Local Health Traditions and Drs. J Idiculla and Ganapathi B. both endocrinologists at St. John's Medical Hospital and College, are the co-Principal Investigators of this project, entitled "A Comparison of Ethnomedical Treatments of Type II, *Diabetes mellitus*." In this study, we are investigating how Ayurvedic Management Therapy may affect Type II *Diabetes mellitus*. We would like permission to interview you about your experiences while we or you fill out the required forms.

This medical history and examination and Ayurvedic medical history and examination will take approximately 45 minutes. With your permission, I would like to record this interview on standard forms so that I may document your details accurately. All information gathered will be kept strictly confidential, and will be stored in my computer and a locked file cabinet in Dr. Venkatasubramanian's office, to which only we will have access. At any time, you can refuse to answer any questions or end this interview without any penalty.

Historically when Ayurvedic medicines are prescribed according to the classical texts by a trained Ayurvedic physician, the formulations are safe and well-tolerated, and toxicity is minimal. Based on a review of the medical literature of the 36 plants and one fish species, thirteen plants show anti-diabetic effect. However, two (*Salacia reticulata* and *Butea frondosa*) have shown anti-fertility activity in animal models. Based on these studies, the amount of *Butea frondosa* and *Salacia reticulata* required for humans to create this possible anti-fertility effect far exceeds the dosages to be prescribed by the Ayurvedic physician in this study.

During the course of this study at each of the five visits you will have blood withdrawn to gauge your blood glucose levels and cholesterol levels. You will then undergo a medical and Ayurvedic examination. You may experience discomfort in answering questions pertaining to quality of life, personal dietary habits, weight, and hygiene. After the examination you will be prescribed an Ayurvedic Management Therapy protocol that will include diet and exercise modification and Ayurvedic medicinal formulations to be taken on a regular basis during the course of the treatment period. We expect a 30 mg/dl reduction in your fasting blood glucose levels. In addition the benefit of your participation is that, in the future, there will be more information on how to help people with Type II, *Diabetes mellitus* from an Ayurvedic management perspective.

We may publish results of the study, but names of people, or any identifying characteristics, will not be used in any of the publications. If you would like a copy of the study, please provide me with your address and I will send you a copy in the future.

If you have any questions about this research, you can call me at The Foundation for the Revitalization of Local Health Traditions (# 98 455 47571). If you have any questions about your rights as a participant in this study, you can contact Hilry Fisher, Sponsored Research, Graduate Center/City University of New York, USA (212) 817-7523, email: hfisher@gc.cuny.edu

Thank you for your participation in the study. I will give you a copy of this form to take with you.

I agree to 5 meetings for medical check-up and monitoring, circle one: Yes No.
I agree to release my medical records for the purpose of this study, circle one: Yes No.

Principal Investigator signature Date Patient signature Date

Appendix I: OUTLINE OF STUDY PROCEDURES

Outline of Study Procedure

Procedures	**Pre-screening**	**Screening**	**Baseline**	**Open Treatment Period**		**Follow-up**
Visit number	0	1	2	3	4	5
Weeks	1	2	3	5	7	8
Time relative to baseline (weeks)	-2	-1	0	+2	+4	+5
Create log of patient enquiry-registration	x					
Obtain informed consent		x				
Administer Quality of life questionnaire		x			x	X
Complete physical exam—includes hip/weight ratio, BP, height		x	x	x	x	X
Complete Ayurvedic exam and protocol intake and information on diet and exercise		x	x	x	x	X
Fasting blood glucose (lab)		x	x	x	x	X
Lipid profile (lab)		x	x		x	X
HbgA1C (lab)		x	x		x	X
Dispense study medication			x	x		
Phone contact to remind patient of next visit, review compliance to Ayurvedic diet and exercise regimen, MF intake, document any adverse effects (in between visits)		x	x	x	x	

Appendix J: CLASSIFICATIONS OF DM2

New Classification for Diabetes

Bottom of Form

New Definitions for the Types of Diabetes	
TYPE 1	Characterized by beta cell destruction, usually leading to absolute insulin deficiency. It has two forms: **Immune-Mediated Diabetes Mellitus:** Results from a cellular mediated autoimmune destruction of the beta cells of the pancreas. **Idiopathic Diabetes Mellitus:** Refers to forms of the disease that have no known etiologies.
TYPE 2	Diseases of insulin resistance that usually have relative (rather than absolute) insulin deficiency. Can range from predominant insulin resistance with relative insulin deficiency to predominant insulin deficiency with some insulin resistance.
Impaired Glucose Homeostasis	A metabolic stage intermediate between normal glucose homeostasis and diabetes. A risk factor for diabetes and cardiovascular disease. **Impaired Fasting Glucose** Fasting plasma glucose higher than normal, and less than diagnostic. **Impaired Glucose Tolerance** Plasma glucose higher than normal, and less than diagnostic, following administration of a glucose load of 75 grams.
Gestational Diabetes Mellitus	Glucose intolerance in pregnancy. The definitions are unchanged from before.
Other Specific Types	Diabetes caused by other identifiable etiologies. Genetic defects of beta cell function (e.g., MODY 1, 2, 3) Genetic defects in insulin action Diseases of the exocrine pancreas (e.g., cancer of the pancreas, cystic fibrosis, pancreatitis) Endocrinopathies (e.g., Cushing's) Drug or chemical induced (e.g., steroids) Infection (e.g., rubella, Coxsackie, CMV) Uncommon forms of immune-related diabetes Other genetic syndromes

On Monday morning, June 23, 1997, at the ADA meeting in Boston, this revised classification system, and revised diagnostic criteria *(below)* were announced. The new

guidelines were a joint activity of committees from the American Diabetes Association and from the World Health Organization; the two separate committees ended up in agreement on the changes (with one exception, screening criteria for gestational diabetes).

This proposal for a new classification of diabetes has been in development for several years. As indicated *above,* the definitions of the terms Type 1 and Type 2 have been revised (and the terms **IDDM** and **NIDDM** are dropped); new cutoff values for blood sugar normality have been defined (see the table *below*). Criteria for children and for the elderly are the same as for other age groups.

Press stories from *The New York Times, CNN* and the *Associated Press* are appended at the end of this webpage.

The official report of these guidelines, and an accompanying editorial, have been published in the July, 1997 issue of **Diabetes Care**, and are available at the American Diabetes Association website. The article is entitled *Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.* (See *reference*, at end of this article).

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Diagnosing Diabetes
From the Boston Beacon (the daily newsletter of the ADA 57th Annual Meeting), Tuesday, June 24, 1997, page 6
(mmol/L / mg/dl)

Stage	**Fasting Plasma Glucose Test (FPG) (Preferred) ***	**Casual Plasma Glucose Test**	**Oral Glucose Tolerance Test (OGTT)**
Diabetes	FPG greater than or equal to 7.0 / 126 **	Casual Plasma Glucose greater than or equal to 11.1 / 200 plus symptoms ***	Two-hour plasma glucose (2hPG) greater than or equal to 11.1 / 200 ****
Impaired Glucose Homeostasis	Impaired Fasting Glucose (IFG) = FPG greater than or equal to 6.1 / 110 and less than 7.0 / 126		Impaired Glucose Tolerance (IGT) = 2hPG greater than or equal to 7.8 / 140 and less than 11.1 / 200
Normal	FPG less than 6.1 / 110		2hPG less than 7.8 / 140

Notes:
* The FPG is the preferred test for diagnosis, although any of the three is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these three tests should be used on a different day to confirm the diagnosis.
** Fasting is defined as no caloric intake for at least eight hours.

*** Casual is defined as any time of day without regard to time since last meal; *symptoms* are the classic ones of polyuria, polydipsia, and unexplained weight loss.
**** OGTT should be performed using a 75 gram glucose load. The OGTT is not recommended for routine clinical

Appendix K: NEW YORK HEART ASSOCIATION CRITERIA FOR FUNCTIONAL CAPACITY AND THERAPEUTIC CLASS

1994 Revisions to Classification of Functional Capacity and Objective Assessment of Patients With Diseases of the Heart

Year Published:
1994
Product Code:
71-0052

In 1928 the New York Heart Association published a classification of patients with cardiac disease based on clinical severity and prognosis. This classification has been updated in seven subsequent editions of *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels* (Little, Brown & Co). The ninth edition, revised by the Criteria Committee of the American Heart Association, New York City Affiliate, was released March 14, 1994. The new classifications are summarized below for the many physicians and scientists who use them to describe the status of individual patients.
A principal change in this edition is terms for the classes. Early editions referred to *functional capacity* and therapeutic classifications. The terms *cardiac status* and *prognosis* were used in the seventh (1973) and eighth (1979) editions. However, *functional capacity* is the term generally used by the medical profession. Therefore, the Criteria Committee is again using that term, which is based on subjective symptoms, and adds as the second category *objective assessment*, which is based on measurements such as electrocardiograms, stress tests, x-rays, echocardiograms, and radiological images. In addition, the Canadian Cardiovascular Society Grading Scale (Campeau L. *Circulation.* 1976;54:522. Letter), which considers anginal symptoms not previously included in the classes, has been incorporated into the new edition.
Shown below are the new terms and definitions.
Criteria for use of the terms *minimal*, *moderately severe*, and *severe disease* cannot be defined precisely. Grading is based on the individual physician's judgment. The objective assessment of a patient with cardiac disease who has not had specific tests of cardiac structure or function is classified as undetermined.
The classification of patients according to cardiac functional capacity is only part of the information needed to plan the management of patients' activities. A prescription for physical activity should be based on information from many sources. Functional capacity is an estimate of what the patient's heart will allow the patient to do and should not be influenced by the character of the structural lesions or an opinion as to treatment or prognosis. A recommendation for physical activity is based not only on the amount of effort possible without discomfort but also on the nature and severity of the disease.
Following are examples of functional capacity and objective assessment classifications.
A patient with minimal or no symptoms but a large pressure gradient across the aortic valve or severe obstruction of the left main coronary artery is classified: Functional Capacity I, Objective Assessment D
A patient with a severe anginal syndrome but angiographically normal coronary arteries is classified: Functional Capacity IV, Objective Assessment A
A patient with acute myocardial infarction, shock, reduced cardiac output, and elevated pulmonary artery wedge pressure is classified: Functional Capacity IV, Objective Assessment D

A patient with mitral stenosis, moderate exertional dyspnea, and moderate reduction in mitral valve area is classified: Functional Capacity II or III, Objective Assessment C

Uncertain Diagnosis

No Heart Disease: Predisposing Etiologic Factor

The diagnostic category *No heart disease: Predisposing etiologic factor* includes patients in whom no cardiac disease is evident but whose course should be followed by periodic examinations because of a history of an etiologic factor that might cause heart disease. These should be recorded as *No heart disease: History of (state the etiologic factor).*

No Heart Disease: Unexplained Manifestation

The diagnostic category *No heart disease: Unexplained manifestation* includes patients with symptoms or signs referable to the heart but in whom a diagnosis of cardiac disease is uncertain at the time of examination. These cases should be recorded as *No heart disease: Unexplained manifestation*, with a further recommendation that reexamination be performed after a stated interval.

When there is a reasonable uncertainty that the symptoms or signs are not of cardiac origin, the diagnosis should be *No heart disease.*

Functional Capacity	Objective Assessment
Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.	**A.** No objective evidence of cardiovascular disease.
Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.	**B.** Objective evidence of minimal cardiovascular disease.
Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.	**C.** Objective evidence of moderately severe cardiovascular disease.
Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.	**D.** Objective evidence of severe cardiovascular disease.

*The Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-256.

Appendix L: STANDARDIZED CONDITIONS FOR WAIST/HIP RATIO AND BODY WEIGHT MEASUREMENTS

Overweight and Obesity
Defining Overweight and Obesity
Overweight and Obesity Among Adults
Recent results of the National Health and Nutrition Examination Survey (NHANES) 1999 indicate that an estimated 61 percent of U.S. adults are either overweight or obese, defined as having a body mass index (BMI) of 25 or more.
Among U.S. adults aged 20-74 years, the prevalence of **overweight** (defined as BMI 25.0–29.9) has increased an estimated 2 percent since 1980, increasing from 33 percent to the 35 percent of the population in 1999 (based on NHANES II and NHANES 1999 data).
In the same population, **obesity** (defined as BMI greater than or equal to 30.0) has nearly doubled from approximately 15 percent in 1980 to an estimated 27 percent in 1999.
Overweight
Overweight refers to increased body weight in relation to height, when compared to some standard of acceptable or desirable weight (NRC p.114; Stunkard p.14). **NOTE:** Overweight may or may not be due to increases in body fat. It may also be due to an increase in lean muscle. For example, professional athletes may be very lean and muscular, with very little body fat, yet they may weigh more than others of the same height. While they may qualify as "overweight" due to their large muscle mass, they are not necessarily "over fat," regardless of BMI.
Desirable weight standards are derived in a number of ways:
By using a mathematical formula known as Body Mass Index (BMI), which represents weight levels associated with the lowest overall risk to health. Desirable BMI levels may vary with age.
By using actual heights and weights measured and collected on people who are representative of the U.S. population by the National Center for Health Statistics. Other desirable weight tables have been created by the Metropolitan Life Insurance Company, based on their client populations.
These sources are consistent with the U.S. Dietary Guidelines and with the National Heart, Lung, and Blood Institute's Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults.

Individuals with a BMI of 25 to 29.9 are considered **overweight**, while individuals with a BMI of 30 or more are considered **obese**.

Obesity
Obesity is defined as an excessively high amount of body fat or adipose tissue in relation to lean body mass. (NRC p114; Stunkard p14) The amount of body fat (or adiposity) includes concern for both the distribution of fat throughout the body and the size of the adipose tissue deposits. Body fat distribution can be estimated by skinfold measures, waist-to-hip circumference ratios, or techniques such as ultrasound, computed tomography, or magnetic resonance imaging.
Overweight and Obesity Among Children and Adolescents
The percentage of children and adolescents who are defined as overweight has more than doubled since the early 1970s.

About 15 percent of children and adolescents are now overweight.
In spite of the public health impact of obesity and overweight, these conditions have not been a major public health priority in the past. Halting and reversing the upward trend of the obesity epidemic will require effective collaboration among government, voluntary, and private sectors, as well as a commitment to action by individuals and communities across the nation.
Body Mass Index (BMI)
BMI is a common measure expressing the relationship (or ratio) of weight-to-height. It is a mathematical formula in which a person's body weight in kilograms is divided by the square of his or her height in meters (i.e., wt/(ht)2. The BMI is more highly correlated with body fat than any other indicator of height and weight (NRC p563).
Individuals with a BMI of 25 to 29.9 are considered **overweight**, while individuals with a BMI of 30 or more are considered **obese**.
What BMI levels are risky?
According to the NIH Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults
all adults (aged 18 years or older) who have a BMI of 25 or more are considered at risk for premature death and disability as a consequence of overweight and obesity. These health risks increase even more as the severity of an individual's obesity increases.
Waist circumference
Waist circumference is a common measure used to assess abdominal fat content. The presence of excess body fat in the abdomen, when out of proportion to total body fat, is considered an independent predictor of risk factors and ailments associated with obesity.
What waist size is risky? Undesirable waist circumferences differ for men and women.
Men are at risk who have a waist measurement greater than 40 inches (102 cm)
Women are at risk who have a waist measurement greater than 35 inches (88 cm)
NOTE: If a person has short stature (under 5 feet in height) or has a BMI of 35 or above, waist circumference standards used for the general population may not apply
.
Waist-to-hip ratio (WHR)
Waist-to-hip ratio (WHR) is the ratio of a person's waist circumference to hip circumference, mathematically calculated as the waist circumference divided by the hip circumference. For most people, carrying extra weight around their middle increases health risks more than carrying extra weight around their hips or thighs. (NOTE: Overall obesity is still more risky than body fat storage locations or waist-to-hip ratio.)
What waist-to-hip ratio is considered risky?
For both men and women, a waist-to-hip ratio of 1.0 or higher is considered "at risk" or in the danger zone for undesirable health consequences, such as heart disease and other ailments connected with being overweight.
What is a good waist-to-hip ratio?
For men, a ratio of .90 or less is considered safe.
For women, a ratio of .80 or less is considered safe.
References
Stunkard AJ, Wadden TA. (Editors) *Obesity: theory and therapy, Second Edition*. New York: Raven Press, 1993.
National Research Council. *Diet and health: implications for reducing chronic disease risk*. Washington, DC: National Academy Press, 1989.

National Institutes of Health. *Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults*. Bethesda, Maryland: Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute, 1998.
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Appendix M: Group 1 Ayurvedic Plants with Animal and Human Studies

Genus, species Common name (Sanskrit)	***Plant part used, preparation, and dosage***	***Design and model***	***Results***	***References***
Biophytum sensitivum (Linn.) DC Samanga	Leaf extract	Rabbits and diabetic rabbits	Observations suggest that the hypoglycemic response of B. sensitivum may be mediated through stimulating the synthesis/release of insulin from the beta cells of Langerhans.	Puri D. 2001. The insulino-tropic activity of a Nepalese medicinal plant Biophytum sensitivum: preliminary experimental study. J Ethno-pharmacol. Nov; 78 (1): 89-93.
Biophytum sensitivum	Leaf extract	Subdiabetic rabbits	The results prove that the plant material has significant hypoglycaemic effect, which is possibly due to pancreatic beta-cell stimulating action.	Puri D, Baral N. 1998. Hypo-glycemic effect of Biophytum sensitivum in the alloxan diabetic rabbits. Indian J Physiol Pharmacol. Jul; 42 (3): 401-6.
Curcuma longa Linn. Nisa, haridra	Dianex includes the aqueous extracts of *Gymnema sylvestre*, *Eugenia jambo-lana*, *Momordica charantia*, *Azadi-rachta indica*, *Cassia auriculata*, *Aegle marmelose*, *Withania somnifera* and *C. longa*.	Diabetic mice Doses: 100-500mg/kg/day orally in acute (6h) and long-term (6wks)	Dianex produced significant hypoglycemic activity in both normal and diabetic animals. It also reversed other diabetic complications in diabetic mice at 250 and 500 mg/kg doses. In our earlier study, Dianex was well tolerated in laboratory animals at higher doses (upto 10 g/kg in mice, acute toxicity; up to 2.5 g/kg in rats, subacute toxicity studies for 30 days) without exhibiting any toxic manifestation. Dianex may be useful in the treatment of diabetes mellitus.	Mutalik S, Chetana M, Sulochana B, Devi PU, Udupa N. 2005. Effect of Dianex, a herbal formulation on experimentally induced diabetes mellitus. Phytother Res. May; 19 (5): 409-15.
Curcuma longa	Fenugreek seed mucilage and spent turmeric (10%)	Diabetic rats	Fenugreek seed mucilage and spent turmeric supplementations were beneficial in alleviating the reduction in maltase activity during diabetes,	Kumar GS, Shetty AK, Salimath PV. 2005. Modula-tory effect of fenugreek seed mucilage and spent turmeric on intestinal and renal disac-charidases in

			however not much change in the activities of sucrase and lactase was observed upon feeding. This positive influence of feeding fenugreek seed mucilage and spent turmeric on intestinal and renal disaccharidases clearly indicates their beneficial role in the management of diabetes.	strepto-zotocin induced diabetic rats. Plant Foods Hum Nutr. Jun; 60 (2): 87-91.
Curcuma longa	Turmeric and curcumin	Diabetic rats	The present studies suggest that curcumin and turmeric treatment appear to have countered the hyperglycemia-induced oxidative stress. Also, treatment with turmeric or curcumin appears to have minimized osmotic stress. Most important, aggregation and insolubilization of lens proteins due to hyperglycemia was prevented by turmeric and curcumin. Turmeric was more effective than its corresponding levels of curcumin. The results indicate that turmeric and curcumin are effective against the development of diabetic cataract in rats.	Suryanarayana P, Saraswat M, Mrudula T, Krishna TP, Krishnaswamy K, Reddy GB. 2005. Curcumin and turmeric delay streptozotocin-induced diabetic cataract in rats. Invest Ophthalmol Vis Sci. Jun; 46 (6): 2092-9.
Curcuma longa	*Curcuma longa* rhizome ethanolic extract	Diabetic mice	These results indicate that turmeric is a promising ingredient of functional food for the prevention and/or amelioration of type 2 diabetes and that curcumin, demethoxycurcumin, bisdemethoxycurcumin, and ar-turmerone mainly contribute to the effects via PPAR-gamma activation.	Kuroda M, Mimaki Y, Nishi-yama T, Mae T, Kishida H, Tsukagawa M, Takahashi K, Kawada T, Nakagawa K, Kitahara M. 2005. Hypogly-cemic effects of turmeric (Curcuma longa L.Rhizomes) on genetically diabetic KK-Ay mice. Biol Pharm Bull. May; 28 (5): 937-9.
Curcuma longa	*Curcuma longa* rhizome extracts: ethanol,	Diabetic mice	These results indicate that both curcuminoids and sesquiterpenoids in turmeric exhibit	Nishiyama T, Mae T, Kishida H, Tsukagawa M, Mimaki Y, Kuroda M, Sashida Y, Taka-

	hexane, ethanol extraction from hexane-extraction residue		hypoglycemic effects via PPAR-gamma activation as one of the mechanisms, and suggest that E-ext including curcuminoids and sesquiterpenoids has the additive or synergistic effects of both components.	hashi K, Kawada T, Naka-gawa K, Kitahara M. 2005. Curcuminoids and sesquiter-penoids in turmeric (Curcuma longa L.) suppress an increase in blood glucose level in type 2 diabetic KK-Ay mice. J Agric Food Chem. Feb 23; 53 (4): 959-63.
Curcuma longa	Hyponidd: extracts of *Momordica cha-rantia*, *Melia azadi-rachta*, *P. marsu-pium*, *T. cordifolia*, *Gymnema sylvestre*, *Enicostemma littorale*, *E. officinalis*, *Eugenia jambolana*, *Cassia auriculata* and *C. longa*.	Diabetic rats Dose: 100 mg/kg and 200 mg/kg for 45 days	Oral administration of hyponidd resulted in significant lowered levels of blood glucose and significant increased levels of hepatic glycogen and total haemoglobin. An oral glucose tolerance test was also performed in experimental diabetic rats in which there was a significant improvement in blood glucose tolerance. Hyponidd administration also decreased levels of glycosylated haemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and alpha-tocopherol. Plasma reduced glutathione and vitamin C were significantly elevated by oral administration of hyponidd. The effect of hyponidd was more effective than glibenclamide (600 microg kg(-1)) in restoring the values to near normal. The results showed that hyponidd exhibits antihyperglycaemic and antioxidant activity in STZ-induced diabetic rats.	Babu PS, Stanely Mainzen Prince P. 2004. Antihyper-glycaemic and antioxidant effect of hyponidd, an ayurvedic herbomineral formulation in streptozo-tocin-induced diabetic rats. J Pharm Pharmacol. Nov; 56 (11): 1435-42.
Curcuma longa	Curcumin	Human	In this study the antioxidant effect of curcumin as a function of changes in cellular	Balasubramanyam M, Kote-swari AA, Kumar RS, Mon-ickaraj SF, Maheswari JU, Mohan

			ROS generation was tested. Our results demonstrated that curcumin clearly abolished both phorbol-12 myristate-13 acetate (PMA) and thapsigargin-induced ROS generation in cells from control and diabetic subjects. We suggest that the antioxidant and antiangeogenic actions of curcumin, as a mechanism of inhibition of Ca2+ entry and PKC activity, should be further exploited to develop suitable and novel drugs for the treatment of diabetic retinopathy and other diabetic complications.	V. 2003. Curcumin-induced inhibition of cellular reactive oxygen species generation: novel therapeutic implications. J Biosci. Dec; 28 (6): 715-21.
Curcuma longa	Aqueous extracts of *Ocimum sanctum* (OS), *Withania somnifera* (WS), *C. longa* (CL), *Azadirachta indica* (AI)	In vitro rat lens	All the four plants were found to inhibit lens AR activity but to different extent. From dose-response curve, OS was found to be the most effective AR inhibitor followed by CL, AI and WS. The IC(50) values of OS, CL, AI and WS were calculated to be 20, 55, 57 and 89 microg/ml, respectively. OS showed a significant inhibition (38.05%) in polyol accumulation followed by CL and AI (28.4 and 25.04%, respectively). WS did not show any effect on polyol level in rat lenses. OS possesses a significant anticataract activity in vitro and its anticataract potential could be related with its AR inhibitory effect.	Halder N, Joshi S, Gupta SK. 2003. Lens aldose reductase inhibiting potential of some indigenous plants. J Ethno-pharmacol. May; 86 (1): 113-6.
Curcuma longa	Turmeric and curcumin	Diabetic rats	Administration of turmeric or curcumin reduced the blood sugar, Hb and glycosylated hemoglobin levels significantly. Turmeric and curcumin	Arun N, Nalini N. 2002. Efficacy of turmeric on blood sugar and polyol pathway in diabetic albino rats. Plant Foods Hum Nutr. Winter; 57 (1): 41-52.

			supplementation also reduced the oxidative stress. Moreover, the activity of SDH (sorbitol dehydrogenase), which catalyzes the conversion of sorbitol to fructose, was lowered significantly on treatment with turmeric or curcumin. These results also appeared to reveal that curcumin was more effective in attenuating diabetes mellitus related changes than turmeric.	
Curcuma longa	Cogent db contains *Azadirachta indica* (AI), *E. Officinalis* (EO), *C. longa* (CL), *Trigonella foenum-graecum* (TF), *S. cumini* (SC), *Tribulus ter-restris* (TT), *T. bel-lirica* (TB), *T. che-bula* (TC), *Rotula aquatica* (RA)	Non-randomized, non-placebo-controlled clinical trial Dose: AI 3g; EO 0.7g; CL 0.8g; TF 0.1g; SC 2g; TT 1g; TB 0.7g; TC 0.7g; RA 1g	At the end of three months it was found that there was a significant decrease in the levels of fasting and postprandial blood glucose, cholesterol, triglycerides, glycated hemoglobin (Hb A[sub 1C]) and fasting insulin in the treatment group compared to the controls. Cogent db did not alter the liver function tests, hematologic parameters, or the kidney function tests. These results concur with earlier animal studies that indicate that Cogent db is safe, reliable, tolerable, and efficacious in the control of type 2 diabetes mellitus.	Shekhar, K.C., Achike, F.I., Kaur G. Kumar, P. and Hashim, R. 2002. A prelim-inary evaluation of the efficacy and safety of Cogent db (an Ayurvedic drug) in the glycemic control of patients with type-2 diabetes. J. Alt Compl Med 8, 4, 445-457.
Emblica officinalis Gaertn. Amalaki, Dhatri	Commercial enzymatic extract SunAmla (Taiyo Kagaku Co. Ltd., Yokkaichi, Japan)	Diabetic rats Dose: 20 or 40 mg/kg of body wt/day or a polyphe-nol-rich fraction of ethyl acetate extract (10 or 20 mg/kg of body wt/day) was given orally for 20 d	Amla extracts showed strong free radical scavenging activity. Amla also showed strong inhibition of the production of advanced glycosylated end products. Oral administration slightly improved body weight gain and also significantly alleviated various serum oxidative stress indices. The	Rao TP, Sakaguchi N, Juneja LR, Wada E, Yokozawa T. 2005. Amla (Emblica officinalis Gaertn.) extracts reduce oxidative stress in streptozotocin-induced diabetic rats. J Med Food. Fall; 8 (3): 362-8.

			elevated serum levels of 5-hydroxymethylfurfural, which is a glycosylated protein that is an indicator of oxidative stress, were significantly reduced dose-dependently. The serum level of creatinine, another oxidative stress parameter, was also reduced. Thiobarbituric acid-reactive substances levels were significantly reduced, indicating a reduction in lipid peroxidation. The decreased albumin levels were significantly improved. Amla also significantly improved the serum adiponectin levels. These results form the scientific basis supporting the efficacy of amla for relieving the oxidative stress and improving glucose metabolism in diabetes.	
Emblica officinalis	Hyponidd: extracts of *Momordica cha-rantia*, *Melia azadi-rachta*, *P. marsu-pium*, *T. cordifolia*, *Gymnema sylvestre*, *Enicostemma littorale*, *E. officinalis*, *Eugenia jambolana*, *Cassia auriculata* and *C. longa*.	Diabetic rats Dose: 100 mg/kg and 200 mg/kg for 45 days	Oral administration of hyponidd resulted in significant lowered levels of blood glucose and significant increased levels of hepatic glycogen and total haemoglobin. An oral glucose tolerance test was also performed in experimental diabetic rats in which there was a significant improvement in blood glucose tolerance. Hyponidd administration also decreased levels of glycosylated haemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and alpha-tocopherol. Plasma reduced glutathione and vitamin C were	Babu PS, Stanely Mainzen Prince P. 2004. Antihyper-glycaemic and antioxidant effect of hyponidd, an ayurvedic herbomineral formulation in streptozo-tocin-induced diabetic rats. J Pharm Pharmacol. Nov; 56 (11): 1435-42.

			significantly elevated by oral administration of hyponidd. The effect of hyponidd was more effective than glibenclamide (600 microg kg(-1)) in restoring the values to near normal. The results showed that hyponidd exhibits antihyperglycaemic and antioxidant activity in STZ-induced diabetic rats.	
Emblica officinalis	Aqueous extract of *E. officinalis* and its major constituent tannoids	Rat lens	Extract inhibited rat lens and recombinant human aldose reductase with IC50 values 0.72 and 0.88 mg/ml respectively. It was demonstrated that the hydrolysable tannoids of *E. officinalis* were responsible for AR inhibition, as enriched tannoids of exhibited remarkable inhibition against both rat lens and human AR with IC50 of 6 and 10 microg/ml respectively. These results indicate that *E. officinalis* tannoids are potent inhibitors of aldose reductase.	Suryanarayana P, Kumar PA, Saraswat M, Petrash JM, Reddy GB. 2004. Inhibition of aldose reductase by tan-noid principles of Emblica officinalis: implications for the prevention of sugar catar-act. Mol Vis. Mar 12; 10: 48-54.
Emblica officinalis	Methanolic extract (75%) of *T. chebula*, *T. bellirica, E. officinalis* and their combination named 'Triphala' (equal proportion)	Diabetic rats Dose: Oral administration of the extracts (100 mg/kg body wt)	These plants were found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro. The concentration of plant extracts that inhibited 50% of lipid peroxidation induced with Fe(2+)/ascorbate were found to be 85.5, 27, 74 and 69 micro g/ml, respectively. The concentration needed for the inhibition of hydoxyl radical scavenging were 165, 71, 155.5 and 151 micro g/ml, and that for superoxide scavenging activity were found to be 20.5, 40.5, 6.5 and 12.5	Sabu MC, Kuttan R. 2002. Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. J Ethnopharmacol. Jul; 81 (2): 155-60.

			micro g/ml, respectively. Oral administration reduced the blood sugar level in normal and in alloxan (120 mg/kg) diabetic rats significantly within 4 h. Continued, daily administration of the drug produced a sustained effect.	
Emblica officinalis	Cogent db contains *Azadirachta indica* (AI), *E. Officinalis* (EO), *C. longa* (CL), *Trigonella foenum-graecum* (TF), *S. cumini* (SC), *Tribulus ter-restris* (TT), *T. bel-lirica* (TB), *T. che-bula* (TC), *Rotula aquatica* (RA)	Non-randomized, non-placebo-controlled clinical trial Dose: AI 3g; EO 0.7g; CL 0.8g; TF 0.1g; SC 2g; TT 1g; TB 0.7g; TC 0.7g; RA 1g	At the end of three months it was found that there was a significant decrease in the levels of fasting and postprandial blood glucose, cholesterol, triglycerides, glycated hemoglobin (Hb A[sub 1C]) and fasting insulin in the treatment group compared to the controls. Cogent db did not alter the liver function tests, hematologic parameters, or the kidney function tests. These results concur with earlier animal studies that indicate that Cogent db is safe, reliable, tolerable, and efficacious in the control of type 2 diabetes mellitus.	Shekhar, K.C., Achike, F.I., Kaur G. Kumar, P. and Hashim, R. 2002. A prelim-inary evaluation of the efficacy and safety of Cogent db (an Ayurvedic drug) in the glycemic control of patients with type-2 diabetes. J. Alt Compl Med 8, 4, 445-457.
Emblica officinalis	Chyawanprash contains *E. officina-lis* in addition to several other herbal products.	Clinical Trial Randomized Controlled Trial Dose: 15 g/d Chyawanprash or 500 mg/d vit C	Chyawanprash reduced postprandial glycemia in the oral glucose tolerance test and reduced blood cholesterol level to a significantly greater extent than vitamin C in healthy adult males.	Manjunatha S, Jaryal AK, Bijlani RL, Sachdeva U, Gupta SK. 2001. Effect of Chyawanprash and vitamin C on glucose tolerance and lipoprotein profile. Indian J Physiol Pharmacol. Jan; 45 (1): 71-9.
Ficus racemosa Linn. Udumbarah, Sadaphalah	Methanol extract of stem bark	Diabetic rats Dose: 200 and 400 mg/kg p.o.	The extract exhibited significant hypoglycaemic activity in both experimental animal models when compared with the control group. The activity was also comparable to that of the effect produced by a standard antidiabetic	Bhaskara Rao R, Murugesan T, Sinha S, Saha BP, Pal M, Mandal SC. 2002. Glucose lowering efficacy of Ficus racemosa bark extract in normal and alloxan diabetic rats. Phytother Res. Sep; 16 (6): 590-2.

			agent, glibenclamide 10 mg/kg. The present investigation established pharmacological evidence to support the folklore claim that it is an antidiabetic agent.	
Mangifera indica Linn. Amra, Cutah	Stem-bark aqueous extract of *M. indica*	Rats and mice Dose: 50-800 mg/kg i.p.	The results of this experimental animal study lend pharmacological credence to the suggested folkloric uses of the plant in the management and control of painful, arthritic and other inflammatory conditions, as well as in the management of adult-onset type 2 diabetes mellitus in some rural African communities.	Ojewole JA. 2005. Antiin-flammatory, analgesic and hypoglycemic effects of Ma-ngifera indica Linn. (Ana-cardiaceae) stem-bark aqu-eous extract. Methods Find Exp Clin Pharmacol. Oct; 27 (8): 547-54.
Mangifera indica	Mangiferin	Diabetic rats Dose: 10 and 20 mg/kg once daily (o.d.)	The present study demonstrated that mangiferin possesses significant antidiabetic, antihyperlipidemic and antiatherogenic properties thus suggesting its beneficial effect in the treatment of diabetes mellitus associated with hyperlipidemia and related cardiovascular complications.	Muruganandan S, Srinivasan K, Gupta S, Gupta PK, Lal J. 2005. Effect of mangiferin on hyperglycemia and atheroge-nicity in streptozotocin dia-betic rats. J Ethnopharmacol. Mar 21; 97 (3): 497-501.
Mangifera indica	Ethanolic extracts of *Lawsonia inermis* leaves, *Holarrhena antidysenterica* bark, *Swertia chirata* whole plant and *Mangifera indica* bark	In vitro	*M. indica* extract was found to be the most potent, with an IC(50) value of 314 microg/ml for alpha-glucosidase inhibitory activity.	Prashanth D, Amit A, Samiulla DS, Asha MK, Padmaja R. 2001. alpha-Glucosidase inhibitory activity of Mangifera indica bark. Fitoterapia. Aug; 72 (6): 686-8.
Mangifera indica	Aqueous extract of the leaves	Diabetic mice	The results of this study indicate that the aqueous extract of the leaves of Mangifera indica possess hypoglycaemic activity.	Aderibigbe AO, Emudianughe TS, Lawal BA. 2001. Evaluation of the antidiabetic action of Mangifera indica in mice. Phytother Res. Aug; 15 (5): 456-8.

Mangifera indica	Aqueous extract of the leaves	Diabetic rats Dose: (1 g/kg)	The aqueous extract given orally did not alter the blood glucose levels in either normoglycemic or STZ-induced diabetic rats. In glucose-induced hyperglycemia, however, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The hypoglycemic effect of the aqueous extract was compared with that of an oral dose of chlorpropamide (200 mg/kg) under the same conditions. The results of this study indicate that the aqueous extract of the leaves possess hypoglycaemic activity. This action may be due to an intestinal reduction of the absorption of glucose.	Aderibigbe AO, Emudianu-ghe TS, Lawal BA. 1999. Antihyperglycaemic effect of Mangifera indica in rat. Phytother Res. Sep; 13 (6): 504-7.
Pterocarpus marsupium Roxb. Asanah, Bijakah, Vijaysar	Water extract of the wood	Diabetic rats Dose: 250 mg/kg	During both acute and sub-acute tests, the water extract showed statistically significant hypoglycemic activity.	Mukhtar HM, Ansari SH, Ali M, Bhat ZA, Naved T. 2005. Effect of aqueous extract of Pterocarpus marsupium wood on alloxan-induced diabetic rats. Pharmazie. Jun; 60 (6): 478-9.
Pterocarpus marsupium	Aqueous extracts of *P. marsupium* Linn bark (PM), *Ocimum sanctum* Linn. leaves (OS) and *Trigonella foenum-graecum* Linn. seeds (FG)	Rats	Results of this study, in addition to previous clinical benefits of PM seen in NIDDM subjects, are suggestive of usefulness of PM bark (Vijayasar) in insulin resistance, the associated disorder of type 2 diabetes; however, OS and FG may not be useful. Though several antidiabetic principles (-epica-techin, pterosupin, marsupin and pterostilbene) have been identified in the PM, yet future studies are	Grover JK, Vats V, Yadav SS. 2005. Pterocarpus marsu-pium extract (Vijayasar) prevented the alteration in metabolic patterns induced in the normal rat by feeding an adequate diet containing fructose as sole carbohydrate. Diabetes Obes Metab. Jul; 7 (4): 414-20.

			required to certify their efficacy and safety before clinical scenario.	
Pterocarpus marsupium	Hyponidd: extracts of *Momordica cha-rantia*, *Melia azadi-rachta*, *P. marsu-pium*, *T. cordifolia*, *Gymnema sylvestre*, *Enicostemma littorale*, *E. officinalis*, *Eugenia jambolana*, *Cassia auriculata* and *C. longa*.	Diabetic rats Dose: 100 mg/kg and 200 mg/kg for 45 days	Oral administration of hyponidd resulted in significant lowered levels of blood glucose and significant increased levels of hepatic glycogen and total haemoglobin. An oral glucose tolerance test was also performed in experimental diabetic rats in which there was a significant improvement in blood glucose tolerance. Hyponidd administration also decreased levels of glycosylated haemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and alpha-tocopherol. Plasma reduced glutathione and vitamin C were significantly elevated by oral administration of hyponidd. The effect of hyponidd was more effective than glibenclamide (600 microg kg(-1)) in restoring the values to near normal. The results showed that hyponidd exhibits antihyperglycaemic and antioxidant activity in STZ-induced diabetic rats.	Babu PS, Stanely Mainzen Prince P. 2004. Antihyper-glycaemic and antioxidant effect of hyponidd, an ayurvedic herbomineral formulation in streptozo-tocin-induced diabetic rats. J Pharm Pharmacol. Nov; 56 (11): 1435-42.
Pterocarpus marsupium	Aqueous extract of *P. marsupium* bark (PM), *Ocimum sanctum* leaves (OS), and alcoholic extract *Trigonella foenum-graecum* seeds	Diabetic rats Dose: PM 1g/kg/day; OS 200mg/kg/day; FG 2g/kg/day	Administration of all the three plant extracts exerted a favorable effect on body weight and blood glucose, the effects were best with PM followed by FG and OS. On the course of cataract development, PM followed by FG exerted anti-cataract effect evident from	Vats V, Yadav SP, Biswas NR, Grover JK. 2004. Anti-cataract activity of Pterocar-pus marsupium bark and Trigonella foenum-graecum seeds extract in alloxan diabetic rats. J Ethnopharma-col. Aug; 93 (2-3): 289-94.

	(FG)		decreased opacity index while OS failed to produce any anti-cataract effect in spite of significant antihyperglycemic activity.	
Pterocarpus marsupium	Vacuum dried 95% ethanolic extract of 24 samples including: *P. marsupium, T. bellirica, T. cordifolia, and Z. officinale*	Diabetic albino rats Dose: 250 mg/kg once, twice or thrice daily, as needed	In all the experiments with different herbal samples, definite blood glucose lowering effect within 2 weeks has been confirmed. Blood glucose values were brought down close to normal fasting level. While evaluating comparative hypoglycaemic activity of the experimental herbal samples, significant blood glucose lowering activities are observed in decreasing order in the following 4 samples: *P. marsupium, T. cordifolia, T. bellirica*, and *Z. officinale*.	Kar A, Choudhary BK, Bandyopadhyay NG. 2003. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol. Jan; 84 (1): 105-8.
Pterocarpus marsupium	Aqueous extract	In-vitro tissue cultures Rats Dose: 1 g/kg PO	The extract was assessed for its effect on glycogen levels of insulin dependent (skeletal muscle and liver), insulin-independent tissues (kidneys and brain) and enzymes such as glucokinase (GK), hexokinase (HK), and phosphofructokinase (PFK). Administration of PM led to decrease in blood glucose levels by 38 and 60% on 15th and 30th day of the experiment. Liver and 2-kidney weight expressed as percentage of body-weight was significantly increased in diabetics ($p < 0.0005$) vs. normal controls and this alteration in the renal weight ($p < 0.0005$) but not liver weight was normalized by feeding of	Grover JK, Vats V, Yadav S. 2002. Effect of feeding aqueous extract of Pterocar-pus marsupium on glycogen content of tissues and the key enzymes of carbohydrate metabolism. Mol Cell Bio-chem. Dec; 241 (1-2): 53-9.

			PM extract. Renal glycogen content increased by over 10-fold while hepatic and skeletal muscle glycogen content decreased by 75 and 68% in diabetic controls vs. controls and these alteration in glycogen content was partly prevented by PM. Activity of HK, GK and PFK in diabetic controls was 35, 50 and 60% of the controls and PM completely corrected this alteration in PFK and only partly in HK and GK.	
Pterocarpus marsupium	Aqueous extract of the bark of *P. marsupium* (PM) and alcoholic extract of seeds of *Trigonella foenum-graecum* (FG) and leaves of *Ocimum sanctum* (OS)	Normal and diabetic rats Dose: PM 1 g/kg po	PM extract significantly (P<0.001) reduced the blood sugar levels from 72.32+/-5.62 to 61.35+/-1.2 mg% 2 h after oral administration and also significantly lowered the blood glucose in alloxan diabetic rats from 202.91+/-5.44 to 85.22+/-11.28 mg% 21 days after daily oral administration (P<0.001). Similarly, reduction was seen with FG extract (74.33+/-4.77 to 60.56+/-1.9 in normal rats and 201.25+/-7.69 to 121.25+/-6.25 in diabetic rats) (P<0.001) and OS (204.48+/-11.0 to 131.43+/-7.86 in normal rats and 73.54+/-3.7 to 61.44+/-2.3 in diabetic rats) (P<0.001). In addition, the extract also showed a favourable effect on glucose disposition in glucose fed hyperglycemic rats.	Vats V, Grover JK, Rathi SS. 2002. Evaluation of anti-hyperglycemic and hypogly-cemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and alloxanized diabetic rats. J Ethnophar-macol. Jan; 79 (1): 95-100.
Pterocarpus marsupium	Extract	Open human trial Newly diagnosed or untreated non-	A flexible dose open trial was undertaken in four centres in India to evaluate the efficacy of an Ayurvedic drug, P. marsupium, in the	Indian J Med Res. 1998 Jul; 108:24-9. Erratum in: [No authors listed] Flexible dose open trial of Vijayasar in cases of

		insulin dependent *Diabetes mellitus* patients 12 wks	treatment of newly-diagnosed or untreated non-insulin dependent diabetes mellitus. By 12 wk, control of blood glucose (both fasting and postprandial levels) had been attained in 67 (69%) of 97 patients studied, and the dose on which control was attained was 2 g of the extract in about 73% of the patients, 3 g in about 16% and 4 g in 10% of the patients. Four patients had to be withdrawn from treatment due to excessively high postprandial blood glucose levels. Among the 93 patients who completed the treatment, both the fasting and post-prandial blood glucose levels fell significantly from the initial means. Mean HbA1c decreased significantly from the initial mean. No significant change was observed in the mean levels of lipids. Other laboratory parameters remained stable during the designated treatment. Also, no side-effects were reported.	newly-diagnosed non-insulin-dependent diabetes mellitus. Indian Council of Medical Research (ICMR), Collaborating Centres, New Delhi. Indian J Med Res Nov; 108:253.
Salacia reticulata Wight Vairi, Pitika	herbal tea containing *S. reticulata* (Kothala Himbutu tea)	Clinical Trial Randomized Controlled Trial 51 patients with type II diabetes mellitus	The HbA1C at the end of drug treatment was significantly lower than after treatment with placebo (6.29 +/- S.D. 1.02 versus 6.65 +/- S.D. 1.04; P = 0.008). A statistically significant fall in HBA1c was seen with the active drug compared to a rise in HbA1C with the placebo group (0. 54 +/- S.D. 0.93) versus -0.3 +/-S.D. 1.05; P < 0.001. The daily mean dose of	Jayawardena MH, de Alwis NM, Hettigoda V, Fernando DJ. 2005. A double blind randomised placebo control-led cross over study of a herbal preparation containing Salacia reticulata in the treat-ment of type 2 diabetes. J Ethnopharmacol. Feb 28; 97 (2): 215-8. Epub 2005 Jan 7.

			Glibenclamide fell by 1.89 (S.D. 6.2) mg in the drug treated group but rose by 2.25 mg in the placebo treated group (P = 0.07). The differences in the metformin dose were not significantly significant in the two groups. We conclude that Kothala Himbutu tea is an effective and safe treatment for type 2 diabetes.	
Salacia reticulata	Aqueous extract of the root bark and stem fractions	Diabetic rats	Hypoglycemic potential of each fraction was evaluated, and the effect of active fraction was investigated in alloxan diabetic rats given long-term oral treatment. A significant hypoglycemic activity was established in the precipitate of methanol fraction, and it was used for the long-term oral treatment. Chronic oral administration of the precipitate from methanol fraction to alloxan diabetic rats twice a day for 120 days improved glucose tolerance and significantly reduced fasting blood glucose, fructosamine, and glycosylated hemoglobin levels. The polydypsia, hyperphagia, and weight loss of the alloxan diabetic rats were also reduced by the treatment. The results suggest that the hypoglycemic effect of *Salacia reticulata* in alloxan diabetic rats may involve an extrapancreatic effect on glucose production or clearance.	Kumara, N.K., Ruvin, V.M., Pathirana, R.N. and Pathirana, C. 2005. Hypogly-cemic activity of the root and stem of Salacia reticulata var. beta-diandra in alloxan diabetic rats. Pharmaceutical Biology 43, 3, 219-225.
Salacia reticulata	Root extract	Wistar rats Dose: orally 10	The extract significantly enhanced post-implantation losses	Ratnasooriya WD, Jayakody JR, Premakumara GA. 2003.

		g/kg during early (days 1-7) and mid-pregnancy(days 7-14)	(control vs treatment). Gestational length was unaltered but the pups born had a low birth weight (P<0.05) and low birth index (P<0.05), fetal survival ratio (P<0.05) and viability index (P<0.05). However, the root extract was non-teratogenic. We conclude that the S. reticulata root extract can be hazardous to successful pregnancy in women and should not be used in pregnancy complicated by diabetes.	Adverse pregnancy outcome in rats following exposure to a Salacia reticulate (Celastra-ceae) root extract. Braz J Med Biol Res. Jul; 36 (7): 931-5. Epub 2003 Jun 26.
Salacia reticulata	Two selenium analogues (10 and 11) of naturally occurring aqueous extract salacinol	In vitro	The syntheses of two selenium analogues (10 and 11) of the naturally occur-ring sulfonium ion, salacinol (3), are described. Salacinol is one of the active principles in the aqueous extracts of *S. reticulata* that is traditionally used in Sri Lanka and India for the treatment of diabetes. Enzyme inhibition assays indicate that 10 is a better inhibitor (K(i) = 0.72 mM) of glucoamylase than 3, which has a K(i) value of 1.7 mM. In contrast, 11 showed no significant inhibition of glucoamylase. Compounds 10 and 11 showed no significant inhibition of barley-alpha-amylase or porcine pancreatic-alpha-amylase.	Johnston BD, Ghavami A, Jensen MT, Svensson B, Pinto BM. 2002. Synthesis of selenium analogues of the naturally occurring glycosi-dase inhibitor salacinol and their evaluation as glycoside-ase inhibitors. J Am Chem Soc. Jul 17;124(28):8245-50.
Salacia reticulata	Salacinol	In vitro Rats	Salacinol showed potent inhibitory activities on several alpha-glucosidases, such as maltase, sucrase, and isomaltase, and the inhibitory effects on serum glucose levels in maltose- and sucrose-	Yoshikawa M, Morikawa T, Matsuda H, Tanabe G, Mura-oka O. 2002. Absolute ste-reostructure of potent alpha-glucosidase inhibitor, Salaci-nol, with unique thiosugar sulfonium sulfate inner

			loaded rats (in vivo) were found to be more potent than that of acarbose, a commercial alpha-glucosidase inhibitor.	salt structure from Salacia reticu-lata. Bioorg Med Chem. May; 10 (5): 1547-54.
Salacia reticulata	Synthetic nitrogen analogue of salacinol	In vitro	A nitrogen analogue 4 of the naturally occurring sulfonium ion salacinol (1), a potent alpha-glucosidase inhibitor isolated from the Ayruvedic medicine *S. reticulata,* was synthesized and its inhibitory activity against alpha-glucosidase tested. Substitution of the sulfur atom in 1 with a nitrogen reduced the activity considerably. The solid-state stereostructure of the related compound (5) was determined on the basis of single crystal X-ray measurement.	Muraoka O, Ying S, Yoshi-kai K, Matsuura Y, Yamada E, Minematsu T, Tanabe G, Matsuda H, Yoshikawa M. 2001. Synthesis of a nitrogen analogue of salacinol and its alpha-glucosidase inhibitory activity. Chem Pharm Bull (Tokyo). Nov;49(11):1503-5.
Salacia reticulata	Water soluble extract	Guinea pigs Dose: oral (64 or 320 mg/kg, 5 x wk/3 wks) or the subcuta-neous (64 mg/ kg,1xwk/3wks)	The antigenicity and phototoxicity of water-soluble extract from *S. reticulata* (SRE) were examined in guinea pigs. In a study of active systemic anaphylaxis reaction, neither the exhibited any anaphylactic reaction. Moreover, sensitization with serum obtained from these animals did not induce passive cutaneous anaphylaxis reaction in normal animals. In a phototoxicity study, oral administration of SRE (320 mg/kg) induced neither erythema nor edema. These results suggest that SRE is not antigenic or phototoxic.	Shimoda H, Asano I, Yama-da Y. 2001. [Antigenicity and phototoxicity of water-soluble extract from Salacia reticulate (Celastraceae)] [Article in Japanese]. Shoku-hin Eiseigaku Zasshi. Apr; 42 (2): 144-7.
Salacia reticulata	The syntheses of two nitrogen analogues (11 and 12) of the naturally	In vitro	Enzyme inhibition assays indicate that salacinol (7) is a weak (K(i) = 1.7 mM) inhibitor of	Ghavami A, Johnston BD, Jensen MT, Svensson B, Pinto BM. 2001. Synthesis of nitrogen analogues of

	occurring sulfoni-um ion, salacinol		glucoamylase, whereas compounds 11 and 12 inhibit glucoamylase with K(i) values in the range approximately 10-fold higher. The nitrogen analogues 11 and 12 showed no significant inhibitory effect of either barley alpha-amylase (AMY1) or porcine pancreatic alpha-amylase (PPA). In contrast, salacinol (7) inhibited AMY1 and PPA in the micromolar range, with K(i) values of 15 +/- 1 and 10 +/- 2 microM, respectively.	salacinol and their evaluation as glycosidase inhibitors. J Am Chem Soc. Jul 4; 123 (26): 6268-71.
Salacia reticulata	Kotalanol	In vitro	A potent natural alpha-glucosidase inhibitor called kotalanol has been isolated from an antidiabetic traditional Ayurvedic medicine, the roots and stems of *S. reticulata*, through bioassay-guided separation. The structure of kotalanol was elucidated on the basis of chemical and physicochemical evidence to be the inner salt comprised of 1-deoxyheptosyl-3-sulfate anion and 1-deoxy-4-thio-D-arabinofuranosyl sulfonium cation. Kotalanol was found to show more potent inhibitory activity against sucrase than salacinol and acarbose.	Yoshikawa M, Murakami T, Yashiro K, Matsuda H. 1998. Kotalanol, a potent alpha-glucosidase inhibitor with thiosugar sulfonium sulfate structure, from antidiabetic ayurvedic medicine Salacia reticulata. Chem Pharm Bull (Tokyo). Aug; 46 (8): 1339-40.
Syzygium cumini (Linn.) Skeels Jambuh	Tea from leaves Dose: 2 g/L H2O, taken as water substitute; plus placebo tablets; placebo tea ;plus glyburide tablets (5 mg 2/d), or	Double-blind, double-dummy clinical trial Patients with *Diabetes mellitus* Type 2	Fasting blood glucose levels decreased significantly in participants treated with glyburide and did not change in those treated with the *Syzygium cumini* tea and in the participants who received placebos from tea and glyburide. BMI, creatinine, ℽ-glutamyl	Teixeira CC, Weinert LS, Barbosa DC, Ricken C, Esteves JF, Fuchs FD. 2004. Syzygium cumini (L.) Skeels in the treatment of type 2 diabetes: results of a random-ized, double-blind, double-dummy, controlled trial. Dia-betes Care. Dec; 27 (12): 3019-20.

	placebo tea plus placebo tablets.		transferase, alkaline phosfatase, SGOT, SGPT, 24-h glicosuria, 24-h proteinuria, triglycerides, and total, LDL, and HDL cholesterol did not vary significantly among the groups.	
	Cogent db contains *Azadirachta indica* (AI), *E. Officinalis* (EO), *C. longa* (CL), *Trigonella foenum-graecum* (TF), *S. cumini* (SC), *Tribulus ter-restris* (TT), *T. bel-lirica* (TB), *T. che-bula* (TC), *Rotula aquatica* (RA)	Non-randomized, non-placebo-controlled clinical trial Dose: AI 3g; EO 0.7g; CL 0.8g; TF 0.1g; SC 2g; TT 1g; TB 0.7g; TC 0.7g; RA 1g	At the end of three months it was found that there was a significant decrease in the levels of fasting and postprandial blood glucose, cholesterol, triglycerides, glycated hemoglobin (Hb A[sub 1C]) and fasting insulin in the treatment group compared to the controls. Cogent db did not alter the liver function tests, hematologic parameters, or the kidney function tests. These results concur with earlier animal studies that indicate that Cogent db is safe, reliable, tolerable, and efficacious in the control of type 2 diabetes mellitus.	Shekhar, K.C., Achike, F.I., Kaur G. Kumar, P. and Hashim, R. 2002. A prelim-inary evaluation of the efficacy and safety of Cogent db (an Ayurvedic drug) in the glycemic control of patients with type-2 diabetes. J. Alt Compl Med 8, 4, 445-457.
Syzygium cumini	Fractions obtained from the seeds	Diabetic rats	These observations indicate that the hypoglycaemic effect of *S. cumini* seeds was due to water soluble gummy fibre and also that water insoluble neutral detergent fibre (NDF) and other constituents of the seeds had no significant hypoglycaemic effects.	Pandey M, Khan A. 2002. Hypoglycaemic effect of defatted seeds and water soluble fibre from the seeds of Syzygium cumini (Linn.) skeels in alloxan diabetic rats. Indian J Exp Biol. Oct; 40 (10): 1178-82.
Syzygium cumini	Aqueous seed extract (5g/kg) Alcoholic seed extract (100 mg/kg)	Diabetic rats	The effect of alcoholic was better than aqueous extract. The effect of both these extracts was better than glibenclamide (600 microg/kg). Thus, our study shows that *S. cumini* seed extracts reduce tissue damage in	Stanely Mainzen Prince P, Kamalakkannan N, Menon VP. 2003. Syzigium cumini seed extracts reduce tissue damage in diabetic rat brain. J Ethnopharmacol. Feb; 84 (2-3): 205-9.

			diabetic rat brain.	
Syzygium cumini	Tea prepared from leaves	Randomized placebo controlled trial 30 non-diabetic volunteers Rats and diabetic rats	In the first study, a randomized, parallel, placebo controlled trial; tea prepared from leaves of *S. cumini* did not present any antihyperglycemic effect. In the animal experiments, we tested the effect of increasing doses of the crude extract prepared from leaves of *S. cumini* administrated for 2 weeks, on the post-prandial blood glucose level of normal rats and rats with streptozotocin-induced diabetes mellitus. The treatment did not produce any antihyperglycernic effect in both models.	Teixeira CC, Rava CA, Mall-man da Silva P, Melchior R, Argenta R, Anselmi F, Al-meida CR, Fuchs FD. 2000. Absence of antihyperglyce-mic effect of jambolan in experimental and clinical models. J Ethnopharmacol. Jul; 71 (1-2): 343-7.
	DZ contains aque-ous extracts of the leaves of *Aegle marmelos*, *Azadira-chta indica* and *S. cumini*, stem of *T. cordifolia* and the seeds of *Trigonella foenum-graecum*			Bano, S., K. Javed and M.A. Jafri. 2000. Effect of a new Unani formulation 'DZ' on blood sugar of normal and alloxan-induced diabetic rats, Indian Journal of Pharmaco-logy 32, 2, 158.
Syzygium cumini	Tea from leaves and seeds	Albino rats Diabetic rats Dose: ranging from 2-64 g/l	None of the tea concentration had any detectable antihyperglycemic effect either in normal or in diabetic rats, suggesting that this plant, prepared in a manner similar to that employed by humans, does not demonstrate an antihyperglycemic effect.	Teixeira CC, Pinto LP, Kess-ler FH, Knijnik L, Pinto CP, Gastaldo GJ, Fuchs FD.1997. The effect of Syzygium cumini (L.) skeels on post-prandial blood glucose levels in non-diabetic rats and rats with streptozotocin-induced diabetes mellitus. J Ethnoph-armacol. May; 56 (3):209-13.
Terminalia bellirica (Gaertn.) Roxb. Vibhitakah,	Vacuum dried 95% ethanolic extract of 24 samples including:	Diabetic albino rats Dose: 250 mg/kg once,	In all the experiments with different herbal samples, definite blood glucose lowering effect within 2 weeks has been	Kar A, Choudhary BK, Bandyopadhyay NG. 2003. Comparative evaluation of hypoglycaemic activity

Aksah	*P. marsupium, T. bellirica, T. cordifolia, and Z. officinale*	twice or thrice daily, as needed	confirmed. Blood glucose values were brought down close to normal fasting level. While evaluating comparative hypoglycaemic activity of the experimental herbal samples, significant blood glucose lowering activities are observed in decreasing order in the following 4 samples: *P. marsupium, T. cordifolia, T. bellirica*, and *Z. officinale*.	of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol. Jan; 84 (1): 105-8.
Terminalia bellirica	Methanolic extract (75%) of *T. chebula*, *T. bellirica, E. officinalis* and their combination named 'Triphala' (equal proportion)	Diabetic rats Dose: Oral administration of the extracts (100 mg/kg body wt)	These plants were found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro. The concentration of plant extracts that inhibited 50% of lipid peroxidation induced with Fe(2+)/ascorbate were found to be 85.5, 27, 74 and 69 micro g/ml, respectively. The concentration needed for the inhibition of hydoxyl radical scavenging were 165, 71, 155.5 and 151 micro g/ml, and that for superoxide scavenging activity were found to be 20.5, 40.5, 6.5 and 12.5 micro g/ml, respectively. Oral administration reduced the blood sugar level in normal and in alloxan (120 mg/kg) diabetic rats significantly within 4 h. Continued, daily administration of the drug produced a sustained effect.	Sabu MC, Kuttan R. 2002. Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. J Ethnopharmacol. Jul; 81 (2): 155-60.
Terminalia bellirica	Cogent db contains *Azadirachta indica* (AI), *E. Officinalis* (EO), *C. longa* (CL), *Trigonella*	Non-randomized, non-placebo-controlled clinical trial Dose: AI 3g; EO 0.7g; CL	At the end of three months it was found that there was a significant decrease in the levels of fasting and postprandial blood glucose, cholesterol, triglycerides, glycated	Shekhar, K.C., Achike, F.I., Kaur G. Kumar, P. and Hashim, R. 2002. A prelim-inary evaluation of the efficacy and safety of Cogent db (an Ayurvedic drug) in the glycemic control of

	foenum-graecum (TF), *S. cumini* (SC), *Tribulus ter-restris* (TT), *T. bel-lirica* (TB), *T. che-bula* (TC), *Rotula aquatica* (RA)	0.8g; TF 0.1g; SC 2g; TT 1g; TB 0.7g; TC 0.7g; RA 1g	hemoglobin (Hb A[sub 1C]) and fasting insulin in the treatment group compared to the controls. Cogent db did not alter the liver function tests, hematologic parameters, or the kidney function tests. These results concur with earlier animal studies that indicate that Cogent db is safe, reliable, tolerable, and efficacious in the control of type 2 diabetes mellitus.	patients with type-2 diabetes. J. Alt Compl Med 8, 4, 445-457.
Terminalia chebula (Gaertn.) Retz. Haritaki. Pathya, Abhava	Methanolic extract (75%) of *T. chebula*, *T. bellirica, E. officinalis* and their combination named 'Triphala' (equal proportion)	Diabetic rats Dose: Oral administration of the extracts (100 mg/kg body wt)	These plants were found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro. The concentration of plant extracts that inhibited 50% of lipid peroxidation induced with Fe(2+)/ascorbate were found to be 85.5, 27, 74 and 69 micro g/ml, respectively. The concentration needed for the inhibition of hydoxyl radical scavenging were 165, 71, 155.5 and 151 micro g/ml, and that for superoxide scavenging activity were found to be 20.5, 40.5, 6.5 and 12.5 micro g/ml, respectively. Oral administration reduced the blood sugar level in normal and in alloxan (120 mg/kg) diabetic rats significantly within 4 h. Continued, daily administration of the drug produced a sustained effect.	Sabu MC, Kuttan R. 2002. Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. J Ethnopharmacol. Jul; 81 (2): 155-60.
Terminalis chebula	Cogent db contains *Azadirachta indica* (AI), *E. Officinalis* (EO), *C. longa* (CL), *Trigonella*	Non-randomized, non-placebo-controlled clinical trial Dose: AI 3g; EO 0.7g; CL	At the end of three months it was found that there was a significant decrease in the levels of fasting and postprandial blood glucose, cholesterol, triglycerides, glycated	Shekhar, K.C., Achike, F.I., Kaur G. Kumar, P. and Hashim, R. 2002. A prelim-inary evaluation of the efficacy and safety of Cogent db (an Ayurvedic drug) in the glycemic control of

	foenum-graecum (TF), *S. cumini* (SC), *Tribulus ter-restris* (TT), *T. bel-lirica* (TB), *T. che-bula* (TC), *Rotula aquatica* (RA)	0.8g; TF 0.1g; SC 2g; TT 1g; TB 0.7g; TC 0.7g; RA 1g	hemoglobin (Hb A[sub 1C]) and fasting insulin in the treatment group compared to the controls. Cogent db did not alter the liver function tests, hematologic parameters, or the kidney function tests. These results concur with earlier animal studies that indicate that Cogent db is safe, reliable, tolerable, and efficacious in the control of type 2 diabetes mellitus.	patients with type-2 diabetes. J. Alt Compl Med 8, 4, 445-457.
Tinospora cordifolia (Willd.) Miers ex Hook.f. & Thoms. Guduci, Amrta	Alcoholic extract of roots	Diabetic rats Dose: 100 mg/kg orally for 6 wks	A significant increase in the concentration of thiobarbituric acid reactive substances in brain along with a decrease in heart was observed in diabetic rats. Decreased concentration of glutathione and decreased activities of superoxide dismutase, catalase and glutathione peroxidase in heart and brain of diabetic rats were also noted. The effect of T. cordifolia root extract was more prominent than glibenclamide (600 microg/kg). Insulin (6 units/kg) restored all the parameters to normal status.	Prince PS, Kamalakkannan N, Menon VP. 2004. Resto-ration of antioxidants by ethanolic Tinospora cordifo-lia in alloxan-induced diabe-tic Wistar rats. Acta Pol Pharm. Jul-Aug; 61(4):283-7.
Tinospora cordifolia	Hyponidd: extracts of *Momordica cha-rantia*, *Melia azadi-rachta*, *P. marsu-pium*, *T. cordifolia*, *Gymnema sylvestre*, *Enicostemma littorale*, *E. officinalis*, *Eugenia jambolana*, *Cassia*	Diabetic rats Dose: 100 mg/kg and 200 mg/kg for 45 days	Oral administration of hyponidd resulted in significant lowered levels of blood glucose and significant increased levels of hepatic glycogen and total haemoglobin. An oral glucose tolerance test was also performed in experi-menttal diabetic rats in which there was a significant improvement in blood glucose tolerance. Hyponidd administration also	Babu PS, Stanely Mainzen Prince P. 2004. Antihyper-glycaemic and antioxidant effect of hyponidd, an ayurvedic herbomineral formulation in streptozo-tocin-induced diabetic rats. J Pharm Pharmacol. Nov; 56 (11): 1435-42.

	auriculata and *C. longa*.		decreased levels of glycosy-lated haemoglobin, plasma thiobarbituric acid reactive substances, hydroper-oxides, ceruloplasmin and alpha-tocopherol. Plasma reduced glutathione and vitamin C were significantly elevated by oral administration of hyponidd. The effect of hyponidd was more effective than glibenclamide (600 microg kg(-1)) in restoring the values to near normal. Hyponidd exhibits antihyperglycaemic and antioxidant activity in STZ-induced diabetic rats.	
Tinospora cordifolia	Alcohol extract of roots for 6 wks	Diabetic rats	Oral administration of the extract resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues. The extract also prevented a decrease in body weight. Thus our study clearly shows that an alcohol extract has a hypoglycemic and hypolipidemic action.	Stanely Mainzen Prince P, Menon VP. 2003. Hypogly-caemic and hypolipidaemic action of alcohol extract of Tinospora cordifolia roots in chemical induced diabetes in rats. Phytother Res. Apr; 17 (4): 410-3.
Tinospora cordifolia	Vacuum dried 95% ethanolic extract of 24 samples including: *P. marsupium, T. bellirica, T. cordifolia, and Z. officinale*	Diabetic albino rats Dose: 250 mg/kg once, twice or thrice daily, as needed	In all the experiments with different herbal samples, definite blood glucose lowering effect within 2 weeks has been confirmed. Blood glucose values were brought down close to normal fasting level. While evaluating comparative hypoglycaemic activity of the experimental herbal samples, significant blood glucose lowering activities are observed in decreasing order in the following 4 samples: *P. marsupium,*	Kar A, Choudhary BK, Bandyopadhyay NG. 2003. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol. Jan; 84 (1): 105-8.

			T. cordifolia, T. bellirica, and *Z. officinale*.	
Tinospora cordifolia	*Momordica charantia* (MC), *Eugenia jambolana* (EJ), *T. cordifolia* (TC) and *Mucuna pruriens* (MP)	Diabetic rats Dose: aqueous MC and EJ: 200 mg/kg p.o., alcohol TC: 400 mg/kg, and MP: 200 mg/kg p.o. d/4 months	The incidence rate of cataract in MC, EJ, TC and MP treated groups at 120 days was only 0, 0, 1 and 2. Oral feeding of MC, EJ, TC and MP extracts for 1 month produced a fall of 64.33%, 55.62%, 38.01% and 40.17%, respectively, in the serum glucose levels in comparison with the 48 h level. After 2 months of treatment, the respective values were 66.96%, 59.85%, 40.41% and 45.63%. MC and EJ prevented the development of cataract while the protective effect was less with TC and MP along with a significant reduction of plasma glucose levels.	Rathi SS, Grover JK, Vikrant V, Biswas NR. 2002. Preven-tion of experimental diabetic cataract by Indian Ayurvedic plant extracts. Phytother Res. Dec; 16 (8): 774-7.
Tinospora cordifolia	Extract of *M. charantia* (MC), *E. jambolana* (EJ), *M. pruriens* (MP), and *T. cordifolia* (TC)	Diabetic mice Dose: MC: 200 mg/kg; TC: 400 mg/kg; MP: 200 mg/kg; EJ: 200 mg/kg for 50 d	The plasma glucose concentration was reduced by 24.4, 20.84, 7.45 and 9.07% respectively. Tail flick latency (TFL) and gastric transit percentage were significantly higher in diabetic controls versus normal controls. *M. charantia* and *E. jambolana* modified it favorably while *M. pruriens* and *T. cordifolia* did not exert any favorable change.	Grover JK, Rathi SS, Vats V. 2002. Amelioration of exper-imental diabetic neuropathy and gastropathy in rats follo-wing oral administration of plant (Eugenia jambolana, Mucuna pruriens and Tino-spora cordifolia) extracts. Indian J Exp Biol. Mar; 40 (3): 273-6.
Tinospora cordifolia	*M. charantia* (MC), *E. jambolana* (EJ), *M. pruriens* (MP) and *T. cordifolia* (TC)	Diabetic rats Dose: daily oral feeding of MS 200 mg/kg; EJ 200 mg/kg; MP 200 mg/kg; and TC extracts for 40 d	Plasma glucose concentrations in STZ-diabetic mice were reduced significantly by the administration of extracts of MC, EJ, TC and MP. Urine volume was significantly higher in diabetic controls and MC, EJ, MP and TC	Grover JK, Vats V, Rathi SS, Dawar R. 2001. Traditional Indian anti-diabetic plants attenuate progression of renal damage in streptozotocin induced diabetic mice. J Ethnopharmacol. Aug; 76 (3): 233-8.

			treatment significantly prevented polyuria. After 10 days of STZ administration, urinary albumin levels (UAE) were over 6 fold higher in diabetic controls as compared to normal controls. Treatment with MC, EJ, MP and TC significantly prevented the rise in UAE levels from day 0 to 40 in comparison to diabetic controls. Renal hypertrophy was significantly higher in diabetic controls as compared to non-diabetic controls. MC and EJ partially but significantlyprevented renal hypertrophy as compared to diabetic controls. TC and MP failed to modify renal hypertrophy.	
Tinospora cordifolia	Aqueous root extract	Diabetic rats Dose: Oral 2.5 g and 5.0 g/kg body wt for 6 wks	Administration of the extract resulted in a significant reduction in thiobarbituric acid reactive substances (TBARS) and an increase in reduced glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD) in alloxan diabetic rats. The effect of the extract was most prominently seen in the case of rats given 5.0 g/kg body weight. The extract was more effective than glibenclamide. Thus our study shows that the extract exhibits antioxidant action in alloxan diabetes.	Stanely Mainzen Prince P, Menon VP. 2001. Antioxi-dant action of Tinospora cordifolia root extract in alloxan diabetic rats. Phytother Res. May; 15 (3): 213-8.
Tinospora cordifolia	Alcoholic extract and lyophilized powder of *Eugenia jambolana*	Animals Dose: EJ 200 mg/kg/d lyophilized powder; TC	In the pilot study (mild diabetes), maximum reduction of 73.51 and 70.37% in glucose levels was seen in animals. The percent reduction in	Grover JK, Vats V, Rathi SS. 2000. Anti-hyperglycemic effect of Eugenia jambolana and Tinospora cordifolia in experimental diabetes

	(EJ) and *T. cordifolia* (TC)	400 mg/kg/d aqueous extract	glucose decreased significantly in the moderate and severe diabetes; 55.62 and 17.72% for EJ and 48.81 and 0% for TC at the similar time intervals. The alteration in hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels in diabetic mice were partially restored by EJ but not by TC.	and their effects on key metabolic enzymes involved in carbo-hydrate metabolism. J Ethno-pharmacol. Dec; 73 (3): 461-70.
Tinospora cordifolia	Aqueous root extra	Diabetic rats	Administration of the extract caused a significant reduction in blood glucose and brain lipids. The extract caused an increase in body weight, total hemoglobin and hepatic hexokinase. The root extract also lowers hepatic glucose-6-phosphatase and serum acid phosphatase, alkaline phosphatase, and lactate dehydrogenase in diabetic rats. Thus extract has hypoglycemic and hypolipidemic effect.	Stanely P, Prince M, Menon VP. 2000. Hypoglycaemic and other related actions of Tinospora cordifolia roots in alloxan-induced diabetic rats. J Ethnopharmacol. Apr; 70 (1): 9-15.
Zingiber officinale Rosc. Ardrakam, Nagaram	Ethanolic extract	Diabetic rats Dose: 200 mg/kg	The results of test drug were comparable to gliclazide (25 mg/kg, orally), a standard antihyperglycaemic agent. The results indicate that extract can protect the tissues from lipid peroxidation. The extract also exhibit significant lipid lowering activity in diabetic rats. The present study is the first pilot study to assess the potential of Zingiber officinale in diabetic dyslipidaemia.	Bhandari U, Kanojia R, Pillai KK. 2005. Effect of ethanolic extract of Zingiber officinale on dyslipidaemia in diabetic rats. J Ethnopharmacol. Feb 28; 97 (2): 227-30.
Zingiber officinale	Ginger extract: gingerol	Mouse culture	Ginger extracts were found to enhance the	Sekiya K, Ohtani A, Kusano S. 2004.

			adipocyte differentiation. Active constituent was purified and identified as gingerol. In the gingerol-treated cells, insulin-sensitive glucose uptake was increased. It is expected that ginger enhance the insulin-sensitivity, and improve chronic disease, such as diabetes.	Enhancement of insulin sensitivity in adipo-cytes by ginger. Biofactors. 22(1-4):153-6.
Zingiber officinale	Juice	Diabetic rats Dose: 4 mL/kg, p.o. daily for 6 wks	Treatment with *Z. officinale* juice produced a significant increase in insulin levels and a decrease in fasting glucose levels in diabetic rats. In an oral glucose tolerance test, treatment was found to decrease significantly the area under the curve of glucose and to increase the area under the curve of insulin in STZ-diabetic rats. Treatment also caused a decrease in serum cholesterol, serum triglyceride and blood pressure. Data suggest a potential antidiabetic activity of the juice of *Z. officinale* in type I diabetic rats.	Akhani SP, Vishwakarma SL, Goyal RK. 2004. Anti-diabetic activity of Zingiber officinale in streptozotocin-induced type I diabetic rats. J Pharm Pharmacol. Jan; 56 (1): 101-5.
Zingiber officinale				Gonlachanvit S, Chen YH, Hasler WL, Sun WM, Owyang C. 2003. Ginger reduces hyperglycemia-evoked gastric dysrhythmias in healthy humans: possible role of endogenous prosta-glandins. J Pharmacol Exp Ther. Dec; 307 (3): 1098-103. Epub 2003 Oct 08.
Zingiber officinale	Vacuum dried 95% ethanolic extract of 24 samples including: *P. marsupium, T. bellirica, T. cordifolia, and Z. officinale*	Diabetic albino rats Dose: 250 mg/kg once, twice or thrice daily, as needed	In all the experiments with different herbal samples, definite blood glucose lowering effect within 2 weeks has been confirmed. Blood glucose values were brought down close to normal fasting level.	Kar A, Choudhary BK, Bandyopadhyay NG. 2003. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol. Jan; 84

			While evaluating comparative hypoglycaemic activity of the experimental herbal samples, significant blood glucose lowering activities are observed in decreasing order in the following 4 samples: *P. marsupium, T. cordifolia, T. bellirica*, and *Z. officinale*.	(1): 105-8.

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Siddha: Dravidian culture is the source of *Siddha* medical arts (originally, a *siddhar* was a devotee of the god Shiva; a *siddhi* is one who has achieved extraordinary power). A number of the early medical classics such as *Agathiya Vaidhya Rathina Churukkam* and *Agashtiya Vaidya Kaviyam* have been attributed to sage Agasthiya, the patron saint of the southern area of Tamil. Agasthiya is said to have communed with the

Gods and to have been gifted with profound knowledge. He is said to have set down the rules of the Tamil language and of Siddha medicine. According to tradition between the tenth and twelfth centuries C.E., eighteen additional Siddhas contributed to the growth of Siddha medicine. Sharma states that the basic concepts of Siddha medicine and Ayurveda are similar; however, differences arise due to local and aboriginal traditions that are based on Dravidian culture.

Tibetan: The seventh-century King Songtsen Gampo facilitated the flowering of Tibetan medicine. Eager to develop relations with neighboring countries, the monarch invited physicians from India, China, and Iran to the Tibetan court. Translations of these different medical traditions into the new Tibetan language occurred at this time and continued under the patronage of later kings. Later, physicians from Kashmir, Nepal, and Turkic regions of Central Asia also contributed to the evolving Tibetan healing arts. Modern-day Tibetan medicine is therefore an amalgam of Asian and Near Eastern medical traditions in addition to Tibetan aboriginal traditions.

Unani: Unani medicine originated in Greece. The Unani theoretical framework is based on the teachings of Hippocrates (460-377 B.C.E.). Galen (131-210 C.E.) also greatly developed Greek medical philosophy and practice. Later noted physicians Rhazes (850-925 C.E.) and Avicenna (aka Ibn Sina 980-1037 C.E.) further developed Unani medicine. Like Tibetan medicine, Unani was influenced by contemporary systems of traditional medicine in Egypt, Syria, Iraq, Persia, India, China, and other Near, Middle, and Far Eastern countries. In the South Asian subcontinent, Arabs introduced the Unani system. When Mongols invaded Persia and Central Asia in the early thirteenth century, later Unani scholars and physicians found refuge in South Asia since India had good relations with Persia, and economic and political conditions proved more favorable.[177] The Delhi Sultan, the Khiljis, the Tughlaqs, and the Mughal (aka Moguls) Emperors provided state patronage to the scholars and even enrolled some as state employees and court physicians. From the thirteenth to seventeenth centuries Unani medicine flourished. Practitioners and scholars who have made valuable contributions to Unani include Abu Bakr Bin Ali Usman Ksahani, Sadruddin Damashqui, Bahwa bin Khwas Khan, Ali Geelani, Akbal Arzani, and Mohammad Hashim Alvi Khan.

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