ABSTRACT

The Chemical Validation for Ayurvedic Medicine Implementation in American Medicine

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America has recently seen a rise in the interest, study, and use of natural remedies in conjunction with the advantages that modern medicine provides. However, there is contention concerning the validity of such natural remedies due to their use for millennia before modern science and technology were able to validate the benefits of such medicinal treatment. This thesis examines the scientific literature of several key spices and herbs used in Ayurvedic medicine—black pepper, cinnamon, fenugreek, garlic, ginger, St. John's wort, and turmeric—to determine the chemical and biochemical validity of the use of such natural components. Based on the substantial literature supporting the physiological advantages of the use of such, an argument is made for the role of natural remedies in preventative and affordable care in the practice of modern American medicine.

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THE CHEMICAL VALIDATION FOR AYURVEDIC MEDICINE IMPLEMENTATION IN AMERICAN MEDICINE

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INTRODUCTION

The Foundation of This Work

The American medical system is complex. On the one hand, it is the product of amazing technological advancements and as such is capable of feats of healing that were previously assumed never to be possible. On the other hand, there are several major problems present, including the high costs, the piecemeal infrastructure and funding, and the high number of uninsured individuals. Among these problems is the fact that the American population seems not to be significantly healthier than other similar countries. If the technology and lengthy training required for medical professionals gives American medicine such an advantage, why are there no results showing in the population's health?

There are several answers to this question, such as poor diet, lack of exercise, and socioeconomic factors, and the effects that each factor may have on another. However, a case may be made that one major answer to this question is that the American medical system lacks key components for holistic physical health of its citizens. Clearly, the significant medical technology and training is not enough. Rather, I would argue that the lack of sufficient preventative health measures and holistic healing models contribute to the continued struggle of the American medical system to provide long-term advantages to its population. Perhaps this is one of the reasons behind the recent rise in interest in alternative medicine. Alternative medicine—including Ayurveda, traditional Chinese medicine, acupuncture, chiropractic medicine, and homeopathy—provide a supplementary method of healing to the traditional method employed by physicians.

Though there is an increase in interest regarding alternative medicine practices, there is simultaneously much contention regarding the validity of the use of these alternative medicine practices. Some see them as made-up, useless attempts at medicine that are at best ignorant and at worst antithetical to science. However, the millennia of use of these alternative medicines should not be discounted, as they would not have lasted for the length of time they did if they had not been effective in some capacity. A better response to the unknown scientific validity of alternative medicine practices would be to develop and accomplish work that examines whether the alternative medical treatments do have a medicinal effect of some sort. In response to this, this thesis seeks to address the topic of the validity, in some small capacity, of alternative medicine, by examining the literature on the chemical validity of seven specific plants used in Ayurveda, an ancient Indian medicine. Following that, a case will be presented on whether and how alternative medicine may be implemented in American medicine.

In the first chapter, the specifics of Ayurveda will be described in order to better understand the nature of this particular alternative medicine practice. As Ayurveda is largely based on naturally occurring remedies for medical treatment, and especially on plants within the natural remedies, it is an ideal alternative medicine to study for the purpose of this work. The history of Ayurveda will also be studied, both in support of its use predominating for the length of time it did and to highlight the differences in modern and ancient medicine.

In the second chapter, four key spices used in Ayurvedic medicine will be studied for two purposes: their biochemical actions and their clinical physiological significance. Black pepper is studied for its effect on the gastrointestinal system and drug

bioavailability, and its antioxidant, anticarcinogenic, anti-inflammatory, and pain-relieving properties. Cinnamon is studied for its role in immune response regulation, increase in insulin function, lipid regulation, and its antioxidant, anti-inflammatory, and neuroprotective properties. Ginger is studied for its anticarcinogenic, cardioprotective, antioxidant, and antinausea properties. Finally, turmeric is studied for its anticarcinogenic, antioxidant, and neuroprotective properties.

In the third chapter, three key herbs used in Ayurvedic medicine will be studied in a manner similar to that of the spices examined in the second chapter. The three herbs being studied are fenugreek, garlic, and St. John's wort. Fenugreek is studied for its role in the regulation of metabolism and regulation of lipids, as well as its anticarcinogenic properties. Garlic is studied for its anticarcinogenic and anti-inflammatory properties. Finally, St. John's wort is studied for its antidepressant and pain relief properties.

In the fourth chapter, the chemical and clinical validity of the spices and herbs examined will be reiterated. The principles of these spices and herbs will be extrapolated to argue the implementation of alternative medicine in American medicine. Two concepts are significant for this argument—that of the importance of preventative medicine and of the financial advantage to incorporating components of Ayurvedic medicine into the modern American medical system.

CHAPTER ONE

The Nature and History of Ayurvedic Medicine

The Ayurvedic system of medicine is considered one of the oldest forms of medicine. It originated in India over five thousand years ago. Ayurvedic medicine, or Ayurveda, is one of the complementary and alternative medicine (CAM) practices. Other CAM practices recognized by the National Cancer Institute (NCI) include Traditional Chinese medicine, acupuncture, naturopathic medicine (NCI, 2022). Some treatments utilized by CAM include meditation, yoga, massage therapy, chiropractic therapy, and dietary supplements. Unlike contemporary Western medicine, Ayurveda focuses on integrating the mind, body, and spirit of a person rather than individual systems. For the purpose of this paper, the philosophical validity of whether or not people have souls will not be argued. It will be taken as true, in order that the biochemical validity of the medicine may be discussed.

Western medicine, which includes American medicine as is recognized today, functions entirely from a biological materialistic worldview. Disease is caused by some physical abnormality in the body or by some pathogen, such as bacteria or viruses. In that view, the best, if not only, way to fix the disease is to get rid of that abnormality, whether by modern pharmaceuticals or surgery. There is no space for alternate causes of disease or illness. However, there are many different forms of medicine that would argue, and even practice, from a different worldview. CAM work from the belief that there may be other causes of disease and illness. These may include things such as spiritual or mental struggles or imbalances (Sharma, 2016). While they may or may not present with any

biological symptoms as required by modern American medicine to be classified as a disease or illness, the patient is still suffering—to which the healthcare provider should feel a desire to heal. This is not to say that modern American medicine is inept; rather, it is excellent for addressing biological maladies, but that these are not the only form of suffering which a healthcare provider can address. It can be argued that American medicine often only treats symptoms rather than properly addressing the underlying cause. Thus, CAM are to be considered supplemental forms of medicine—they do not replace, but rather can be used alongside modern American medicine in order to enhance the healing and wellbeing of patients.

The word 'Ayurvedic' comes from two Sanskrit words: *ayur*, meaning "life," and *veda*, meaning "knowledge." Putting these together, Ayurveda means "knowledge of life." It came to be referred to in this manner due to the understanding of both the human body as well as understanding about the natural world that the Ayurvedic healer possessed (Dobbins, 2019). "Ayurveda is nothing but the knowledge of the unity of the body, senses, mind and soul which in turn increases a life longitivity of the human body" (Tiwari, *et al*., 2021).

Principles of Ayurveda

The mind and body are inherently connected. With the two being so intertwined, any change in the mind will cause some sort of relational change to the body; similarly, any change in the body will cause some sort of change to the mind. There are three components to a person. These three—physical existence (body), mental existence (mind), and personality (spirit)—each exist as their own unique element. However, they do influence the others (Mills, 2019). This holistic approach to medicine differs from

American medicine's school of thought. While there has been more research showing the connection between and influence of mental health on physical health and vice versa, the connection to the personality or spirit of a person is missing.

One of the differences between Ayurveda and contemporary American medicine is that Ayurvedic medicine has its basis in balance. Medical intervention is needed when something in the person is out of balance. This can occur when there is a disconnect between mind and body, or between the person and nature, or other such imbalances.

Another one of the major differences between Ayurveda and contemporary American medicine is that Ayurveda is non-invasive. Treatment is given with balance and the holistic person in mind. Prescriptions are entirely natural, i.e., things from the natural world, to bring or maintain balance with the earth. These can take the form of herbal medicines, meditation, yoga, massage, special diets, and medical oils, among others. This paper will be looking specifically at the use of herbal medicines, though the other sources of healing should not be neglected in one's recognition of Ayurveda.

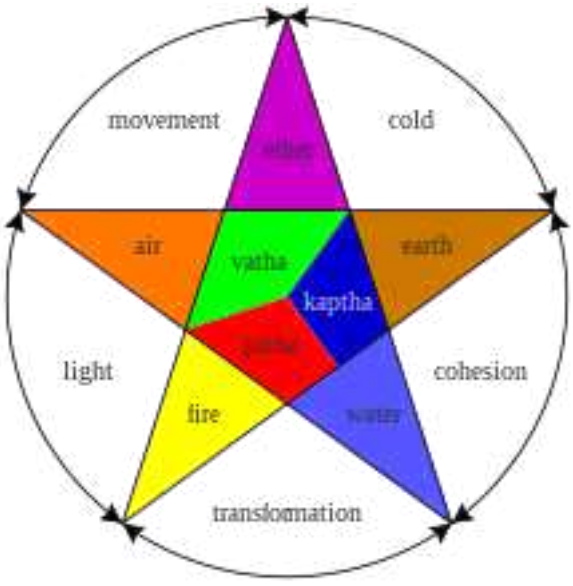

Figure 1: Tridosha of Ayurveda. (Krishnavedala, 2013.)

Three universal, fundamental energies regulate natural processes and thus maintain the balance of the healthy individual. These energies are collectively called the Tridosha (Fig. 1). Individually, they are *vātha* (air), *pitha* (bile and fire), and *kaptha* (phlegm, earth and water). They function at both the macro- and microcosmic level, which means that the same processes that govern human physiology also govern the physiology of the universe. The balance between these three energies is found in five elements: earth, air, fire, water, and ether. For each of these elements there are ten pairings of qualities that affect the balance. These include cold/hot, soft/hard, smooth/coarse, heavy/light, dull/sharp, unctuous/dry, stable/mobile, minute/gross, viscous/liquid, and non-slimy/slimy. An imbalance of these bodily and mental components, the doshas, results in disease (Mishra, *et al*., 2001).

An important note to be made is that there are two theories about individual balance of the energies. One view holds that the doshas are the same for everyone—every single person has an equal amount of *pitha*, *kaptha*, and *vātha* if she is healthy. The other view holds that the balance between the doshas is not universal. That is to say, not everyone has the same balance between, or amounts of, the Tridosha. Instead, each person is made up of her own particular balance (Mishra, *et al*., 2001). One might have more *pitha* than others, while another might have less *kaptha* than others. According to this view, an Ayurvedic healer must not only know what to diagnose to correct an imbalance, he must also be able to discern or discover how the particular patient is composed and find balance from there.

Components of Ayurveda

Historically and currently, Ayurveda has eight components governing its practice (Dutt, 1899). These eight are:

- Internal Medicine (*Kayachikitsa*)
- General Surgery (*Shalya Tantra*)
- Otorhinolaryngology (*Shalakya Tantra*)
- Pediatrics and Obstetrics/Gynecology (*Kaumara-bhrtya*)
- Psychiatry (*Bhutavidya*)
- Toxicology (*Agada Tantra*)
- Nutrition, Detoxification and Rejuvenation (*Rasayana Tantra*)
- Fertility and Virility (*Vajikarana*)

Due to differences in translation, there are several English iterations of the original names of each of these components. The terms given above will be used throughout this paper. Of these eight components, two are surgical in some capacity: *shalya tantra* and *kayachikitsa*. While they are important components, much of Ayurvedic medicine utilizes the natural remedies that the other components can apply in practice.

Diagnosis

Ayurveda has eight different ways to diagnose illness. *Nadi* focuses on the pulse, *mootra* on urine, *mala* on stool, *jihva* on the tongue, *shabda* on speech, *sparsha* on touch, *druk* on vision, and *aakruti* on appearance. For an Ayurvedic healer to diagnose patients, a physical examination is required. Healers use their five senses to discern what the problem is and where it originates (Dutt, 1899). For example, a healer might listen to

observe any differences in breathing and speech, or use touch to observe any change in a patient's pulse or skin.

One consideration of the modern practice of Ayurvedic medicine is telehealth. Telehealth here refers to the provision of medical services by use of telecommunication technology. Because Ayurveda does not have or use the conveniences of modern medicine, its utilization of things such as telehealth has been limited. While some things can still be done from afar over a live video call, such as listening to the patient's respiration, there are still limits to telemedicine in regards to Ayurveda, as well as other CAM practices. All of the senses are limited to the quality of the video call. Poor lighting, loud levels of background noise, and a distracted patient, among others, are all factors that lower the quality and thus effectiveness of diagnosis and the following treatment. A few of the senses—touch and smell—cannot be used at all by the physician. Though the patient can pass along that information, by describing his own observations based on touch and smell, they are not always accurate or helpful. All of these things can be inconvenient at best and problematic or misleading at worst, leading to misdiagnosis and potentially even exacerbation of the disease by prescribing the wrong medicine. However, due to Ayurvedic medicine being more based upon physical observations, it is that much more reliant upon the accuracy of physical observations compared to modern medicine.

Treatment

As previously mentioned, traditionally, two of the eight branches of Ayurveda are surgical, those being *kayachikitsa*, internal medicine, and *shalya tantra*, general surgery. However, for the purposes of this paper, Ayurvedic medicine is being considered only in

a supplemental light, which is to say only in conjunction with modern American medicine. Because modern American medicine is biology-centric and relies on and utilizes much more advanced technology, surgery will be left under the jurisdiction of modern American medicine. Contemporary Ayurveda, then, will focus on building and then maintaining a healthy lifestyle in order to maintain a balanced metabolic system. Thus, most surgeries and invasive procedures are done in hospitals and using modern medical technology for better success. Ayurveda is then used as preventative or enrichment medicine for smaller medical issues in addition to the modern medicine for emergent or invasive needs.

This relationship could be considered similar to that of the internal balance within modern American medicine between the primary care physician and specialists. Primary care physicians are responsible for the longitudinal and broad health of their patients. Longitudinally, primary care physicians care for their patients over the course of the patient's entire life, unless the patient should change physicians for some reason. This means that primary care physicians are responsible for the long-term health consequences of their patients. Thus, they deal with the habitual health behaviors—exercise, smoking, diet, and more. Additionally, primary care physicians are responsible for the broad overall health of their patients. It is the role of the primary care physician to know and understand the whole body, though at a less detailed knowledge or skill level compared to that of a specialist. Using that broad knowledge, the primary care physician is able to regulate smaller or more common health problems. When the disease or injury goes beyond the depth of knowledge or skill of the primary care physician, or requires immediate and complicated intervention, the primary care physician refers the patient to a

specialist. The specialist, with a much more detailed knowledge and skill level but on a much smaller scope, is then able to address that particular need before sending the patient back to the primary care physician.

The relationship between Ayurvedic and other CAM with modern American medicine can be seen as analogous to this model of primary care physicians and specialists. Ayurvedic healthcare providers are concerned with the long-term and overall health of a patient—meaning, keeping her in balance. This balance is achieved by two types of treatment—nourishing and depleting. A patient may have too much or too little of one or more of the Doshas or of the five elements governing the Tridosha. Healing, in this light, is then achieved by the addition or subtraction of relevant components. Additionally, Ayurvedic healthcare providers are able to address the health issues that may arise from some cause other than biological that may affect patients' day-to-day living. This increases the overall well-being of the patients over time. When there is a medical problem too great or too complicated for Ayurveda to address well, modern American medicine provides its skill and technological advantage to heal the patient. With this in mind, the methods of treatment according to Ayurveda will now be considered.

The medicinal use of plants is the most important facet of Ayurvedic treatment. Over 90% of treatments are plant based (Dymock, *et al*., 1890). Various components of the plants are used, including the fruit, leaves, roots, bark, berries, and seeds. William Dymock, along with others, wrote a history of the various botanical drugs used in British India in the 19th century. This comprehensive summary includes the history, habitat, microscopic structure, description, toxicology, and uses of each plant used medicinally at

that time. Because there are hundreds of different plants all with varied uses that are involved in Ayurvedic medicine, as Dymock described, not every plant used for treatment will be listed here. Instead, some of the most common and most useful plants will be described in further detail.

In addition to the many plants used, Ayurveda utilizes several other natural sources for treatment. These include animal products, minerals, alcohol, and oils. The primary animal products used are milk, bones, and fat. Minerals commonly used historically include arsenic, copper, gold, lead, and sulfur. Often, minerals were mixed into botanical remedies, a practice called *rasashastra.*

Alcohols used for treatment are referred to as *madya*. This is said to increase *pitta*, or bile and fire, and decrease the other two *dosha*, *vātha* and *kaptha*. This method of treatment is considered fast-acting and "enters into minute pores of the body and cleaning them, spreads quickly and produces looseness of joints" (Sekar, 2007). Different types of *Madya* are categorized according to their fermentation process and the ingredients used. Some categories include: fruit-based, fermented with vinegar, sugar-based, and tonic wines. *Madya* are used for a variety of treatments, such as purging, creating dryness, loosening joins, and improving taste when combined with other treatment methods such as plant-based consumptive treatment (Sekar, 2007).

Oils are another method of treatment utilized by Ayurveda. These are primarily used topically, though they can be consumed as well. The most common use of oil is with massage. Other uses include smearing with oil, applying oil to the affected area, oil pulling, where oil is used similar to mouthwash, and *shirodhara*, the anointing of one's forehead with oil. An additional use of oil is, along with tar, to stop bleeding.

Because plants were the primary method of treatment, these will be the focus of this study of integrating Ayurveda and modern American medicine. This is not to decrease the importance of other methods of treatment used in Ayurvedic medicine. Given the holistic nature of Ayurveda, the many facets and various routes which practitioners employ for healing ought not be surprising, and indeed, expected. The full scope of Ayurveda will not be covered in detail here. Because the purpose of this paper is to use the biochemical activity of natural plant remedies as used by Ayurvedic medicine, such as spices and herbs, to make an argument for their incorporation into modern American medicine, the other treatment components will not be discussed beyond what already has been covered. While there may be an argument for greater incorporation of those other methods of treatment into mainstream American medicine, that must be considered in some other paper.

History of Ayurveda

The history of Ayurveda will now be described. Ayurveda is concerned an ancient practice of medicine because it predates the written word in its country of origin. For the purpose of this work, Ayurveda will be discussed in four periods of Indian history. These are the Vedic Period, Puranic Period, Indian Middle Ages, and Modern Period (Fig. 2). Each historical period included is due to the advancements or characteristics of the Ayurveda within the given period. The Vedic Period describes the origin of Ayurveda, even before surviving written texts. The Puranic Period is characterized by the first written texts of Ayurvedic observations. Three compendia, *Charaka Samhita*, *Sushruta Samhita,* and *Bhela Samhita*, are the primary historical texts described. Translation and spread of Ayurvedic practice to other countries is observed in the Indian Middle Ages.

Finally, the section on the Modern Period describes the continued use of Ayurveda within the past century and a half, as well as its spread to America.

Historical Period	Dates
Vedic Period	c. 1500 – 500 BC
Puranic Period	c. 500 BC – 500 AD
Indian Middle Ages	c. 500 – 1700 AD
Modern Period	c. 1850 – present

Figure 2: Historical Periods of Ayurveda and Their Given Dates

Vedic Period (c. 1500 – 500 BC)

Some scholars would argue that Ayurveda has existed since 3000 BC. However, the surviving text of that time and in the region—the Indus script—has not been deciphered, so this argument is cast into doubt. There is, however, historical evidence that the practice of Ayurveda dates back to the first millennium BC. According to Indian historical records, this period, has the first documented use of herbs medicinally to heal ailments (Tiwari, *et al*., 2021). At this time there were no written collections of Ayurvedic practice or treatments; instead, the knowledge was passed down by word of mouth.

At its origin, Ayurvedic medicine started as a magico-religious practice, though there is debate about the specific means by which it first came about. According to the mythological account of the history of Ayurveda, Brahmâ, the Hindu god of creation, gave four treatises of the sciences to humanity—the science of law, of the bow, of music,

and Ayurveda, the science of life (Dutt, 1899). This treatise gave a systematic description of health, the causes of disease, and the cures thereof. It was originally shared with the gods, until humanity had become so diseased and full of suffering that the gods convened and decided to bring the knowledge of medicine to humankind. Dhanwantari, a physician or holy sage, was chosen to be the one to leave heaven to teach the practice of medicine to people. He has since been regarded as the god of Ayurveda and believed to be reincarnated as King Divodāsa of Varanasi (Girindranāth, M, 1977).

Many view Greece as the mother of medical science, considering the work of Hippocrates and others. However, there is an account, following 330 BC when Alexander the Great conquered the Persian Empire, stating that an individual from India offered, "I shall send to the great conqueror your master…a physician who has such skill that he can restore the dead" (Wise, 1867). This shows that there was, by that point, already a strong practice of medicine in India. There is also a case to be made that Hippocrates gained a portion of his medical knowledge from India and other eastern countries. This is based on the fact that there are several medicinal plants from India mentioned in Hippocrates' writings.

A quick note to be added here: there may be contention to call the use of plants as medicine a science. However, the root word of science, Latin *scire*, means "to know." Though it is not the same systematic, technologically assisted method of research "science" is often used to refer to now, Ayurveda was considered a science per the understanding of science at the time because it is the knowledge of medicine. This knowledge was based upon the natural world because the natural world was the foundation of all information. This explains why Ayurveda is so rooted in balance,

specifically balance with the earth: with the earth as the source of all knowledge, any problem in the human body has some relation to the earth.

Puranic Period (c. 500 BC - 500 AD)

The Puranic period, according to Indian chronology, is when written accounts of Ayurveda are first observed. Specifically, there are three main texts that remain to this day: *Charaka Samhita*, *Sushruta Samhita,* and *Bhela Samhita* (Tiwari, *et al*., 2021). Each of these are compendia of Ayurvedic knowledge, similar to the Hippocratic compendium of Greek medical knowledge. They are compiled by several individuals together. There has been research and debate about the dating of these texts over the centuries, though all sources date them as ancient texts.

The *Charaka Samhita*, literally "Charaka's Compendium," is written in a form similar to that of Plato—a dialogue between a teacher and a student on a variety of topics (Dutt, 1899). This text is quite large, containing one hundred twenty chapters divided into eight separate sections. Throughout the text, the student asks many questions of the teacher, on matters philosophical and practical. By doing so, the author is able to give information relevant not just to the practical needs of medicine, but also on the philosophy of Ayurveda from which it functions. The text includes details on the eight components of Ayurveda. It is also credited to be one of the first texts to give a systematic description of the causes and cures for particular diseases, as well as being the first written text with an objective standard by which to perform a clinical examination.

The *Sushruta Samhita* was written, like the *Charaka Samhita*, by multiple authors. The primary author listed is Sushruta, who claims to be a pupil of King Divodāsa, the incarnation of the one who originally brought Ayurveda to humanity. The

Sushruta Samhita was written after the *Charaka Samhita*. Both texts contain a significant amount of similar information, though the *Sushruta Samhita* has something which the *Charaka Samhita* does not cover: surgery. The *Sushruta Samhita* is considered one of the first texts describing surgical training, procedures, and instruments (Dutt, 1899). For example, it is the first record of rhinoplasty known, and describes fifteen different methods of this surgical procedure, some of which are still used in some form today. It is also one of the earliest texts stating that students of medicine ought to learn about the human body and its functioning by dissecting a dead body.

The *Bhela Samhita* is written similarly to that of the *Charaka Samhita*—as a dialogue between teacher and student. Here, the teacher is Atreya, one of the great Ayurvedic sages, conversing with his pupil Bhela. Several other individuals take part in the conversation at various points, each of whom asks questions about specific topics. For example, Gurdalu Bhekin asks Atreya about medical topography. This text is also similar to the *Charaka Samhita* in the contents, as both deal with the eight components of Ayurveda and state agreeing arguments and opinions on many topics. There are some differences, however. The *Bhela Samhita* discussed internal medicine in more detail and is written in a more concise and comprehensible way.

Indian Middle Ages (c. 500 AD – 1200 AD)

During this time, Ayurvedic medicine began to be practiced in countries beyond Indian. More texts of Indian medicine were compiled. Both *Charaka Samhita* and *Sushruta Samhita* were translated initially into Chinese and then later into both Arabic and Persian languages. By the twelfth century, translations of Indian medicine had made

it to Europe. Surgical techniques of the *Sushruta Samhita* were used by Italian Renaissance families in Sicily and Bologna (Harrison, 2016).

As the Ayurvedic texts were translated and being spread around the world, the practice of Ayurveda itself was becoming more standardized. The spread of the methods of diagnosing and treating disease and injury meant more and more healthcare providers were using the same methods around the world. As they were increasingly used, the treatments were progressively becoming more specific as the knowledge from case studies regarding any particular disease increased.

There is a distinction in the greater history of India between the Middle Ages and the Late Middle Ages, spanning approximately from 1200 to 1700 AD. However, there were no great advancements or changes made to the practice of Ayurveda during this time, as it had already been established in previous historical periods, so it is not discussed in detail in this work.

Modern Period (c. 1850 – present)

The Indian Modern Period is considered to have begun 1857-1858 when northern India revolted and then abolished the rule of the East Indian Company over the nation (Metcalf, 2001). Ayurveda is still largely practiced in India in modern times. One study found that up to 80% of the Indian population uses Ayurveda, individually or in combination with conventional modern medicine. Due to its prevalence, the Indian government has passed several bills regarding the standardization and qualifications of practicing Ayurveda.

Because Ayurveda is one of the few medical systems being practiced today that started in ancient times, there has been debate about whether and to what degree

Ayurveda practice should be modernized to better syncretize with modern medical practices. This sparked a debate in India in the first decades in the twentieth century between those wanted Ayurveda to remain unchanged, what is called *śuddha* (pure) Ayurveda, and those who wanted to modernize Ayurveda, what is called *aśuddha* (impure) Ayurveda. This debate continues in India today.

Ayurveda was introduced to the West in the twentieth century. In doing so, Ayurveda was adapted to better cater to the American medical system. In some cases, this was due to proposing that Ayurveda be held to American standards of modern medical research. By adapting Ayurveda for Western culture, a number of ethical issues are raised, especially regarding the authenticity and thus validity of Ayurveda as a medical practice.

Ayurveda was adapted for Western use primarily by two people—Baba Hari Dass and Maharishi Mahesh Yogi. Baba Hari Dass is recognized as the primary person who brought Ayurveda to America in the 1970s. He brought several Ayurvedic instructors to America to allow Ayurvedic medical training to take place in America. However, even with his contributions, the United States do not license or regulate the practice of Ayurveda in any state. Maharishi Mahesh Yogi led Ayurveda in Switzerland, opening the first Ayurvedic clinic there in 1987. As recently as 2015, the Swiss government recognized a diploma in Ayurveda. However, Maharishi Mahesh Yogi introduced and taught an approach distinct from traditional Ayurveda—the Maharishi Vedic Approach to Health (MVAH). This approach, more psychological in practice than that of the traditional form, focuses on the importance of consciousness and positive emotions for health.

Though Ayurveda has been introduced and is practiced in America, it is not a popular or widely used medical practice. According to several studies, Ayurveda lacks scientific soundness. Many of the treatments used have not shown to actually have any medicinal effect. Because of this, and due to the American push for advancement in medicine and medical technology, Ayurveda remains sparsely used in America, though there are some Ayurveda-based pharmaceutical drugs available in America today, such as the laxative Senekot. However, by looking into the biochemical mechanisms employed by various Ayurvedic natural remedies, an argument for its incorporation into American medicine may be made. Thus, the scientific literature regarding the scientific literature of seven Ayurvedic spices and herbs will now be examined in detail, in order to determine the scientific validity of the use of Ayurvedic and other alternative medicines in America today.

CHAPTER TWO

The Chemical Foundation of Key Spices Used in Ayurveda

Spices comprise a large portion of Ayurvedic remedies. This is not surprising, considering how India is known for its spices. They are the reason ambassadors from other countries traveled to India and established trade routes. A spice is here defined as a piece of a plant used, be it fruit, seed, flower, root, or other component, crushed to a loose powder, used in small quantities, usually for consumption. The spices used are employed for a variety of reasons—flavor, color, and as a preservative, to name a few. However, many of the spices have medicinal effects as well. These medicinal effects vary based on the spice and how it is used to effect healing.

Ayurvedic medicine, as mentioned previously, is not based upon scientific research, given its history dating back to before a defined scientific method. However, this is not to say that there was no basis or criteria by which medicine was practiced. It was still evidence-based; this evidence was just different technology than what is expected or required in modern times. Much of Ayurveda, along with other ancient medical practices, was based on observation and trial-and-error. One could look at an individual's diet and compare his health with others. For example, a woman who includes ginger in her cooking is observed to be less nauseous during pregnancy than her peers who did not cook with ginger to the same degree. Medical treatments could also be determined via a trial-and-error method. Mentally, orally, or physically recording the effects of a particular treatment on a person's health is an effective, albeit inefficient, method for determining how to treat various illnesses and injuries.

There are numerous spices used in Ayurvedic medicine, too many to describe all of them within this paper. Instead, a few of the key spices used will be described in detail and these principles extrapolated to cover more broadly the other spices used in Ayurvedic medicine. This is not to assume that research demonstrating the validity of medicinal use of one spice extends to the validity of medicinal use of a different spice; rather, it is to combat the argument that Ayurvedic medicine in its entirety is outdated and of no use. Instead, after explaining the experimentally-determined validity of some spices, it will be argued that a more in depth conversation regarding the use of natural remedies, such as spices, ought to be held. First, however, the scientific research of the biochemical actions of the select few spices will be analyzed in detail in order to determine the validity of the use of the spices in Ayurvedic medical treatment. This will, in turn, show how accurate the observational and trial-and-error methods in deciding medical treatment are compared to modern scientific research. The spices chosen for in-depth study are black pepper, cinnamon, ginger, and turmeric.

Black Pepper

Black pepper (*Piper nigrum*) is considered by some to be the "king of the spices" (Aggarwal, 2009). It has been used around the world, primarily for food flavoring, for several thousand years, as far back as 2000 BC in Indian cooking. Additionally, peppercorns were considered an important and valuable trading good. Black pepper was one of the spices motivating the European desire to establish trade routes with India. It was also used for preservation of food in the Middle Ages, though that required a much higher quantity than is necessary for its use in flavoring. An added benefit of using black pepper to preserve food, such as meat, was the extra flavor given to that preserved meat

when it was later consumed. Currently, ground pepper is one of the most commonly used spices globally. Black pepper, in spice form, is derived from the plant, which belongs in the Piperaceae family. The spice is prepared by cooking unripe berries in hot water. This heat causes the cell membrane to rupture, releasing enzymes that give the spice its characteristic dark color when dried. Once dried, the seeds are often ground and added to food in that form. Alternatively, the seeds can be left to mature before being cooked, dried, and then used in its whole form, referred to as peppercorn.

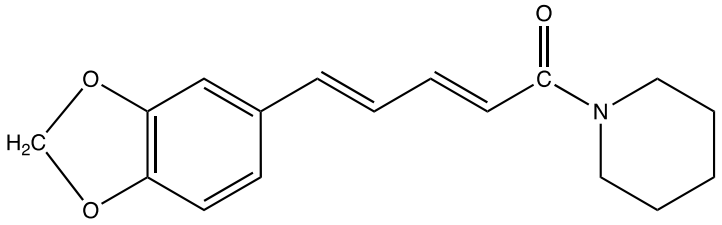

Figure 3: Structure of Piperine

The plant is native to India and has been used for medical purposes for thousands of years as well. The active component of black pepper, piperine (Fig. 3), has multiple medicinal effects in addition to its flavorful nature and antimicrobial properties which allow it to function as a food preservative. These effects include influence on the gastrointestinal system, inhibition of drug-metabolizing enzymes, enhancing effects on drug bioavailability, antioxidant properties, tumor inhibitory and antimutagenic properties, as well as various other physiological effects (Srinivasan, 2009). These effects are due primarily to how piperine acts as an inhibitor to gastrointestinal enzymes responsible for drug metabolism, such as CYP1A1, CYP1A2, CYP2D6, CYP3A4, and P-glycoprotein. “The mode of action of this alkaloid in various medicinal effects is undoubtedly its bioavailability enhancing influence on various structurally and

therapeutically diverse drugs. Piperine's potential to increase the bioavailability of drugs when pretreated or co-administered is of great clinical significance" (Srinivasan, 2009). Alkaloid here refers to a naturally occurring organic compound containing a nitrogen group, as seen above, which has known pronounced physiological effects on humans.

There are multiple experimentally validated effects that piperine, and thus black pepper, have on the gastrointestinal system. These include, among others, digestive stimulant action, antidiarrheal property, and a positive influence on absorptive function. Regarding piperine's digestive stimulative action, it stimulates the digestive enzymes of both the pancreas and the small intestine, including lipase, amylase, trypsin, and chemotrypsin (Platel and Srinivasan, 2000). By stimulating these digestive enzymes, black pepper increases the overall digestion and metabolism. Piperine had an antidiarrheal effect against castor oil induced diarrhea, suggesting that it acts as an inhibitor to prostaglandins, along with arachidonic acid and magnesium sulfate induced diarrhea (Bajad, *et al.*, 2001). Piperine has also been found to significantly increase the absorptive function of the small intestine by stimulating the activity of γ-glutamyl transpeptidase (γ-GT) and increasing amino acid uptake, specifically in the jejunum (Johri, *et al.*, 1992). The effects on γ-GT activity was a change in the kinetic behavior between the enzyme and its substrate, showing that piperine actually causes a change in the lipid environment and membrane around the enzyme. It is also hypothesized in a separate study that the increase in drug bioavailability, as discussed shortly, also may contribute to this increase in absorptive function (Khajuria, *et al.*, 2002).

Piperine, through several clinical trials, has been shown to enhance drug bioavailability. Piperine increases the half-life of pharmaceutical drugs and delays their

excretion. This in turn enhances the effect of the drug itself, because it is active in the body longer due to its delayed metabolism. It has an inhibitory effect on a group of liver and gastrointestinal enzymes, called cytochrome P450 enzymes, known to be important for drug metabolism. These include CYP1A1, CYP1A2, CYP2D6, CYP3A4, and P-glycoprotein. CYP3A4 and P-glycoprotein are expressed in hepatocytes, which are the liver cells responsible for much of a body's first pass elimination of drugs, so the inhibitory effect of piperine can also help decrease the early elimination of particular drugs (Hu, *et al.*, 2005). Certain drugs that piperine have been found to influence include: phenytoin (epilepsy), propranolol (hypertension), rifampicin (tuberculosis), and theophylline (lung medication) (Srinivasan, 2009).

The antioxidant properties of piperine are also relevant for clinical treatment. Piperine is an inhibitor of lipid peroxidation and also quenches free radicals and reactive oxygen species in the body. Oxidative damage, due to the presence of these free radicals and reactive oxygen species, among others, can cause oxidative stress. This cell and tissue death due to oxygen species is extremely harmful and has been suggested as major causes for things such as cancer and atherosclerosis (Pizzino, *et al*., 2017).

Piperine has additionally been shown to have antimutagenic and tumor suppressive activity toward certain cancers. One study found it to effectively decrease mutations induced by ethyl carbamate, a promutagen (El Hamss, *et al.*, 2003). It also has protective and suppressive properties against lung carcinomas. This was observed to be caused by the aforementioned antioxidant activity of piperine, which had a cytoprotective effect on experimental lung cancer in mice (Selvendiran, *et al.*, 2003). Additionally, piperine enhances the activity of specific detoxifying enzymes, including glutathione

transferase, quinone reductase, and UDP-glucuronosyl transferase, which also contributes to piperine's antioxidative and antimutagenic properties.

Piperine also has been known to have anti-inflammatory properties. This is due to piperine's inhibitory effect on neutrophil adhesion to the endothelium in the body's inherent inflammatory response to damage or foreign bodies (Kumar, *et al.*, 2007). This inhibitory effect occurs because piperine is able to block the expression of certain cell adhesion molecules, E-selectin, intracellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1), which is induced by TNF-α, tumor necrosis factor-alpha. Piperine works by blocking the translocation and activation of the transcriptional regulator of those cell adhesion molecules (NF-κB) by blocking its inhibitory protein (I-kBα). Because of this anti-inflammatory activity of piperine, black pepper can be considered a natural source or precursor to NSAIDs, non-steroidal anti-inflammatory drugs.

Additionally, recent research shows that piperine also functions as a TRPV1 vanilloid agonist. One study, using whole-cell patch-clamp electrophysiology, stated that piperine produced clear agonist activity of the human TRPV1 vanilloid receptor (McNamara, *et al*., 2005). When compared with capsaicin, the active component of chili peppers and the prototypical TRPV1 agonist, piperine was found to be a less potent agonist but had greater efficacy than capsaicin, though it had a propensity for receptor desensitization. TRPV1 is known to be expressed in pain pathway and gastrointestinal system human sensory neurons (Hayes, *et al*., 2000; Ward, *et al*., 2003). As such, piperine is a potential route for further study into pharmaceutical intervention of gastrointestinal problems and neuropathic pain. "Since piperine has been used to

stimulate the gastrointestinal tract, it could be helpful for conditions such as diarrhea and irritable bowel syndrome, which are not easily managed by standard care" (Srinivasan, 2009). Thus, piperine's role as a vanilloid agonist could be used for treatment in a variety of health problems in a way that modern pharmaceuticals cannot.

One negative effect of piperine is that of its effect on gastric mucosa. Piperine was observed, using aspirin as a positive control group, to cause an increase in gastric microbleeding and gastric cell exfoliation. It was also found to cause a significant increase in parietal and pepsin secretions along with a decrease in potassium (Myers, *et al.*, 1987). These results, from a single-dose experimental study, show similar negative effects on gastric mucosa due to piperine as to aspirin.

Cinnamon

Cinnamon is a well-known and broadly used spice that has been around for millennia. It was documented in Chinese and Egyptian texts 4000 years ago and has been used as a spice, flavoring agent, preservative, and pharmacological agent throughout history (Panickar, *et al.*, 2009). There are two different types of cinnamon—Cassia cinnamon and Ceylon cinnamon. Cassia cinnamon, though more affordable than Ceylon cinnamon, contains a much higher level of coumarin, a plant compound toxic to several human organs, including the liver and kidney (Wang, 2013). Regarding the pharmacological uses of cinnamon, several studies have shown the various biochemical and physiological effects that cinnamon produces. These include antioxidant activity, brain activity, and effects on glucose, insulin, and lipid metabolism.

Cinnamon, as a spice, derives from the bark of the small evergreen tree *Cinnamomum verum.* Cinnamon oil, the main constituent of the bark, is comprised of (a)

cinnamic acid, (b) cinnamic alcohol, and (c) cinnamaldehyde (Fig. 4). Cinnamaldehyde has anesthetic, antibacterial, anti-inflammatory, antiulcer, and antiviral properties, though it also functions as a prooxidant, which is problematic in human health (Panickar, *et al.*, 2009). Cinnamic acid, along with its derivatives, has both antioxidant and antihyperglycemic properties.

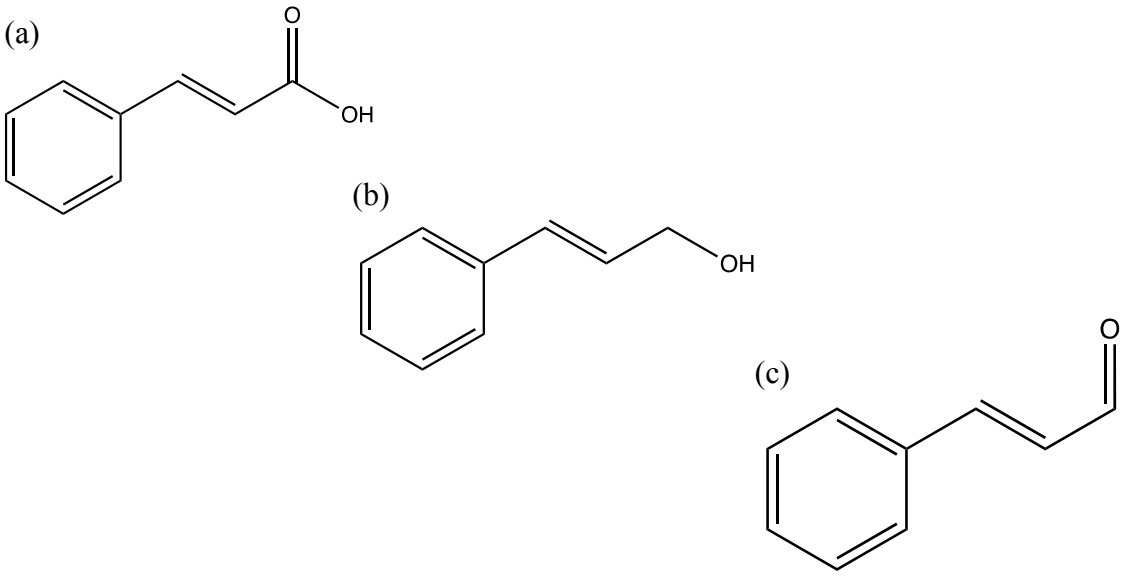

Figure 4: Structure of (a) Cinnamic Acid, (b) Cinnamic Alcohol, and (c) Cinnamaldehyde

Cinnamon is a known antioxidant. However, when cinnamaldehyde was isolated, it was found that it has prooxidant properties (Gowder and Devaraj, 2006). Cinnamic acid, on the other hand, does have antioxidant properties, along with its derivatives. The primary mechanism by which these work is lowering thiobarbituric acid-reactive substances and by increasing glutathione peroxidase activity (Lee, *et al.*, 2001). The action of a specific class of derivative, 2-alkoxydihydrocinnamates, function as agonists of peroxisome proliferated-action receptor (PPAR), which is similar to that of glitazone drugs currently used by diabetic patients. (Martin, *et al.*, 2005). Additionally, as a

carboxylic acid, cinnamic acid inherently has antioxidant properties by reducing other agents as it is oxidized into cinnamaldehyde.

Anti-inflammatory tristetraprolin (TTP) is a protein that attaches to and denatures mRNA coding for proteins such as TNF-α. TNF-α is one of a group of tumor necrosis factors, which are inflammatory cytokines responsible for signaling the body's acute immune response. By denaturing the mRNA responsible for a specific cytokine, the acute immune response is decreased. Aqueous solution of cinnamon was found to significantly increase TTP protein and mRNA levels by up to sixfold (Cao, *et al.*, 2007). Thus, cinnamon also has an anti-inflammatory effect.

Glucose is an important metabolite for many biochemical pathways and functions, one of which is maintaining host immunity. Macrophages, one of the human body's major types of immune cells, requires glucose for mounting an effective immune response to foreign agents. Glucose is required for an increase in macrophage glycolysis, which is necessary to power the antimicrobial inflammation and pathogen killing responsible for removing said foreign agents (Tucey, *et al.*, 2018). The transport of glucose into and out of cells occurs via glucose transporter (GLUT) proteins. One study found that components of cinnamon increased the mRNA of, and thus the equivalent amount of, GLUT1 proteins by threefold, suggesting that cinnamon has a role in regulating the body's immune response (Cao, *et al.*, 2008).

Cinnamon also has a significant effect on insulin. It is responsible for increasing insulin activity through an increase in the uptake of glucose. When compared with forty-eight other spices, herbs, and medicinal extracts known to have insulin-potentiating activity, cinnamon had a greater increase in insulin activity at more than a 20-fold

increase in activity, compared to the next greatest increase by witch hazel. Adding aqueous extract of cinnamon thus is similar to adding more insulin, which is important when considering chronic insulin resistance diseases, such as type 2 diabetes, since this results in an increase in insulin sensitivity in the patient (Panickar, *et al.*, 2009).

In addition, cinnamon has a role in neural function. An insulin deficiency was found to cause, at least partially, the neurodegenerative pathology of Alzheimer's Disease (AD). When insulin and cinnamon were given, there was a significant decrease in the cell death associated with AD (Panickar, *et al.*, 2009). Other neural effects of cinnamon include attenuation of cell necrosis in oxygen deficient conditions, such as stroke (Panickar and Norenberg, 2005).

Finally, cinnamon was also found to have a beneficial effect on dyslipidemia, which is the imbalance of various lipids in the body, such as cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. Dyslipidemia is a risk factor for a number of other, more serious health problems, particularly cardiovascular ones, such as hypertension atherothrombosis, and myocardial infarction. Cinnamon has been found to have lipid lowering properties in several studies, both animal and clinical. High fructose diet rats that were given cinnamon were found to be lacking the elevated levels of triglycerides, LDL, and cholesterol that are associated with a high fructose diet (Kannappan, *et al.*, 2006). Cinnamon was also found to counteract the increase in systolic blood pressure associated with the spontaneous hypertension of a high-sucrose diet to a near-normal level (Preuss, *et al.*, 2006).

Ginger

Ginger is a spice commonly known for both its flavorful use in food preparation and its therapeutic use for medicinal purposes. It has been used around the globe since ancient times for various purposes, including treating nausea and vomiting during pregnancy (Nigam, *et al*., 2009). The ginger plant, *Zingiber officinale*, is native to both India and China, which accounts for its use in natural remedies since it was first recorded. It is also mentioned in the Quran, which indicates that ginger was present in Arab countries at least since 650 AD, when the Quran was first written (Nigam, *et al*., 2009). The main active ingredient of ginger is [6]-gingerol (Fig. 5), which is a nonvolatile pungent compound. However, it is thermally unstable, giving slightly different properties of fresh and thermally-dried ginger.

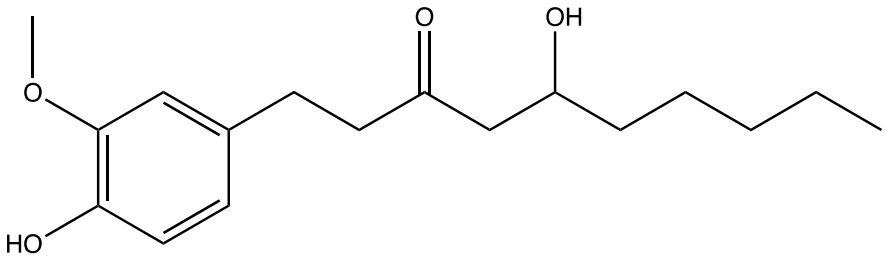

Figure 5: Structure of [6]-gingerol

Ginger, similar to other spices discussed here and elsewhere, also has been found, through various *in vitro* studies, to have anticarcinogenic properties via its effect on the nuclear factor NF-κB. Ginger inhibits the activity of this protein by suppressing the phosphorylation of its inhibitory protein, I-κBα (Aggarwal and Shishodia, 2006). It also contributes to inducing apoptosis, keeping mutated cells from continuing to live and form a tumor. Ginger participates in apoptosis by increasing the activity of NAG-1 and G(1)

by decreasing the activity of cyclin D1 (Lee, *et al.*, 2008). Ginger also functions as a COX2 inhibitor (Lantz, *et al.*, 2007). Cancers that have been shown to be effected by ginger include skin, pulmonary, breast, gastrointestinal, pancreatic, renal, prostate, and ovarian cancer in humans. Animal studies have also shown promise with skin, gastrointestinal, colon, breast, and prostate cancers.

Additionally, ginger possesses cardioprotective properties. It is able to protect from and treat cardiovascular problems, such as high blood pressure. This spice is able to effectively function in this way because of its specific inhibition of the voltage-dependent sodium channels that are required for the electric signals that pump the heart and cardiovascular system.

Just as the other spices have some sort of antioxidant property, so does ginger. Ginger is effectively able to reduce injury risks, such as high blood pressure. Gingerol was found to be as effective as vitamin C in lowering lipid peroxidation in rats (Ahmed, *et al.*, 2000). This antioxidant property also ties into anti-inflammatory and anticarcinogenic functioning, due to how oxidative stress and inflammation are related to tumor promotion and thus cancer formation and progression.

Finally, ginger has been found to have strong anti-nausea effects against things such as motion and sea sickness, pregnancy-induced nausea and vomiting, postoperative nausea and vomiting, and chemotherapy-induced nausea and abdominal discomfort in various clinical trials. Thus, scientific evidence, through various laboratory and clinical studies, shows the validity of the use of ginger for various different uses, including those for which ginger has been used for millennia. Currently, ginger is most commonly used medicinally for nausea due to motion sickness and chemotherapy (Nigam, *et al.*, 2009).

Turmeric

Turmeric is a brightly-colored yellow spice common in Indian cuisine, especially in curry powder. Its main active component is curcumin (Fig. 6), though turmeric also has 28 phytocompounds in addition to curcumin (Lin and Lin-Shiau, 2009). One of the main medicinal uses of turmeric, i.e., curcumin, is that of using it against cancer in its initiation and promotion stages. Though curcumin is of great benefit because of its anticarcinogenic properties, it is also of great interest currently because it has a wide range of uses for various disorders without appreciable side effects, unlike many modern pharmaceutical drugs. One meta-analysis has also shown turmeric to be effective in treating the symptoms of joint arthritis (Daily, *et al*., 2016).

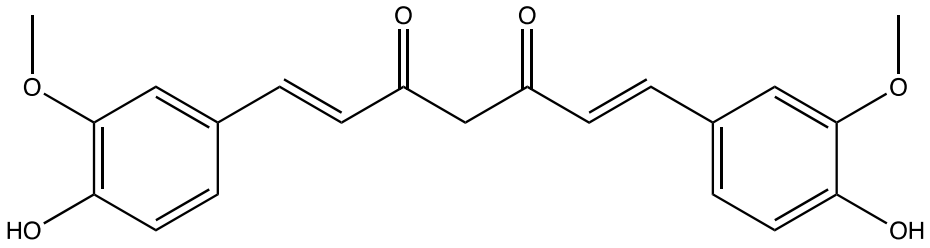

Figure 6: Structure of Curcumin

In several different animal model studies, curcumin has been shown to inhibit carcinogenesis, the process by which normal cells are transformed into cancer cells. This occurs in several different tissues, including the epidermis, duodenum, and colon. Turmeric also assists in potentiating the induction of apoptosis, or programmed cell death. Apoptosis is an important mechanism by which the body kills malfunctioning, mutated, or infected cells before they cause larger problems for the tissue and the body. Without apoptosis, there is an increase in tumors, due to their originating with cell

mutations. The inhibition of NF-κB signaling plays a major role in chemoprevention of cancer. The inhibition of NF-κB signaling also contributes to curcumin's, and thus turmeric's, anti-inflammatory property. This connects with the anticarcinogenic properties of turmeric due to chronic inflammation being a factor in several stages of tumor development and growth.

Turmeric is a strong inhibitor of reactive oxygen species (ROS). It is what is referred to as an ROS scavenger, which means it is part of the human body's natural system whereby ROS and reactive nitrogen species are fought and removed from the body by particular molecules. ROS include superoxide anions, hydroxyl radicals, and hydrogen peroxide, among others. They occur when there is excess oxygen in a particular system, causing too many or too strong of oxygen bonds to be formed, when there is insufficient reduction of the oxygen, or when both scenarios occur (Robak and Marcinkiewicz, 1995). Curcumin in particular reacts with superoxide anions, hydroxyl radicals, singlet oxygen, nitric oxide, and peroxynitrite (Lin and Lin-Shiau, 2009). By affecting enzymes such as cyclooxygenase-2 (COX2), lipoxygenase, nitric oxide synthase, and xanthine oxidase, curcumin inhibits the amount of reactive oxygen species produced that could cause oxidative stress and other problems, if left unchecked.

Curcumin also has been found to have some neuroprotective effects. Due to its anti-inflammatory and antioxidative properties, in addition to its "outstanding safety profile and number of pleiotropic actions with potential for neuroprotective efficacy" (Lin and Lin-Shiau, 2009), curcumin is a strong contender for preventative treatment for molecular damage to neurons (Bishnoi, *et al.*, 2008). Preliminary results have shown that dietary curcumin has large potential for use in preventative treatment of major

neurodegenerative diseases such as Alzheimer's, Parkinson's, and stroke with minor, if any, negative side effects (Cole, *et al.*, 2007).

Each of these four spices—black pepper, cinnamon, ginger, and turmeric—has been shown to have a variety of different properties and uses. Multiple studies have demonstrated that these properties of the spices are proven experimentally valid in their effects and medicinal uses. Black pepper has been found to have an effect on the gastrointestinal system and drug bioavailability, along with antioxidant, anticarcinogenic, anti-inflammatory, and pain relief properties. Cinnamon has a role in immune response regulation and lipid regulation, it increases insulin function, and it possesses antioxidant, anti-inflammatory, and neuroprotective properties. Ginger possesses anticarcinogenic, cardioprotective, antioxidant, and antinausea properties, while turmeric was found to have anticarcinogenic, antioxidant, and neuroprotective properties. Thus, though Ayurvedic medicine is rooted in ancient medicinal practices, particular components of it remain relevant and useful in modern times. Now, the biochemical and experimental validity of various other Ayurvedic plants will be discussed in greater detail.

CHAPTER THREE

The Chemical Foundation of Key Herbs Used in Ayurveda

Spices, as discussed in the previous chapter, comprise a large part of Ayurvedic medicine and the predominant focus of current scientific study regarding Ayurveda. We now turn to another plant-based method of healing used in the practice of Ayurvedic medicine—herbs. These are distinguished from spices in that they are used while still in the original plant component, be that leaves, bark, flowers, or otherwise, rather than crushed into a powder. Note, however, that there is much overlap, as most herbs can be crushed into spices and vice versa. For the sake of organization, the criterium used to distinguish between the two for the purpose of this paper is the form in which a particular plant is predominantly used in American culture today. For example, cinnamon, though also available as whole cinnamon sticks, is predominantly consumed in powder form as a spice, whereas garlic is more often used as a whole bulb than it is dried and crushed into a powder. The herbs that will be discussed in detail here are fenugreek, garlic, and St. John's wort.

Fenugreek

Fenugreek, of the Fabaceae family, is native to many East European and Asian countries and has been used for cooking as far back as 1500 BC (Chevallier, 2000). This brightly-colored seed has been used in Indian cuisine for curry powders, and its leaves have been used as condiments and greens. In addition to its uses in cooking, fenugreek has also been used for medicinal purposes, not just in Ayurvedic medicine, but also in Chinese and Native American remedies. One use of fenugreek is that of increasing

lactation in breastfeeding mothers (Khan, *et al.*, 2017). It has also been used to prevent and control chronic diseases such as diabetes, gastrointestinal problems, high cholesterol and inflammation (Jain, 1991). Recent studies have shown that fenugreek can be used to control chronic conditions such as cancer, diabetes, and obesity. The main bioactive component of fenugreek that makes these effects possible is diosgenin (Fig. 7), which is a steroid. A second bioactive compound is (4)-hydroxyisoleucine; both of these compounds are exclusively of plant origin and cannot be synthesized in mammalian tissue (Raju and Rao, 2009). Two main effects of diosgenin, and thus fenugreek, are those on the metabolic processes of the body and activity against cancer.

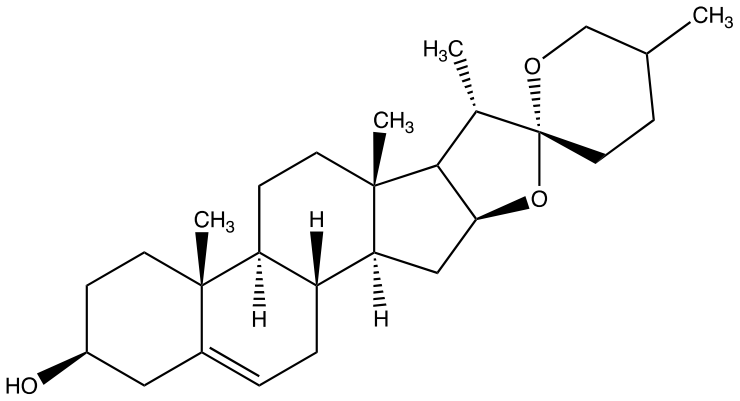

Figure 7: Structure of Diosgenin

Fenugreek is an especially beneficial herb with regards to metabolic diseases. Multiple animal studies have shown that fenugreek lowers serum cholesterol (Sauvaire, *et al.*, 1991), triglyceride, and low-density lipoprotein, including in dogs (Valette, *et al.*, 1984) and rats (Stark and Madar, 1993). These findings have been shown to be similar or replicated in human intervention trials with dietary fenugreek. Lowering of both serum

cholesterol and triglyceride levels are seen in human trials (Sowmya and Rajyalakshmi, 1999). These effects are especially relevant to diabetes patients.

Two distinct types of diabetes currently are recognized—type I, or insulin-dependent, and type II, also known as insulin-independent diabetes mellitus. In type I diabetes, a predominantly genetic disease, the body produces little or no insulin for processing glucose circulating in the blood. Type 2 diabetes, on the other hand, is the result of a long-term buildup of circulating glucose in the blood. This overworks the pancreas and, if left untreated, causes the pancreas to be unable to produce enough insulin to process the high amount of glucose. In addition to this, there is often a problem in insulin signaling pathways that further decreases the amount of insulin produced. Type II diabetes is often observed in obese individuals. Diabetes, in turn, is associated with an increase in circulating serum cholesterol in the blood, such as low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL), and a decrease in high density lipoprotein (HDL), which removes serum cholesterol—all of which can then lead to clots forming thromboses, embolisms, and other cardiovascular problems. In addition, several herbs and other natural medicinal treatments target the inhibition of fatty acid synthase, which is also beneficial in managing obesity (Tian, *et al*., 2004). Fenugreek, specifically, was found to be beneficial for managing both type I and type II diabetes, which currently have no cure. Fenugreek seeds were found to decrease blood glucose and serum cholesterol, LDL, and VLDL in type I diabetic patients (Sharma, *et al*., 1990). This was especially seen to have an effect on the glucose tolerance test and 24-hour urinary glucose excretion in the insulin-dependent diabetic patients. In type 2 diabetic patients, lower serum cholesterol, triglyceride, and LDL levels were observed along with an

increase in high-density lipoprotein (HDL) in the fenugreek seed treatment group in a double blind placebo study (Geberemeskel, *et al.*, 2019). Thus, fenugreek has been found to be remarkably important for managing the metabolic processes that must constantly be monitored in a common and yet currently incurable disease.

There are several other related metabolic diseases in which fenugreek has been found to have a beneficial effect. Fenugreek, in rat (Stark and Madar, 1993), dog (Valette, *et al*., 1984), and human (Sowmya and Rajyalakshmi, 1999) studies was found to lower hypercholesteremia. Diosgenin was isolated in multiple rat studies to also lower hypercholesteremia (Juarez-Oropeza, *et al*., 1987; Kwon, *et al*., 2003; Son, *et al*., 2007). Fenugreek in the diet of regular rats was beneficial in treating hyperinsulinemia by stimulating insulin-producing pancreatic islet β-cells (Petit, *et al*., 1993). This insulin-stimulating action was found to be due to the function of the amino acid (4)-hydroxyisoleucine (Broca, *et al*., 2004). In a separate study of obese rats, fenugreek was found to significantly alleviate hepatic steatosis, or fatty liver disease (Raju and Bird, 2006). All of these metabolic benefits were obtained with no significant harmful effects, making fenugreek a highly useful treatment for metabolic diseases, including diabetes.

The other predominating medicinal use for fenugreek is that of its anticarcinogenic actions. These anticarcinogenic properties have been observed in both *in vivo* and *in vitro* studies. Diosgenin specifically has been found to have effects on cell growth, cell cycle and apoptosis, and fatty acid and cholesterol biosynthetic pathways.

The *in vivo* studies on diosgenin and fenugreek, while limited, have promising results regarding the anticarcinogenic properties of fenugreek. In a rat colon cancer study, dietary fenugreek, when given during initiation or promotion cancer stages, inhibited the

formation of precancerous lesions in the colon (Raju, *et al*., 2004). By being administered during these stages, fenugreek can both prevent and stop the development of precancerous lesions in the colon. This effect was also observed with isolated diosgenin, demonstrating the bioactive nature of the compound. A separate rat study found that the long-term dietarily administered fenugreek seeds, over the course of thirty weeks, significantly reduced the occurrence and quantity of colon tumors (Devasena and Menon, 2003). Fenugreek also protects against colon carcinogenesis by modulating hepatic oxidative stress (Devasena and Menon, 2007). One study found that diosgenin suppressed the incidence of colon tumors, both invasive and non-invasive, by up to 60%, and did so by reducing tumor cell proliferation (Malisetty, *et al*., 2005). An *in vivo* study regarding breast tumors show that fenugreek also reduces the occurrence and quantity of breast tumors (Amin, *et al*., 2005). Taken together, these *in vivo* studies demonstrates anticarcinogenic effects of diosgenin individually and fenugreek as a whole.

Diosgenin and fenugreek also have anticarcinogenic properties as inhibitors of tumor cell growth. There are a number of various tumor cells that diosgenin and its analogs have been found to be cytotoxic toward. Diosgenin and three of its analogs inhibit the tumor cell growth of C6 rat glioma cells (Chiang, *et al*., 1991). Diosgenin causes cytotoxicity to myelogenous leukemic KBM-5 cells (Shishodia and Aggarwal, 2006) and other analogs similarly inhibit human myelogenous leukemic K562 cells (Hu, *et al*., 1997). One study, testing the cytotoxicity of a diosgenin analog against sixty human cancer cell lines, found the compound to inhibit tumor cell growth in leukemia, lung, colon, central nervous system, melanoma, and renal cancer (Hu and Yao, 2002). Diosgenin itself has been found to have similar inhibitory effects in human breast

carcinoma (Li, *et al*., 2005), colon carcinoma (Wang, *et al*., 2004; Raju and Bird, 2007), erythroleukemia (Leger, *et al*., 2004), leukemia (Liu, *et al*., 2005), and osteosarcoma (Moalic, *et al*., 2001; Corbiere, *et al*., 2003). All of these studies demonstrate how diosgenin, and thus fenugreek as a whole, may function to inhibit the cell growth of tumor cells.

Secondly, fenugreek has anticarcinogenic actions in its inhibition of the cell cycle and induction of apoptosis. Diosgenin arrests the cell cycle and induces apoptosis in osteosarcoma cells by activating p53 and binding NF-κB (Corbiere, *et al*., 2004). The cell cycle of leukemic KBM-5 cells was found to be arrested at the sub-G1 phase and inhibited TNF-dependent NF-κB activation (Shishodia and Aggarwal, 2006). In human breast cancer cells, specifically in estrogen receptor-positive MCF-7 breast cancer cells, diosgenin induced the activity of p53, the tumor suppressor gene (Sowmyalakshmi, *et al*., 2005). From these various studies, it can be understood that diosgenin, along with other compounds found in fenugreek, follow several mechanisms of inhibiting the cell cycle and/or inducing apoptosis, depending on the type of cell on which fenugreek is acting.

Third and finally, fenugreek functions to counteract the upregulation of fatty acid synthesis that occurs in many cancers. This upregulation of fatty acid synthesis can be considered oncogenic in this context, as fatty acid synthesis denotes and aids in growth and survival advantages over other nearby cells and tissues, which a particular tumor then uses to continue growing, and not for the fatty acid synthesis pathway's inherent function as an anabolic energy storage process for future use (Menendez and Lupu, 2007). Diosgenin was found, in one particular study, to inhibit the expression of fatty acid synthase (FAS), the catalyzing enzyme in fatty acid synthesis, in HER2 breast cancer

cells, with FAS as a potential target for additional cancerous cells outside the breast as well (Chiang, *et al*., 2007). Additionally, tumor cells show a marked increase in the expression and activity of 3-hydroxy-3-methylglutaryl Co-enzyme A (HMG-CoA) reductase, which is the rate-limiting enzyme in cholesterol biosynthesis (Hentosh, *et al*., 2001). However, there is not a substantial enough body of literature to determine if the anticarcinogenic activity of this particular enzyme is targeted by diosgenin (Yang, *et al*., 2004).

In conclusion, fenugreek and its major bioactive compound diosgenin have two primary medicinal attributes—action against metabolic diseases and cancer. Diosgenin and fenugreek were found to have a significant effect on metabolic diseases, especially in type I and II diabetes patients. Diosgenin and fenugreek also have anticarcinogenic activity via their actions to inhibit tumor cell growth, arrest the cell cycle and induce apoptosis, and regulate the fatty acid synthesis pathway.

Garlic

Garlic, or *Allium sativum*, has been used in dietary capacities since ancient times. It is first recorded in the Codex Ebers, a medical papyrus from Egypt around 1550 BC cataloging various therapies and treatments for diseases. Garlic was there listed to be helpful with bites, headaches, heart problems, tumors, and worms (Kuttan and Thejass, 2009). Egyptians were not the only ones to use garlic for medicinal purposes—Babylonians, Chinese, Greeks, Indians, Phoenicians, Romans, and Vikings also have been found to have used garlic (Block, 1985). Modern scientific research on garlic and its plant family began with Louis Pasteur in the mid-nineteenth century, when he recorded the antibacterial properties of garlic (Pasteur, 1858). Garlic primarily has been found to

have cancer-preventative and cardiovascular effects, including antihypertensive, antithrombotic, and atherosclerosis prevention.

The medicinal properties of garlic, as well as the rest of the *Allium* family, are believed to be due to the organosulfur compounds in garlic that are released when it is processed. At least 33 different types of organosulfur compound have been identified in garlic, though they are not often isolated because they have such similar properties and actions. The characteristic scent and taste of garlic is due to allicin, which, as a highly unstable compound, decomposes into oil soluble organosulfur compounds, such as diallyl sulfide (Fig. 8). Diallyl sulfide is the primary compound studied regarding garlic's medicinal uses and is assumed equivalent to garlic for the purposes of the results and implications of the studies performed. Diallyl sulfide (DAS) has anti-inflammatory and anti-angiogenesis effects as well as effects on carcinogen metabolism, immunomodulation, cell cycle progression, signal transduction pathways, and apoptosis.

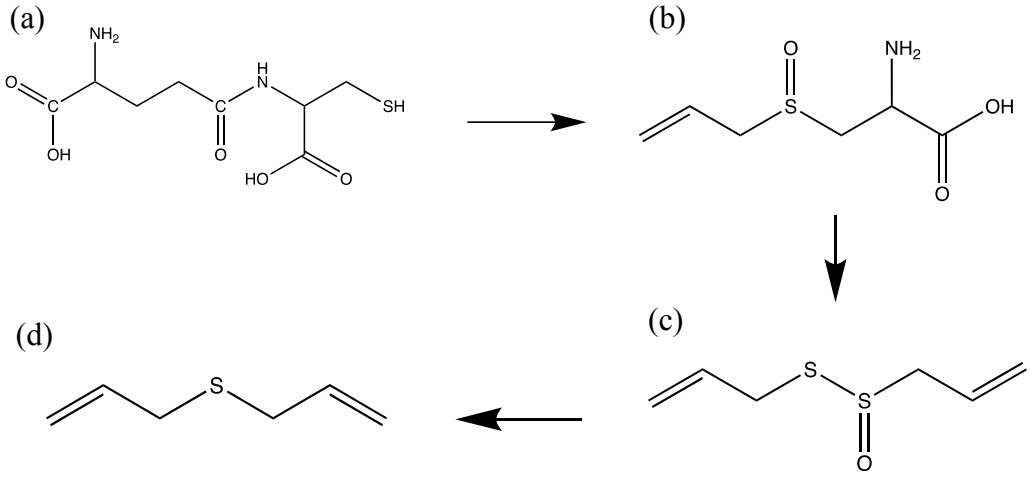

Figure 8: The chemical reactions of garlic to naturally occurring organosulfur compounds: (a) γ-Glutamyl cysteine to (b) Alliin to (c) Allicin to (d) Diallyl sulfide

Most notably, DAS has strong activity against chemically-induced cancer through a variety of different mechanisms. One of these mechanisms that DAS affects is phase 1 metabolism. Many carcinogens are not reactive in their natural form; rather, they are metabolically activated to become electrophilic reactants. This is primarily done by oxidation, though hydrolysis and reduction are occasionally components as well, all of which work to make the carcinogens more hydrophilic. This process, called phase 1 metabolism, is primarily accomplished by cytochrome P450 enzymes (CYPs). When procarcinogens become electrophilically reactive, they can interact with DNA to cause point mutations, leading to changes that are known to be precursors to cancer, such as inactivating tumor suppressor genes and activating proto-oncogenes. DAS, among other organosulfur compounds in garlic, have been shown to inhibit these phase 1 enzymes. DAS competitively inhibits the cytochrome P450 2E1 enzyme (Brady, *et al.*, 1991) via pseudo-first-order kinetics. P450 2E1 enzyme is important for activating a number of low-weight environmental chemical compounds. Thus, by inhibiting the actions of this enzyme, DAS and other garlic compounds are able to block some portion of the chemotoxicity and carcinogenesis of the cell due to those chemical compounds (Kuttan and Thejass, 2009).

Additionally, DAS induces the actions of phase 2 enzymes. These enzymes are responsible for metabolism involving detoxification. They work as protection against carcinogenesis and mutagenesis caused by toxic compounds, often by adding large polar groups in order to both prevent further transformation and to increase elimination of the modified metabolites. The main two phase 2 metabolism enzymes are NAD(P)H quinone reductase (QR) and glutathione S-transferases (GSTs). Multiple animal studies have

shown that DAS specifically works as an inducer of phase 2 enzymes, especially GSTs. One study found that administration of DAS, along with other related garlic compounds, induced the expression of both alpha and pi class GSTs in mice liver, lung, and forestomach cells (Hu, *et al*., 1996). In a different study, DAS treatments were found to increase GST expression by 12 to 16.7-fold (Green, *et al.*, 2007). Another study found DAS to function as a potent quinone reductase inducer in mice forestomach and lung cells (Singh, *et al.*, 1998). These studies, among others, show that DAS and other garlic compounds function as phase 2 enzyme inducers, causing an anticarcinogen effect.

Garlic also functions as an anticarcinogenic compound via inducing apoptosis. DAS does this by modulating the levels of Bcl-2 proteins in cancerous cells (Karmakar, *et al.*, 2007). DAS-induced apoptosis is associated with various other apoptosis-inducing processes, including the down-regulation of nuclear factor-κB (NF-κB) (Hong, *et al.*, 2000). DAS has also been shown to induce apoptosis in human colon cancer cells (Sriram, *et al*., 2008). This was found to occur through a variety of processes, including increased production of reactive oxygen species (ROS) and increased expression of caspase-3, a protease apoptotic enzyme. A separate study found that DAS up-regulates the expression of p53, a tumor suppressor gene, along with the expression of Bax, a proapoptotic protein (Kalra, *et al.*, 2006).

A final way that garlic is anticarcinogenic is in its effect on angiogenesis. Angiogenesis, the development of new blood vessels to support tissue growth, is a major factor in the growth of tumors. Because no tissue can outgrow its blood supply without cell death, angiogenesis is especially important for tumor growth due to the rapid proliferation of cancerous cells. Thus, one way to inhibit cancer is by inhibiting

angiogenesis and thus starving the carcinogenic cells of their needed blood supply. Some proangiogenic factors that stimulate the growth of those new blood vessels include vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), acidic and basic fibroblast growth factor (aFGF and bFGF), tumor necrosis factor (TNF), and matrix metalloproteinases (MMPs). DAS inhibits melanoma growth in mice studies via inhibiting VEGF pathways and thus reducing the circulating VEGF levels, which is accomplished by down-regulating the mRNA expression of VEGF. DAS's ability to inhibit VEGF pathways was also found to prevent and decrease angiogenesis in human umbilical vein endothelial cells (Kuttan and Thejass, 2009). Additionally, DAS has been found to have an effect on MMPs by promoting an endogenous inhibitor of MMPs, tissue inhibitor of metalloproteinase-1 (TIMP 1). MMPs are considered proangiogenic factors because they are able to degrade the extracellular matrix, allowing VEGF to accumulate and switch on angiogenesis.

In addition to being an anticarcinogenic herb, garlic also works as a modulator of inflammation, though inflammation and carcinogenesis are often linked together. Chronic inflammation leads to up-regulation of enzymes in the affected tissue(s), such as nitric oxide synthase (NOS) and cyclooxygenase-2 (COX-2). NOS is responsible for synthesizing nitric oxide (NO), which is helpful in the body's inflammation response. However, in too great quantities, NO is associated with the pathogenesis of cancer via reactive NO-species-mediated reactions and can also act as an endothelial growth factor, which has previously been stated as a factor promoting angiogenesis, an important process included in the growth of a tumor (Kuttan and Thejass, 2009). COX-2, the other enzyme up-regulated with chronic inflammation, is responsible for converting

arachidonic acid into prostaglandins. Prostaglandins, beyond their normal function as proinflammatory mediators, have also been found to inhibit apoptosis, suppress immune function, and increase the proliferation and invasiveness of cancer cells (Kuttan and Thejass, 2009). Multiple studies have shown that DAS has an effect on both of these enzymes. One found that DAS caused a decrease in colon carcinogenesis by reducing the expression of both NOS and COX-2 (Sengupta, *et al*., 2006). DAS was found to diminish pulmonary fibrosis in the lung tissue of rats due to both reducing the activation of NOS and NF-κB and downregulating inflammatory cytokines such as tumor necrosis factor-α (TNF-α) (Kalayarasan, *et al*., 2008). Many other studies show the dual action of DAS in reducing the expression of both NOS and COX-2 in a variety of different cells (Chang and Chen, 2005). Taken together, these effects cause a reduction in inflammation mediated by DAS.

In total, these results show that garlic, and its chemically active compound, diallyl sulfide, has multiple beneficial effects on both carcinogenesis and on inflammation. Regarding carcinogenesis, DAS inhibits phase 1 enzymes, induces phase 2 enzymes, induces apoptosis, and inhibits angiogenesis. Regarding inflammation, DAS reduces the expression of both nitric oxide synthase and cyclooxygenase-2, two enzymes that mediate the body's inflammatory response. These studies, taken together, show that DAS can suppress the growth of cancer cells both in culture and *in vivo* without being limited to one particular carcinogen or tissue. It works not just on one portion of carcinogenesis, but on all three—initiation, proliferation, and metastasis.

St. John's Wort

St. John's wort, or *Hypericum perforatum*, is an herb that has been used in folk medicine for over two thousand years (Gupta and Moller, 2003). It is a perennial herb that grows naturally in Western Asia, Europe, North Africa, and America. St. John's wort gets its name from St. John's Feast Day, a festival that occurs around the time of the summer solstice in late June, which is the approximate time that the herb blooms. The herb is a shrub with red buds and yellow flowers that produces a red, blood-like sap when rubbed between the fingers. This sap is comprised of the majority of the bioactive compounds of St. John's wort. In religious settings, the herb was hung over doors and in houses to protect the people living in the houses from demons and their curses. It has long been used for various medicinal purposes. As far back as the 13th century, St. John's wort is listed by the School of Salerno as "the herb that chases away the devil," and in 1525 is denoted as being useful in treating melancholy and depression by Paracelsus (Gupta and Moller, 2003). As awareness and acceptance of mental health struggles and illnesses have recently become more predominant, a rise in the study of this herb for its medicinal effects has been observed. The main active compound of St. John's Wort is hypericin (Fig. 9), though there are many other flavoids in the herb that are active in addition to hypericin. St. John's wort has been established as effective in treating both depression and headaches, among other things.

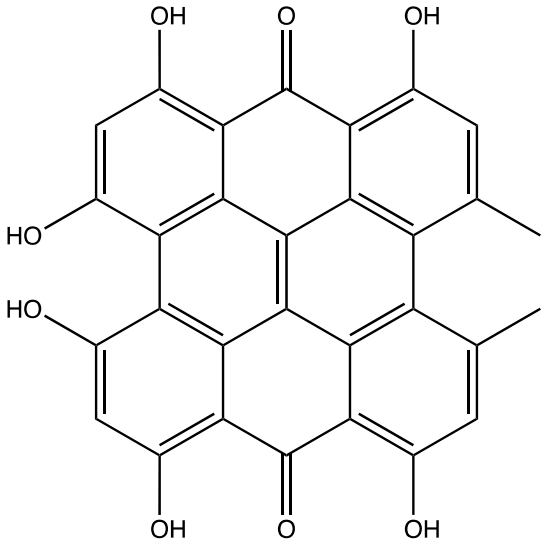

Figure 9: Structure of Hypericin

St. John's wort extract has now been studied extensively for its antidepressant action. The pharmacological interactions and consequences of St. John's wort extract with induced behavioral changes such as learned helplessness have been studied with rodents (Porsolt, *et al*., 1991). St. John's wort acts as a weak inhibitor of monoamine oxidase activity (Cott, 1997). Monoamine oxidase (MAO) is the family of enzymes primarily responsible for the breakdown of neurotransmitters in the brain such as serotonin, dopamine, and norepinephrine. Most pharmaceutical antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), function by blocking the reuptake of neurotransmitters in order to maintain neurotransmitter presence in the brain where they can continue stimulating neural activity. MAO inhibitors (MAOIs), on the other hand, function by inhibiting the enzyme that degrades the neurotransmitters, rather than merely keeping the neurotransmitters from reuptake. Thus, though the overall result of both SSRIs and MAOIs is the same—longer retention of neurotransmitters for action potentials—the mechanism by which they accomplish this is different. John's wort was

found to inhibit the reuptake of serotonin, dopamine, and norepinephrine with approximately equal affinity to each other and compared to other antidepressants (Perovic and Muller, 1995; Muller, *et al*., 1998).

Another way in which St. John's wort is beneficial is in its pain management property. Specifically, St. John's wort has been found to be effective with migraine headaches and cranial and facial nerve pain, as it is closely related to the effect it has upon neurotransmitters as previously discussed. One study found St. John's wort to be effective in treating chronic migraine patients, regarding both the severity and frequency of migraines experienced (Mirzaei, *et al*., 2011). One case study focuses on trigeminal neuralgia, a type of chronic nerve pain that involves sudden, severe facial pain. The patient focused on in the case study—a 53-year-old Hispanic female—was experiencing 30-40 attacks of pain per day, each lasting for 5-10 seconds upon any oral activity such as talking or chewing. She had no symptoms upon returning less than a week later after ingesting a St. John's wort homeopathic preparation (Assiri, *et al*., 2017). Not only that, but it was suggested that the patient cease the St. John's wort treatment for two months to verify that it was indeed the St. John's wort causing the pain to lessen. The patient attempted to decrease or stop the treatment but "as soon as she tried, the pain came back so she resumed treatment" (Assiri, *et al*., 2017). However, there are doubts regarding the efficacy of homeopathic treatments, considering that they are often so dilute that the bioactive compounds are ineffective, so more research into the validity of homeopathic treatment of St. John's wort is needed to be definitive. Thus, St. John's wort also demonstrates effective pain management regarding migraine headaches, though its homeopathic efficacy regarding cranial and facial pain is debated.

In conclusion, these three herbs—fenugreek, garlic, and St. John's wort—each demonstrate various health benefits. Fenugreek primarily works against metabolic diseases and cancer. Garlic is anti-inflammatory and significantly anticarcinogenic. St. John's wort is effective in managing depression and pain. The health benefits of each of the herbs here described have been scientifically examined and found valid in their efficacy. Now, one must consider the application of the knowledge gained—that of implementing the spices and herbs into American medicine in order to truly benefit from the valid scientific and clinical health benefits that have been found.

CHAPTER FOUR

The Implementation of Ayurveda in American Medicine

Having looked at theses spices and herbs, now the discussion regarding whether they should be implemented more into American medicine, and, if that is the case, how to accomplish it will be addressed. They have been shown to have scientifically significant medicinal effects—a summary will be given for each of the seven plants previously discussed, with a focus on their clinical use.

Black pepper was found to have an effect on the gastrointestinal system and drug bioavailability, and antioxidant, anticarcinogenic, anti-inflammatory, and pain relief properties. It serves as a stimulant for both digestive and absorptive action in the gastrointestinal system, as well as an antidiarrheal, primarily by stimulating γ-glutamyl transpeptidase, a digestive enzyme. By inhibiting cytochrome P450 enzymes, black pepper also increases the half-life of drugs to increase the drug's bioavailability. Another major function of black pepper is its inhibition of neutrophil adhesion molecules by blocking the inhibitory protein (I-kBα) of the transcriptional regulator (NF-κB) of the cell adhesion molecules. Finally, black pepper also works as a TRPV1 vanilloid agonist, which causes its identifiable scent and taste. All of these together mean that black pepper can work clinically to stimulate metabolism, as an anti-inflammatory supplement, and to enhance the effects of prescribed medications.

Cinnamon has a role in immune response regulation and lipid regulation, increases insulin function, and possesses antioxidant, anti-inflammatory, and neuroprotective properties. It functions as an anti-inflammatory primarily by increasing

TTP, the protein that inhibits TNF-α, one of the cytokines responsible for the body's acute immune system. It also increases insulin, helpful toward diabetes, and glucose activity, which is necessary for the body's immune response. Cinnamon also is neuroprotective, so it is beneficial in preventing neurodegenerative diseases such as Alzheimer's Disease.

Ginger possesses anticarcinogenic, cardioprotective, antioxidant, and antinausea properties. Its anticarcinogenic action is primarily worked against the nuclear factor NF-κB. It also is a COX-2 inhibitor. One of the strongest and most well-known actions of ginger is its antinausea properties. It is often used to treat motion sickness and morning sickness due to pregnancy, though its other roles as an anticarcinogenic, cardioprotective, and antioxidant compound should not be forgotten.

Turmeric was found to have anticarcinogenic, antioxidant, and neuroprotective properties. Its anticarcinogenic activity, similar to those previously discussed, also works via inhibition of NF-κB. Turmeric also is a significant inhibitor of reactive oxygen species, allowing the body to rid itself of nitrogenous waste safely. Like cinnamon, turmeric is neuroprotective and has been found to be of benefit as preventative treatment for neurodegenerative diseases such as Alzheimer's and Parkinson's.

Fenugreek has a role in the regulation of metabolism and regulation of lipids, as well as anticarcinogenic properties. A significant clinical application of the chemical properties of fenugreek is its prevention and control of chronic conditions such as diabetes, high cholesterol, and inflammation due to its negative effect on serum cholesterol in an individual's body. Like the spices, fenugreek also has anticarcinogenic

activity, as it inhibits both the formation and growth of cancerous lesions by activating p53 and inhibiting NF-κB.

Garlic possesses both anticarcinogenic and anti-inflammatory properties. It inhibits cytochrome P450 enzymes, which are involved in some of the initial mechanisms leading to chemically-induced cancer. It also inhibits NF-κB, as have others, further demonstrating its importance in preventing cancer. It also prevents cancer by inducing apoptosis through increased expression of the enzyme caspase-3 and inhibiting angiogenesis through blocking VEGF pathways. Garlic also reduces the expression of both NOS and COX-2, both of which are involved in inflammation and may induce cancer growth.

Finally, St. John's wort was found to have two major functions—that of an antidepressant and as a provider of pain relief. It functions as an antidepressant by inhibiting the degradation of neurotransmitters via the enzyme monoamine oxidase. It also serves as a pain reliever, especially for the head and neck.

All of these spices and herbs have thus been found to be both chemically and clinically effective in different ways. Now, a case for American medicine to incorporate these spices and herbs in some way will be made. The need for better preventative medicine and the financial advantage that incorporating these spices and herbs provide are both strong arguments for their inclusion. Both of these will be discussed in more detail in an argument for their implementation in American medicine.

A disclaimer is required here—this work is not comprehensive enough to make a case for all of the various forms of alternative medicine, or even for all of Ayurveda, to be implemented into modern American medicine. Rather, this is an argument based upon

the specific spices and herbs studied in detail in this work. However, this is extrapolated to then state that Ayurveda and other alternative medicine should be considered more in depth regarding whether and how much of those particular practices should be incorporated more into traditional medicine practices. Both phrases 'spices and herbs' and 'alternative medicine' will be used throughout this chapter, but this is not to use them interchangeably. The argument is instead based on the specific spices and herbs to then raise attention to Ayurveda and alternative medicine as a whole based upon the argument.

First, the argument for the need for better preventative medicine in America. At this moment, America is one of the best countries to be in for emergencies, surgeries, and transplants. As has been previously stated, the strong presence and advancements in medical technology have made America the place to be for effective healthcare when one is in need of major or emergency medical treatment, such as major surgical procedures or organ transplants. However, even with all this technology, America is not close to being the top country for overall population health among developed countries. In fact, "[f]or many indicators of health, the United States ranks as the country with the highest prevalence of problems. This includes functioning heart disease, stroke at some ages, diabetes, and obesity" (Crimmins, *et al*., 2010). In 2021, the average life expectancy for Americans was 76.1 years compared to the 82.4 year life expectancy in comparable countries (Rakshit, *et al*., 2022). Perhaps the American medical system has had to become as adept and proficient in major procedures as it now is because of the lack of preventative medicine present in America as a whole. Thus, there is a greater need for preventative medicine, which is here defined to be health measures taken to prevent disease acquisition before it occurs.

The spices and herbs discussed in this work, along with other scientifically-validated Ayurvedic and other alternative medicine treatments are one effective route by which preventative medicine can better be addressed in America, for several reasons. For one, spices, herbs, and other natural remedies are easily incorporated into health. They can quickly and easily be added to an individual's everyday meals and drinks, with the added benefit of many of them possessing enjoyable flavor when consumed. These spices and herbs are also relatively inexpensive to incorporate into the population's everyday health, as they are readily available in locations where people may purchase the bulk of their food already. There will be more on the financial advantage of using alternative medicine as preventative medicine later.

Additionally, there are no major, if any, adverse side effects with the use of these spices and herbs, so there is no danger in their utilization for preventative medicine—unlike much of pharmaceutical use, which often comes with a long list of potential adverse side effects. For example, of the seven spices and herbs examined here, all but one have no adverse side effects observed in the studies included. The one exception to this is black pepper and its effect on gastric mucosa. Though even then, the adverse effects of black pepper are equal to that of aspirin on the stomach lining, so it is still not worse than other pharmaceutical options. As always, however, discernment and caution is recommended with any potential for harmful side effects with long term use. This is contrasted with data that shows that increased use of antibiotics in a year increased the risk of breast, esophageal, gastric, lung, pancreatic, and prostate cancers (Boursi, *et al*., 2015). Not only that, but one report estimates that "in the course of the coming decade, medication overload—the result of taking multiple prescription drugs at the same time—

will cause the premature death of 150,000 older people in the United States" (Axe, 2021). Thus, there are minimal negative consequences and multiple positive reasons why these spices and herbs of Ayurvedic medicine should be implemented as preventative medicine in America.

In addition to Ayurveda's role as preventative medicine, it also provides a financial advantage compared to traditional American medicine. The cost of healthcare in America continues to grow dramatically on both an individual and national level. Total healthcare spending went from approximately $1.4 trillion, or 13.3% of gross domestic product (GDP), in 1996 to approximately $3.1 trillion, or 17.9% GDP, in 2016. The average cost per person in 1996 was $5259, whereas the average cost per person in 2016 was $9655 (Dieleman, *et al*., 2020). As can be seen by this, the high cost of healthcare in America is problematic for many of its citizens. The spices and herbs examined here, as well as many others used in Ayurvedic medicine, have the advantage of being significantly less expensive than most pharmaceutical drugs. Many can be accessed with ease at the regular grocery store or supermarket that people frequent for their usual dietary purchases. One additional advantage of Ayurvedic medicine is the natural basis of its healing—the significant use of plants allows for another method of making healthcare affordable. Various herbs can be grown at home, depending upon the climate zone of the land, which further reduces the cost for individuals. These can then be easily incorporated into people's diet with little to no side effects, as previously mentioned, and with no additional cost.

Another way in which the incorporation of Ayurvedic medicine into preventative American medicine is financially advantageous is in its long term benefits. With better

preventative health, fewer visits to the hospital or doctor's office are needed, thus further reducing cost by lowering the number of times one must pay to go in to see the doctor. This would have an overall positive effect on the long-term financial status of not just the individuals, but also of the American healthcare system as a whole. The opportunity for fewer emergency room visits, caused by better preventing health risks necessitating a trip to the emergency room, by those who cannot pay or who are entirely without health insurance will reduce the cost of healthcare for the American government and healthcare industry. There also could be a large financial gain in decreasing the amount of antibiotics purchased due to a reduced need for them following better preventative health. This would be especially beneficial considering that at least 30% of the roughly 260 million antibiotic prescriptions written per year are unnecessary, according to the Centers for Disease Control (CDC, 2022; CDC, 2017).

For one example of the financial benefits, one survey found that in America the cost of one Humalog insulin vial went from $21 in 1996 to $275 in 2017—an over 1200% increase in just over twenty years (Frieden, 2018). This increase in price is consistent with widespread cost increases of insulin in America over the past several decades. Even with insurance, the cost of insulin can be too great for some individuals to afford, such as 23-year-old Alec Smith, whose insurance required a $7600 deductible on top of a $440 monthly premium (Rajkumar, 2020). While type I diabetes cannot be prevented, as it is a genetically-inherited autoimmune disease, type II diabetes, often caused by risk factors such as obesity and physical inactivity, does have the possibility of being prevented. Fenugreek, as has been discussed, showed significant effects on diabetic patients. Black pepper can also be of use, as it increases metabolism, which can in turn

aid in avoiding obesity. Both of these can be utilized preventatively before someone becomes obese and greatly increases the risk of becoming type II diabetic—at a much more affordable cost than insulin costs once the individual is diabetic. This is just one example of how preventative medicine is of significant financial advantage for both individuals in and the nation of the United States.

While there are strong arguments for the implementation of Ayurveda, along with other complementary and alternative medicines, into American medicine, this is not to say that there are no problems that might rise or continue to prevail. One such problem is that of those in poverty not going to the hospital unless necessary to begin with. For those in poverty, and especially those with no health insurance, going to the hospital or doctor's office for annual physical examinations or for small, non-emergency health problems may not be possible for the majority of this population. If this is the case, stronger preventative medicine may not realistically reduce healthcare costs for the individuals or for America as a whole. However, that does not negate the fact that better preventative health still betters the overall health and quality of life of patients, poverty-stricken or not, regardless of the financial impact.

Instead, this problem can be seen as a case for a bigger argument—that of a larger responsibility for population health at a national level rather than an institutional or individual one. If preventative medicine were invested in on a national level, rather than being left in the hands of individual physicians and their particular patients, the financial advantages of better preventative health have a greater possibility of being realized. Reducing the rate of obesity in America, for example, would provide a significant financial decrease in healthcare cost. Due to the problems that might face individuals in

poverty and/or without health insurance, leaving the burden of preventative medicine entirely on them will not be successful. However, if preventative health is taken up as a national cause and investment, the financial advantages that preventative alternative medicine provide can significantly benefit the whole nation.

There is also a potential problem in the self-administrative aspect of preventative medicine, especially as it relates to spices and herbs (Sugito, *et al*., 2019). Because they are ingested orally and almost exclusively as additives to a person's normal dietary intake, physicians cannot manage the exact amount that patients are taking in any given time (Ekor, 2014). While this is true, consider also the reality that patients often don't even take pharmaceutical medicine as prescribed to do. In fact, the affordability and ease of buying a spice from the local supermarket or grocery store and then incorporating it into one's regular meals could be considered easier than remembering to take pills at specific times. Regardless of whether patients are as regimented in taking spices and herbs as prescribed, there is still benefit to doctors recommending them as preventative health, as even some degree of patients increasing their spice and herb intake can be beneficial for their health. There is also the added benefit of generational health increasing over time as better food practices, including a diet with greater intake of spices and herbs, are ingrained in children as they grow and have children of their own. Additionally, spices and herbs are safer for patients, in that when not taken exactly as prescribed there are little to no harmful side effects, unlike some pharmaceutical drugs. Thus, even with the potential problems of self-administering medicine, the risks in doing so with alternative medicines such as spices and herbs are low while the potential benefits are high.

This work is by no means a comprehensive study of the specific spices and herbs of Ayurveda, or of alternative medicines. One factor behind this is the limitations of scope allowed for a work of this magnitude; however, another contributing factor is the lack of scientific literature available regarding these topics. That being said, this thesis serves to compile some of the relevant studies then to make an argument that time and effort should be devoted to studying these topics in more breadth and depth. There are several avenues which further research can pursue.

One area for further study is the efficacy of other methods of treatment which Ayurveda employs. As stated in the first chapter, Ayurveda is a holistic medicine that employs various substances and practices for healing, including things such as physical exercise like yoga, meditation, alcohol, oil, and minerals. Because this paper has been concerned exclusively with plant-based treatments, each of the other treatment forms has a significant amount of space for research into their scientifically-validated efficacy and implementation in American medicine. Beyond Ayurveda, there is also a case to be made for further research regarding other natural medicines such as homeopathy and Traditional Chinese Medicine. Ayurveda, for the purpose of this work, was taken to apply to the other forms of complementary and alternative medicine, but they are by no means the same practice of medicine. Further study is needed first to determine all the differences between Ayurveda and other alternative medicine practices and then to determine how those differences affect their efficacy and implementation into American medicine (Jansen, *et al*., 2021).

There are also areas for research that deal more closely with the content studied within this work. If Ayurveda were to be implemented into American medicine in an

official capacity, more research should be done in the amount of the various spices and herbs, among the other treatment methods, to be prescribed or taken in a specific dose. This is beneficial for two reasons—first, because long-term studies need to be done to determine how much is needed to gain the best health benefits over a lifetime; and second, to better determine if there are any long-term adverse side effects that come with Ayurvedic spices and herbs that have yet to be known due to the lack of lifelong studies. Additionally, more studies need to be conducted to ethically determine if the results from rat and other animal studies also apply to human studies and to what degree they do if so. Another area for study is regarding the multifaceted nature of most of these spices and herbs. As was discussed, each of the seven discussed here had at least two applications, if not more. With this in mind, more research can be done to determine the differences between the multiple properties of each spice and herb—for example, whether differences in the preparation of the plant bring out the different medicinal properties. Finally, more research should be aimed at Ayurvedic spices and herbs as merely long-term preventative medicine or whether there is a case for particular substances to be used as prescribed agents.

Thus, after looking at these seven spices and herbs and recognizing their medicinal validity, an argument has been made for the implementation of alternative medicine—such as the spices and herbs of Ayurveda—into American medicine. This is based on two fundamental arguments. One, that preventative medicine is important, lacking in America, and can be supplemented by alternative medicine. Two, that there is a financial advantage, both for individuals and for the nation, for the spices and herbs of

Ayurvedic medicine to be implemented. These two arguments provide a strong basis for the argument to implement Ayurvedic medicine into modern American culture.

Thus, these seven spices and herbs—black pepper, cinnamon, ginger, turmeric, fenugreek, garlic, and St. John's wort—provide examples of the chemical validity of Ayurveda and other alternative medicines in scientific literature, which then are the foundation for the argument of their implementation in American medicine.

CONCLUSION

A Summary of the Findings and Argument with Future Directions

The purpose of this work was to examine the chemical validity of seven specific plants used in Ayurvedic medicine. The seven spices and herbs chosen for study were black pepper, cinnamon, ginger, turmeric, fenugreek, garlic, and St. John's wort. Each of these were examined in detail to determine whether or not the scientific literature validates their use in the practice of medicine.

Black pepper was found to have an effect on the gastrointestinal system and drug bioavailability, and antioxidant, anticarcinogenic, anti-inflammatory, and pain relief properties. Cinnamon has a role in immune response regulation and lipid regulation, increases insulin function, and possesses antioxidant, anti-inflammatory, and neuroprotective properties. Ginger possesses anticarcinogenic, cardioprotective, antioxidant, and antinausea properties. Turmeric was found to have anticarcinogenic, antioxidant, and neuroprotective properties. Fenugreek has a role in the regulation of metabolism and regulation of lipids, as well as anticarcinogenic properties, while garlic possesses both anticarcinogenic and anti-inflammatory properties. Finally, St. John's wort was found to have two major functions—that of an antidepressant and as a provider of pain relief.

While there are multiple distinctions between these seven spices and herbs—ginger for nausea, St. John's wort for depression, to name a couple—there are predominant properties that many of the plants discussed here have in common. Anti-inflammatory, antioxidant, and anticarcinogenic properties are shared by many, if not all

of the spices and herbs previously examined in greater detail. Many even share the same enzymes upon which they act. These similarities point to two things. First, that naturally-occurring medicinal plants are diverse, but have a large amount of overlap. Second, that with the amount of similarity that is present, there is a great resource for supplementary medicine readily available on the earth.

Following the study of the spices and herbs individually, the validity of which as medicinal treatments has substantially been demonstrated, an argument was put forth for the implementation of these Ayurvedic spices and herbs as complementary medicine in America. These spices and herbs function significantly well as preventative health measures, of which America has need. Additionally, incorporating Ayurvedic and other alternative medicine practices into traditional modern American medicine will be financially advantageous to both individuals in need of it as well as the nation as a whole.

However, this work is not the final stand or argument—it is only the beginning. There are many areas that require more study, some of which have broadly been discussed previously. More research on the chemical and medicinal validity of the various other plants used in Ayurveda, as well as those of other alternative medicine practices are needed before a comprehensive argument for the implementation of alternative medicine into American medicine on a broad scale can successfully be made. The scientific backing of these ancient medicine practices has begun and needs to continue in order to better the health of the American population.

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