Chapter 4

Historical Use of Botanical Medicine

The use of botanicals as medicines has been practiced by various cultures for many thousands of years. Until very recently, the biochemistry and mechanisms of action regarding these substances has remained largely unknown. However, of late, serious scientific effort has begun in order to elucidate the underlying processes by which many plant based substances demonstrate their healing activity.

Introduction

4A

The history of plant chemicals began approximately 1.5 billion years ago, when algae first evolved in the primordial sea. About 435 to 500 million years ago the first known land plants began to appear in wet mud at the edge of bodies of fresh water (1). Once on land, plants enjoyed access to more sunlight, carbon dioxide, and minerals, which they transformed into stored sugars and oxygen.

As millions of years passed, plants grew in size and differentiated. Their evolution escalated approximately 375 million years ago, when many began to

rely on two types of spores, male and female, for reproduction. The next major step was the appearance of gymnosperms, seed-producing plants such as present-day pine trees.

Further sophistication came with angiosperms, or flowering plants, which enclose their seeds in an ovary, usually encased inside a flower. This development occurred about 150 million years ago. The appearance of angiosperms quickly dominated other plants and became one of the most widespread life-forms.

Archaeologists have discovered pollen from at least eight species of flowers in the dirt of a Neanderthal burial cave in Iraq dating back 60,000 years (2). All eight species are still found in Iraq, and seven are traditionally used to treat wounds, dysentery, asthma, inflammation, toothache, and other ailments.

The mythology of plants as palliatives and life-enhancing agents is as old as written language. In the *Epic of Gilgamesh,* a Sumerian prose poem dating from before 2,000 B.C., a god tells the hero, who has just arrived at the mouth of the rivers at the ends of the Earth, “Gilgamesh, you came here exhausted and worn out. What can I give you so that you can return to your land? I will disclose to you a thing that is hidden…..There is a plant….whose thorns will

prick your hand like a rose. If our hands reach that plant you will become as a young man again.

Gilgamesh decides to test the plant, but he and his ferryman stop to eat some food. The story continues: 'Gilgamesh went down and was bathing in the water. A snake smelled the fragrance of the plant, silently came up and carried off the plant" (3).

Gilgamesh was the best known story in the Middle East at a contemporaneous time point with events recorded in the Bible. Its influence is evident in descriptions of the Garden of Eden, where the snake reappears, boasting about a fruit that grows on the "tree of knowledge of good and evil." Eat it and you become immortal, the snake promises. The fruit of another tree, the "tree of life," says the snake, makes you "live forever." These two trees, in turn, appear in the Koran, the holy book of Islam, which has its own Garden of Eden story.

Chinese myths dating back thousands of years likewise describe Penglai, Fangzhang, and Yingzhou, islands with palaces of gold and silver, pure white birds, and animals, and magic herbs that provide immortality. More recently, a Han epic from the 4th to 5th centuries A.D. mentions the "herb of deathlessness."

This herb, according to legend, “seems to have the form of sprouts of water-grass, (with leaves) three to four feet long. If this plant is laid upon a man who has been dead for (as much as) three days, he will come to life again at once. If it is eaten, it will give longevity and immortality.”

The actual medicinal relationship between plants and humans has, of course, been far more than mythical. Collecting medicinal plants and documenting their effects are among mankind’s oldest professions.

Furthermore, the desire for medicinal plants has been fundamental to commercial trade. As soon as people in one part of the world established contact with other societies, one of their first activities was to exchange medicinal plants, as well as their experience and knowledge about them. Known written records regarding medicinal plants date back at least 5,000 years to the Sumarians, who lived in Mesopotamia; the Babylonians, another Mesopotamian civilization, dating to the second millennium B.C.; and the Egyptians, whose Nile River-based culture began to flourish around 3,000 B.C.

Two other ancient civilizations, in India and China, are still thriving after thousands of years, and utilize herbal methodology that is only now being recognized as valuable by Western science. Their continued use of these

ancient substances offer lessons that could be invaluable as modern research attempts to obtain more pharmaceutical drugs from plants, as well as endeavors to better understand herbal medicine.

4B

Worldwide Use of Herbal Therapies

The term *herb* refers to a plant that is used for medicinal purposes. For many individuals, especially those living in the third world, herbal medicines are the only therapeutic agents available. In 1985, the World Health Organization estimated that perhaps 80 percent of the world population relied on herbs for primary health care needs (4). This widespread use of herbal medicines is not restricted to developing countries, as it has been estimated that 30 to 40 percent of all medical doctors in France and Germany rely on herbal preparations as their primary medicines (5).

Throughout the world, but especially in Europe and Asia, a tremendous renaissance in the use and appreciation of herbal medicine has taken place. In Germany, estimates show that over $4 billion dollars are spent on herbal products each year. In Japan, the figure is thought to be even higher. Herbal products represent a major economic force in the United States as well, with an estimated annual sales figure of $3.3 billion dollars for 1998 and rising (6).

Until very recently many mainstream scientists believed that most chemicals produced by flowering and other plants were useless waste products of the plants' basic metabolism, labeling these chemicals "secondary metabolites" to distinguish them from the "primary metabolites" such as sugars and amino acids essential for the plants' basic life functions.

The rebirth of herbal medicine, especially in developed countries, is largely being driven by the renewed interest of scientific researchers. During the last ten to twenty years, research efforts have yielded an explosion of scientific information concerning plants, crude plant extracts, and various constituents from botanical substances formulated as medicinal agents.

For the past 25 years, approximately 25 percent of all prescription drugs in the United States have contained active substances obtained from plants. Digoxin, codeine, colcicine, morphine, vincristine, and yohimbine are examples of this fact. Many over-the-counter preparations are composed of plant compounds as well. It is estimated that more than $11 billion dollars in plant-based medicines are purchased each year in the United States alone, and $43 billion dollars worldwide (7). One advantage herbal medicines possess over synthetic drugs is that, as a rule, herbal preparations are often less toxic than their synthetic counterparts and can offer less risk of side effects.

However, the contralateral position, as expressed by traditional western medicine, has often suggested that the popularity of botanical medicine derives much of its putative benefit from the placebo effect, rather than any intrinsic medicinal properties. The placebo effect is the measurable or observable effect on a person or group that has been given a placebo treatment.

A placebo is an inert substance, surgery or therapy, used as a control in an experiment or given to a patient for its possible or probable beneficial effect. Why an inert substance, surgery or therapy would be effective, is still not completely understood.

Many believe the placebo effect is *psychological*, due to either a real effect caused by *belief* or to a subjective delusion. If one believes the pill will help, it will help. Or, a person's physical condition does not change but they *feel* like it has. For example, Irving Kirsch, a psychologist at the University of Connecticut, believes that the effectiveness of Prozac and similar drugs may be attributed almost entirely to the placebo effect. In a study published [in June, 1999], Kirsch and...Guy Sapirstein...analyzed 19 clinical trials of antidepressants and concluded that the expectation of improvement, not

adjustments in brain chemistry, accounted for 75 percent of the drugs' effectiveness. (8)

"The critical factor," says Kirsch, "is our beliefs about what's going to happen to us. You don't have to rely on drugs to see profound transformation." In an earlier study, Sapirstein analyzed 39 studies, undertaken between 1974 and 1995, of depressed patients treated with drugs, psychotherapy, or a combination of both. In that study, he determined that 50 percent of the drug effect is due to the placebo response.

A person's beliefs and hopes about a treatment, combined with their suggestibility, may have a significant biochemical effect. It is known that sensory experience and thoughts can effect neurochemistry and that the body's neurochemical system affects and is affected by other biochemical systems, including the hormonal and immune systems. Thus, there is likely some truth to the theory that a person's hopeful attitude and beliefs are very important to their physical well-being and recovery from injury or illness.

However, it may be that much of the placebo effect is not a matter of mind over molecules, but of mind over behavior. A part of the behavior of a "sick" person is learned. So is part of the behavior of a person in pain. In short, there is a certain amount of role-playing by ill or hurt people. Role-

playing is not the same as dissembling. The behavior of sick or injured persons is socially and culturally based to some extent. The placebo effect may be a measurement of changed behavior affected by a belief in the treatment. The changed behavior includes a change in attitude, in what one says about how one feels, and how one acts. It may also affect one's body chemistry. The psychological explanation seems to be the one most commonly believed. Perhaps this is why many people are dismayed when they are told that the effective drug they are taking is a placebo.

Doctors in one study successfully eliminated warts by painting them with a brightly colored, inert dye and promising patients the warts would be gone when the color wore off. In a study of asthmatics, researchers found that they could produce dilation of the airways by simply telling people they were inhaling a bronchiodilator, even when they weren't (9). Patients suffering pain after wisdom-tooth extraction got just as much relief from a non-functioning application of ultrasound as from a real one, so long as both patient and therapist thought the machine was functional. Fifty-two percent of the colitis patients treated with placebo in 11 different trials reported feeling better -- and 50 percent of the inflamed intestines actually appeared imporoved upon assessment with a sigmoidoscope. (10) Clearly, such effects are not purely psychological.

Some believe that at least part of the placebo effect is due to an illness or injury taking its natural course. We often heal in time if we do nothing at all to treat an illness or injury. The placebo is sometimes mistakenly thought to be effective when, in fact, the body is spontaneously healing itself.

However, spontaneous healing and spontaneous remission of disease cannot explain all the healing or improvement that takes place because of placebos, or because of active medications or treatments, for that matter. People who are given no treatment at all often do not do as well as those given placebos or real medicine and treatment.

Another theory gaining popularity is that a process of treatment that involves showing attention, care, affection, etc., to the patient/subject, a process that is encouraging and hopeful, may itself trigger physical reactions in the body which promote healing. There is certainly data that suggest that just being in the healing situation accomplishes something. Depressed patients who are merely put on a waiting list for treatment do not do as well as those given placebos. And when placebos are dispensed for pain management, the course of pain relief follows the same course one would expect with an active pharmaceutical.

The peak relief comes about an hour after it's administered, as it does with the real drug, and continues along the same path. If placebo analgesia was the equivalent of giving nothing, a more random pattern would be expected. (Dr. Walter A. Brown, psychiatrist, Brown University) Dr. Brown and others believe that the placebo effect is mainly or purely *physical* and due to physical changes which promote healing or feeling better.

Clearly, these physical changes are not caused by the inert substance itself, so what is the explanatory mechanism for the placebo effect? Some investigators believe the *process* of administration may be key. It is thought that the touching, the caring, the attention, and other interpersonal communication that is part of the controlled study process (or the therapeutic setting), along with the hopefulness and encouragement provided by the experimenter/healer, affect the mood of the subject, which in turn triggers physical changes such as release of endorphins. This process reduces stress by providing hope or reducing uncertainty about what treatment to take or what the outcome will be. It is thought that the reduction in stress may prevent or slow down further harmful physical changes from occurring.

This process-of-treatment hypothesis would help explain how inert homeopathic remedies and the questionable therapies of many "alternative" health practitioners present ostensibly measurable efficacy. It would also

explain why pills or procedures used by traditional medicine work until they are shown to be worthless.

In the 1960's, a young Seattle cardiologist named Leonard Cobb conducted a unique trial of a procedure then commonly used for angina, in which doctors made small incisions in the chest and tied knots in two arteries to try to increase blood flow to the heart. It was a popular technique -- 90 percent of patients reported that it helped -- but when Cobb compared it with placebo surgery in which he made incisions but did not tie off the arteries, the sham operations proved just as successful. The procedure, known as internal mammary ligation, was soon abandoned. (11)

Whether the placebo effect is mainly psychological, or misunderstood spontaneous healing, or due to a process characterized by showing care and attention, or due to some combination of all three may not be ascertainable with complete confidence. But the powerful effect of this phenomenon should not be in doubt.

H. K. Beecher evaluated over two dozen studies and calculated that about one-third of those in the studies improved due to the placebo effect ("The Powerful Placebo," 1955) (12). Other investigations calculate the placebo effect as being even greater than Beecher claimed. For example, studies have

shown that placebos are effective in 50 or 60 percent of subjects with certain conditions, e.g., "pain, depression, some heart ailments, gastric ulcers and other stomach complaints." Further, as effective as many new psychotropic drugs seem to be in the treatment of various brain disorders, some researchers maintain that adequate evidence has not been established from studies to demonstrate beyond all doubt that the new drugs are more effective than placebos. Placebos have also been shown to cause unpleasant side-effects. There are even reports of people becoming addicted to placebos.

Patients can become dependent on nonscientific practitioners who employ placebo therapies. Such patients may be led to believe they're suffering from imagined "reactive" hypoglycemia, nonexistent allergies and yeast infections, dental filling amalgam "toxicity," or that they're under the power of Qi or extraterrestrials. And patients can be led to believe that diseases are only amenable to a specific type of treatment from a specific practitioner regardless of empirical data to the contrary. It has been medico-ethical dilemmas such as these which has long dissuaded many Western physicians from even considering botanically based therapies for the treatment of somatically based disease.

However, with the advent of a growing sophistication in the elucidation and preparation of herbal medicine, a new era in the use of botanically based

therapies may be at hand. Appreciation among western scientists and practitioners is growing for the healing properties that many herbal medicines possess. As modern medicine gains more knowledge and understanding about health and disease, it is adopting therapies that are more natural and, concomitantly, less toxic. Lifestyle modification, stress reduction, exercise, dietary changes, and many other traditional holistically grounded therapies are becoming much more popular in standard medical circles.

4C

Herbal Preparation

The potencies or strengths of herbal extracts are generally expressed in two ways. If they contain known active principles, their strengths are commonly expressed in terms of the content of these active principles. Otherwise, the strength is expressed in terms of concentration. For example, herbal tinctures are typically formulated at a 1:5 concentration. A tincture is an extract, usually herbal, and usually made in a vehicle of water and alcohol, although there have been tinctures compounded using acetic acid, chloroform and glycerin. The term Tincture is still pharmaceutical in implication, so the FDA periodically objects to its use in the herb industry (13).

There are many alternative methods for preparing herbs in concentrated forms, in ours and other cultures (the Unani honeys, the pills used in Ayurveda and TCM), but trying to emulate a tincture with other media results in inferior products, and a moral waste of Plant Energy. By way of contrast, a 4:1 concentration is more typical of a solid botanical extract.

The term *standardized extract* refers to an extract guaranteed to contain a “standardized” level of active compounds. This form is generally accepted in Europe and is has begun to be adopted in the United States as well (14). Standardized extracts arose out of the need to create a uniform product for clinical trials. Broadly speaking, there are two types. One is based on identifying and quantifying an extract to a characteristic chemical *marker compound*.

A marker extract establishes that a specified amount of a marker compound is present in the finished product. It must be noted that a marker does not represent the active constituents but is selected as a biochemical constituent characteristic of the plant. In many cases, if this process uniformly increases all plant constituents to an intended level. In general, the insoluble compounds, such as cellulose and fiber, are excluded. In some cases the concentrated extracts remain dried and powdered while in others they are

mixed with a neutral material such as corn starch, and in still others, the extract is mixed with the fine granules of the whole herb.

The most important distinction is that *marker extracts* are not based on the concentration of a proven active constituent, but are used for positive identification or to create a higher degree of uniform potency. Active constituent extracts identify and concentrate one or more herbs as *active constituents*, thus bringing them closer to the level of chemical isolates.

This means that other naturally occurring constituents are displaced at the expense of one or a number of compounds. An active constituent extract, therefore, regulates a specific biochemical constituent to a level that may not be naturally found in the plant. Concentrating 95% curcuminoids, for instance, in a standardized turmeric extract creates a product that while derived from the crude herb, is not expected to be naturally found concentrated at that level. This leaves only 5% of the other turmeric constituents with which the curcumin is combined.

The range of sophistication in the processing of herbs is tremendous—from crude herb to highly concentrated standardized extracts. The endpoint result is a spectrum of efficacy that varies from negligible to clinically and

scientifically demonstrable. Nonetheless, there are some stages all share. The next section describes some of the common processes involved in the production of herbal preparations.

4D

Collecting/harvesting

When plants are collected from their natural habitat they are said to be "wild-crafted". In contrast, when they are grown, utilizing commercial farming techniques, they are said to be "cultivated". Collection of plants from cultivated sources ensures that the plant collected is the same one desired.

When an herb is wild-crafted, there is a much greater chance that the wrong herb will be picked, a situation that could lead to serious consequences. The use of analytical methods can be employed to ensure that this problem does not occur.

The mode of harvesting varies from hand labor to the use of sophisticated equipment. However, the mode of cropping is not as important as the temporal aspect of harvesting: a plant should be harvested only when the

part desired contains the highest possible level of active compounds. This is safeguarded only through the use of analytical techniques.

4E

Drying

After harvesting, most herbs have a moisture content of 60 to 80 percent and cannot be stored without drying. This is necessary so that important compounds can be protected from breakdown by microbial and other contaminating factors.

The majority of herbs in widespread use today require relatively mild conditions for drying. Commercially, most plants are dried within a temperature range of 100 to 140 degrees Fahrenheit. During drying, the plant material must not be damaged or suffer losses that would prevent it from conforming to accepted standards. With proper drying, the moisture content of the herb will be reduced to less than 14 percent (15).

4F

Garbling

Garbling refers to the separation of the; portion of the plant to be used from other parts of the plant, dirt, and other extraneous matter. This step is often done during collection. Although there are machines that perform garbling, this process is still often performed by hand.

4G

Grinding

Grinding an herb involves mechanically breaking down either leaves, roots, seeds, or other parts of a plant into a uniform size shape and consistency; suitable for encapsulation or extraction. Grinding is employed in the production of crude herbal products as well as in the initial phases of extracts. Often the material must be prechopped or minced before feeding it into a grinder.

A number of machines can be used to grind herbs, but the most widely used is the hammer mill. The hammers, arranged radially, follow the rotation of the shaft to which they are attached, breaking up the material that is fed into the machine from above. Other types of grinders include knife mills and teeth mills.

4H

Extraction

The process of extraction is used in making tinctures, fluid extracts, and solid extracts. In this context, extraction refers to the separation by physical or chemical means, of the desired material from a plant with the aid of a solvent.

The U.S. health food industry often uses alcohol and water mixtures as solvents to extract soluble compounds from herbs. Occasionally liposterolic extraction, involving the use of lipophilic solvents as well as hypercritical CO2, is performed. An example of this process is known in the industry as high pressure extraction.

High-pressure extraction can be used for the separation of both solid and liquid raw substances, the former being fed batch-wise to an extraction vessel, while the latter is extracted continuously in counter-current columns. Liquid CO2 flows from collecting vessels to a transfer pump, which compresses it to the required extraction pressure where the gas is heated to the extraction temperature and transferred to the extraction vessel or column. The substances

to be extracted are dissolved in the heated CO2 as they pass through the vessel.

This CO2 mixture, laden with the dissolved substance, is then fed to a separator. By adjusting the pressure and/or temperature, the dissolving power of the CO2 in the separator is reduced, thus causing the extracts to be precipitated. This may take place at several stages, thereby allowing extract fractions of different qualities to be obtained. The gaseous CO2 from the separator is liquefied in a refrigerated condenser and collected in a collecting vessel where it may be reutilized again. The use of several vessels for the extraction of substances in this method permits virtually semi-continuous operation.

Most extracts produced by small manufacturers involve the use of maceration procedures. The simplest process consists of soaking the herb in the alcohol/water solution for a period of time, followed by filtering. Typically, this process will yield a lower quality extract at a higher price because the solvent, usually alcohol, cannot be reused.

It is, in this form, sold to the customer. Since tinctures are 1:5 concentrates, this means 80 percent of the mixture is alcohol and water and only 20 percent herbal material. Tinctures are generally not as cost effective

or as stable as solid extracts. The primary reason for this is that tinctures may vary between 1 part of herb to 5 to 6 parts of liquid vs. extracts which generally contain a ratio of 1 part herb to 1 part liquid.

Larger manufacturers utilize more elaborate techniques to ensure that an herb is fully extracted and that the solvent is reused. For example, countercurrent extraction is often used. In this process, the herb enters into a column of a large percolator composed of several columns.

The material to be extracted is pumped at a given temperature and rate of speed through the different columns, where it mixes continuously with solvent. The extract-rich solvent then passes into another column, while fresh solvent once again comes into contact with herbal material as it is passed into a new chamber. In this process, complete extraction of health-promoting compounds can be achieved. The extract-rich solvent is then concentrated by the techniques described below.

4l

Concentration

After extraction of the herb, the resulting solutions can be concentrated into fluid extracts or solid extracts. In large manufacturing operations, the

techniques and machines used ensure that the extracted plant components are not damaged.

These machines work by evaporating the solvent, thus isolating the plant compounds. The solvent vapors pass into a condenser, in which they recondense to liquid form and can be used again. The result is separation of the extracted materials from the solvent, so that the final product is a pure extract and the solvent can be used repeatedly.

4J

Excipients

An excipient is an inert substance added to a preparation, such as an herbal tincture, to give it a certain form or consistency. The same excipients used in the manufacture of drug preparations as well as vitamin and mineral supplements are often used in the production of tablets and capsules containing herbs or herbal extracts. Many manufacturers will provide a list of excipients contained in their products.

4K

Analytical Methods in Preparing Botanical Therapies

Improvements in analytical methods have led to definitive improvements in harvesting schedules, cultivation techniques, storage, activity, stability of active compounds, and product purity. All of these gains have resulted in tremendous improvements in the quality of herbal preparations now available.

For example, optimal activity and quality collection should be done at a time when the active ingredient is present in the greatest amount. Improvements in analysis have led to more precise harvesting of many herbs. Methods currently utilized in evaluating herbs and their extracts include the following:

- Organoleptic
- Microscopic
- Physical
- Chemical/physical
- Biological

Organoleptic may be defined as the “impression of the organs”. Organoleptic analysis involves the application of sight, odor, taste, touch, and

occasionally even sound, to identify the plant. The initial sight of a plant or extract may be so specific that it is sufficient for identification. If this is not sufficient, the plant or extract may have a characteristic odor or taste. Organoleptic analysis represents the most basic form of herbal quality analysis.

Microscopic evaluation is indispensable in the initial identification of herbs, as well as in elucidating small fragments of crude of powdered herbs, adulterants (e.g., insects, animal feces, mold, and fungi), and characteristic tissue features of the plant. Every plant possesses a characteristic tissue structure, which can be demonstrated through the study of tissue arrangement, cell walls, and configuration when samples are properly stained and mounted.

In crude plant evaluation, physical methods are often employed to determine the solubility, specific gravity, melting point, water content, degree of fiber elasticity, and other physical characteristics. For example, sophisticated techniques, such as high pressure liquid chromatography (HPLC) and nuclear magnetic resonance (NMR), are often used to separate out molecules. The readings from these machines provide a chemical "fingerprint" as to the nature of chemicals contained in the plant or extract. These techniques are invaluable in the effort to properly and fully identify herbs, as well as standardized extracts. The plant or extract can then be evaluated by various biological methods to determine pharmacological activity, potency, and toxicity.

Various chemical/physical methods are also used to determine the percentage of active principles, alkaloids, flavonoids, enzymes, vitamins, essential oils, fats, carbohydrates, protein, or crude fiber present. The final analytical process requires more precise assays to determine quality. Sophisticated techniques, such as high-pressure liquid chromatography and nuclear magnetic resonance, are often used to separate molecules. The readings from these machines provide a chemical "fingerprint" as to the nature of chemicals contained in the plant or extract. These techniques are invaluable in the effort to identify herbs, as well as to standardize extracts.

The plant or extract can then be evaluated by various biological methods, such as *in vitro* assays as well as *in vivo* animal studies, in order to determine pharmacological activity, potency, and toxicity associated with the compound being considered.

4L

Use of Botanicals in Modern Medicine

Plants have utilized extraordinary chemicals for more than 3.5 billion years. However, the use of botanical therapy in Western Medicine is presently enjoying a resurgence unprecedented at any time in contemporary

history. At the dawn of the twenty-first century, more Americans are looking to "nontraditional" healers, as opposed to simply considering mainstream Western medicine, as a first line approach when faced with illness or debility (16).

A climate of sterility, as well as one-sidedness of Western medicine in treating certain disorders has compelled many people to investigate alternatives. Many of these choices--aromatherapy, ayurevdeic medicine, chiropractic, herbalism, naturopathy—feature natural substances as healing tools.

4M

Aromatherapy

Essential oils, have been revered for their fragrance and spirit for thousands of years by the ancient Egyptians, Greeks, Romans, Chinese, Japanese, Native Americans, and East Indians. It is only recently that many are re-discovering the healing qualities of ancient plant medicine - today referred to as "aromatherapy."

As an art and science, aromatherapy is actually a highly complex and developed heath care area. In definition, aromatherapy is the use of naturally distilled essences and extracts of bark, leaves, petals, resins, rinds, roots, seeds, stalks, and stems of aromatic plants. When used in the form of essential oils, they can promote a sense of well being, as well as offer therapeutic

qualities. As ancient and modern people have discovered, the healing properties of botanicals have a variety of benefits within a holistic framework of health.

Specific essential oils can be used to treat common conditions such as nasal congestion, indigestion, insomnia, arthritis, earache, headache, and sore throat. On an inner realm, there are also certain essential oils that can be utilized in purifying the spirit and stabilizing the individual's psychological and emotional state. It is believed by some that those who incorporate aromatherapy into their health practices enjoy higher levels of creativity and positive self-esteem.

When absorbed into the skin, essential oils have been shown to form new skin cells, calm inflammation, and relieve soar muscles (17). When inhaled, select oils may help relieve nasal congestion, clear headaches, and assist in relaxation. Methods on how to use essential oils are: spray mists, nebulizer diffusers, in the bath/shower, compress, massage, as well as colognes and perfumes. Examples of specific oils that may assist in attaining a calming effect are rose, sandalwood, and neroli oils. Ginger, peppermint, rosemary, and bergamot are believed to serve as stimulants, and believed beneficial for energy and wakefulness.

Reflecting on the power of aroma, Helen Kellar observed: "Smell is a potent wizard that transports across the thousands of miles and all the years we have lived. The odors of fruits take me to my southern home, to my childhood of frolics in the orange orchard. Other odors instantaneous and fleeting cause my heart to dilate joyously or contract with remembered grief. Even as I think of smells my nose is full of scents that start to awake sweet memories of summers gone and ripening fields far away."

4N

Ayurveda

Ayurveda is a holistic system of healing which evolved among the Brahmin sages of ancient India some 3000-5000 years ago (18). There are several aspects of this system of medicine which distinguish it from other approaches to health care:

1. It focuses on establishing and maintaining balance of the life energies within us, rather than focusing on individual symptoms.

2. It recognizes the unique constitutional differences of all individuals and therefore recommends different regimens for different types of people. Although two people may appear to have the same outward symptoms, their

energetic constitutions may be very different and therefore call for very different remedies.

3. Ayurveda is a complete medical system which recognizes that ultimately all intelligence and wisdom flows from one Absolute source (Paramatman). Health manifests by the grace of the Absolute acting through the laws of Nature (Prakriti). Ayurveda assists Nature by promoting harmony between the individual and Nature by living a life of balance according to her laws.

4. Ayurveda describes three fundamental universal energies which regulate all natural processes on both the macrocosmic and microcosmic levels. That is, the same energies which produce effects in the various galaxies and star systems are operating at the level of the human physiology--in your own physiology. These three universal energies are known as the Tridosha.

5. Finally, the ancient Ayurvedic physicians realized the need for preserving the alliance of the mind and body and offers mankind tools for remembering and nurturing the subtler aspects of our humanity. Ayurveda seeks to heal the fragmentation and disorder of the mind-body complex and restore wholeness and harmony to all people.

4O

Chiropractic

Chiropractic medicine is defined as a health profession concerned with the diagnosis, treatment and prevention of mechanical disorders of the musculoskeletal system, and the effects of these disorders on the function of the nervous system and general health. There is an emphasis on manual treatments including spinal manipulation or adjustment. Under Chapter 112 of the Massachusetts General Laws, Section 89, chiropractic is defined as the science of locating and removing interference with the transmission or expression of nerve force in the human body, by the correction of misalignments or subluxations of the bony articulations and adjacent structures, more especially those of the vertebra column and pelvis, for the purpose of restoring and maintaining health. X-ray and analytical instruments may be used for the purposes of chiropractic examinations (19).

Chiropractic is based on the philosophy that the relationship between structure and function in the human body is a significant health factor. The relationships between the spinal column structure and the nervous system functions are the most significant. The doctor of chiropractic (D.C.) is a primary care, first-contact physician. The chiropractic physician bases treatment upon a foundation of diagnostic information gathered through

physical examination, patient history, clinical laboratory results (blood chemistries, urinalysis, etc.), diagnostic imaging (X-rays, MRIs, etc.), and other diagnostic measures in addition to evaluations unique to chiropractic.

Following development of a diagnostic impression, the chiropractic physician may care for the patient through the application of spinal and extravertebral manipulations. Care may also include nutritional counseling, physiological therapeutics, acupuncture, trigger point therapy, lifestyle counseling, emotional support, stress management, and other related therapies.

4P

Herbalism

Herbalism may be defined simply as the practice of using herbs to help provide the body with an environment of health and the ability to heal itself. As previously discussed, there are many ways to administer herbs such as fresh or dried, in infusions, tinctures, decoctions, ointments, and compresses.

4Q

Naturopathy

Naturopathic medicine is a distinct system of healing - a philosophy, science, art and practice which seeks to promote health by stimulating and supporting the body's inherent power to regain harmony and balance. Although the term naturopathy was first used at the turn of the century, the philosophical basis and many of the methods of naturopathic medicine are ancient, some dating back at least to 400B.C., when Hippocrates became famous for his treatment of disease in accordance with natural laws. In fact, although Hippocrates is called the Father of Medicine, modern medical science completely ignores the self-evident laws of health laid down by him, which state:

- Only nature heals, providing it is given the opportunity to do so;

- Let food be your medicine and let medicine be your food;

- Disease is an expression of purification;

- All disease is one.

The philosophy of naturopathic medicine is based upon three basic principles. The first principle is that the body possesses the power to heal itself

through its internal vitality and intelligence. This vital force is the foundation of naturopathic philosophy and all the naturopathic practitioner does is to create the most favourable conditions to stimulate and enhance this healing power of nature.

The second principle is that disease is a manifestation of the vital force applying itself to the removal of obstructions to the normal functioning of organs and tissues. The naturopathic practitioner always seeks to discover and remove the basic causes of disease whether they be; Chemical; i.e. an imbalance in the chemistry of the body fluids due to dietary deficiency or dietary excess, retention of waste products due to inefficient functioning of the lungs, kidneys and bowels, or poor circulation of body fluids; Mechanical; i.e. muscular tensions, strained ligaments, stiff joints, poor posture due to occupational factors, as well as spinal misalignments, leading to an interference in the functioning of the nervous system and the musculoskeletal system generally; Psychological; i.e. impaired function induced by stress, which may be due to worries and upsets in personal and domestic life and/or anxieties and pressures at work.

The third principle is that naturopathic medicine is a holistic approach to health. In other words, disease affects the whole person - body, mind and spirit, and not simply an isolated organ or system. Each person responds in

unique ways to his or her environment, each has individual strengths, weaknesses and needs. Their body's reactions to the same stress may be very different depending on their level of health, inherited tendencies, previous medical history, etc. In treating the whole person the naturopathic practitioner searches for causes at many levels, and attempts to eliminate the fundamental cause of illness, not simply to remove symptoms.

The future of Western healing may not be a total shift to alternative medicine. Rather, a complementary hybrid of sorts appears to be forming, between traditional and non-traditional methodologies. And natural products and botanically derived therapies should prove to be an integral part of this process (20).

There are many noteworthy examples wherein botanicals have shown remarkable benefit as alternatives to pharmaceutical approaches to dealing with human afflictions. Among these are the substances Gugolipid and Feverfew.

4R

Gugolipid

General description

Gugulipid is derived from the mukul myrrh tree (*Commiphora mukul),* a small thorny tree 4 to 6 feet tall that is native to Arabia and India. In its natural setting, the tree remains essentially free of foliage for most of the year. Its bark is ash-colored and comes off in rough flakes, exposing the underbark, which also peels off. On injury, the tree exudes a yellowish gum resin that has a balsamic odor. The oleoresin is referred to as “gum guggul” or “guggulu.” This resin is used for medicinal purposes. When tapped during the winter the average tree yields 700-900 grams of resin (21).

4S

Chemical composition

Guggulu contains a mixture of diverse chemical constituents that can be separated into several fractions (22). The first step in the fractionation process involves mixing guggulu with ethyl acetate, yielding a soluble and an insoluble fraction.

The insoluble fraction, containing the carbohydrate constituents, is toxic and is the major reason why extracts of the soluble portion are preferred to crude gum guggul for medicinal use. The insoluble portion has no demonstrable pharmacological activity other than toxicity (23).

In contrast, the soluble portion possess significant cholesterol-lowering and anti-inflammatory activity. The soluble portion can be further separated into basic, acid, and neutral fractions. The neutral portion possesses primarily cholesterol-lowering activity, while the acidic portion is noted for its anti-inflammatory composition.

On further purification of the neutral portion, it was found that the ketone fraction contains the most potent anti-cholesterolemic properties. The ketone fraction is composed of C^{21} or C^{27} steroids, with the major components being Z- and E-guggulsterone. These compounds are considered the major active components of gum guggul and its extracts.

For medicinal purposes, a standardized extract known as gugulipid, which contains a minimum of 50 mg of guggulsterones per gram, is regarded as the most beneficial in terms of safety and efficacy. In addition to guggulsterones, the gum resin of C. mukul contains diterpenoids (cembrene-A and mukulol), pentosan, pentoses, furfural, D-galactose, fructose, L-arabinose, 4-methyl ether of D-glucoronic acid, the guggultetrols (esters of C18, C19, and C20 polyhydroxylated saturated hydrocarbons), and steroids derived from pregnane and cholestane (24). Upon steam distillation, the gum resin furnishes

an aromatic essential oil. The oil contains the monoterpenes myrcene, camphorene, polymyrcene and caryophyllene.

The aerial parts of C. mukul contain beta-sitosterol, myricyl alcohol, and many amino acids (cysteine, histidine, lysine, arginine, aspartic acid, serine, glutamic acid, threonine, alanine, proline, tryosine, tryptophan, valine, leucine, and isoleucine). The flowers are rich in flavonoids, most notably quercetin (25).

4T

History and folk use

Guggulu is a highly valued botanical medicine in the Indian system of medicine, *Ayurveda*. It is included in formulas for a variety of health conditions including rheumatoid arthritis and lipid disorders. The classic Ayurvedic medical text, the *Sushrutasamhita*, describes in detail the usefulness of guggul in the treatment of obesity and other disorders of metabolism, including "coating and obstruction of channels."

Inspired by this description, researchers began studying, in well-designed scientific studies, the clinical effectiveness of gum guggul and its

extracts in disorders of lipid metabolism—specifically, its ability to lower serum cholesterol and triglyceride levels, and, concomitantly, promote weight loss.

This research has resulted in the development of a natural cholesterol-lowering agent that is safer and more effective than many cholesterol-lowering drugs, including niacin. Gugulipid was granted approval in India for marketing as a lipid-lowering drug in June 1986. However, for reasons not entirely certain, its use in western culture remains somewhat limited.

4U

Pharmacology

The pharmacology of gugulipid focuses primarily on its ability to lower serum cholesterol and triglyceride levels.

4V

Cholesterol- and triglyceride-lowering effects

A number of studies in humans and animals have shown that gum guggul exerts effective lipid-lowering activity. The effect on cholesterol is particularly beneficial, as guggul lowers very low-density lipoprotein (VLDL) cholesterol and low-density lipoprotein (LDL) cholesterol while simultaneously elevating high-

density lipoprotein (HDL) cholesterol, thus offering protection against heart disease due to atherosclerosis (26).

The primary mechanism of action for gum guggul and for gugulipid's anti-cholesterolemic activity has been shown to be the stimulation of liver metabolism of LDL cholesterol. Guggulsterones have been shown to increase the uptake of LDL cholesterol from the blood by the liver.

However, another activity of guggulsterone effecting lipid levels may be its ability to stimulate thyroid function (27). This thyroid-stimulating effect may be responsible for some of gugulipid's weight loss benefit.

4W

Prevention and reversal of atherosclerosis

In addition to lowering lipid levels, gum guggul and its extracts, including gugulipid, prevent the development of atherosclerosis and aid in the regression of preexisting atherosclerotic plaques in animals. This implies that it may have a similar effect in humans. Gum guggul and its extracts mildly inhibit platelet aggregation and promote fibrinolysis, implying that they may also prevent the development of a stroke or embolism (28).

4X

Cardioprotective activity

In addition to its lipid-lowering activity, guggul may also promote cardiovascular health through its ability to act as an antioxidant and to inhibit platelet aggregation. Three studies showing guggul's potential as an antioxidant were reviewed. The effect of guggulsterones on the oxidative modification of lipid and protein components of LDL induced by copper (Cu++) in vitro was examined in a 1997 study. Guggul-sterones inhibited the generation of lipid peroxidation products in a concentration dependent manner. In the same investigation, guggulsterones also inhibited the formation of hydroxyl (OH-) free radicals created in a nonenzymic system in a concentration dependent manner. In 1989, guggulsterones (50 mg/kg) were given to rats after induction of myocardial necrosis with isoproterenol. In myocardial necrosis, increased levels of lipid peroxides, xanthine oxidase activity and a lowering of superoxide dismutase is observed, which may lead to increased formation of free radicals with subsequent cardiac cell damage. In the dietary modification trial discussed above, a decrease in the production of lipid peroxides was observed among the guggul group, suggesting a 33% decline in oxidative stress. No change in lipid peroxide production was observed in the placebo group (29).

A study conducted by Mester and colleagues in 1979 showed total inhibition of platelet aggregation in vitro induced by adenosine diphosphate (ADP), serotonin, and adrenaline by isolated E-and Z-guggulsterones (30).

4Y

Anti-inflammatory activity

The guggulsterone fraction of gum guggul exhibits significant anti-inflammatory action in experimental models of inflammation (31). Its activity in models of acute inflammation is comparable to approximately one-fifth that of hydrocortisone, and equal to phenylbutazone and ibuprofen.

In models of chronic inflammation, it was shown to be more effective than hydrocortisone, phenylbutazone, and ibuprofen in reducing the severity of secondary lesions. The anti-inflammatory action is thought to be due to inhibition of delayed hypersensitivity reactions.

4Z

Clinical applications

The primary clinical application of gugulipid is in the treatment of hypercholesterolemia. Research indicates that gugulipid offers considerable benefit in the prevention and treatment of atherosclerotic vascular disease, the leading cause of death in the United States (32).

Gugulipid appears most indicated in type IIb and type IV (LDL/VLDL) hyperlipidemias. In human clinical trials testing gugulipid, cholesterol levels typically dropped 14 to 27 percent in a 4 to 12 week period while triglyceride levels dropped from 22 to 30 percent (33). Table 2 shows the effect of gugulipid on serum cholesterol in comparison to other lipid-lowering drugs.

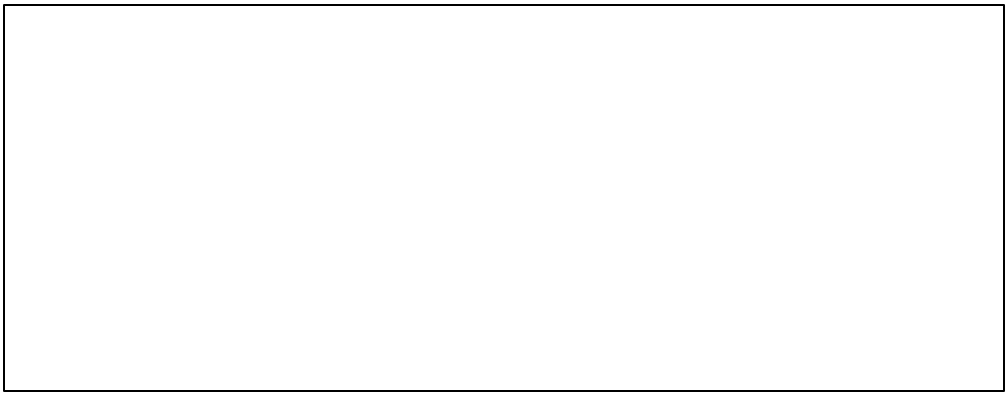

Table 2: Serum lipid effects of gugulipid compared to standard drugs

However, while the drugs are associated with significant toxicity, appropriate extracts of gugulipid produce no side effects. In addition to the excellent safety record as demonstrated in human studies, safety studies in animals have demonstrated gugulipid to be virtually nontoxic.

4AA

Dosage

While the crude oleoresin (gum guggul), alcohol extract, and petroleum ether extract have all been shown to exert lipid-lowering as well as anti-inflammatory action, they have also been associated with undesirable side effects (skin rashes, diarrhea, etc.) at the dosage required to produce a clinical effect.

Gugulipid, the standardized extract of the gum guggul, not only has greater clinical efficacy, but patients tolerate it much better than they do crude or purified gum guggul. The dosage of gugulipid is based on its guggulsterone content.

Clinical studies demonstrate that 25 mg of guggulsterone three times per day is an effective treatment for elevated cholesterol levels, elevated triglyceride levels, or both. For a 5 percent guggulsterone content extract this translates to an effective does of 500 mg three times per day (34).

4BB

Toxicity

The side effects of crude gum guggul, and of alcoholic and petroleum ether extracts are discussed above. In clinical studies, gugulipid has not displayed any negative side effects, nor has it adversely affected liver function, or hematological parameters (35).

Safety studies in rats, rabbits, and monkeys demonstrate gugulipid to be nontoxic. It does not possess any teratogenic/fetotoxic effects and is therefore considered safe to use in pregnancy. In mice the LD50 (50 percent lethal dose) is 1,600 mg/kg both via PO (oral) and IV (intra-venous) delivery (36).

4CC

Conclusions

For centuries, guggul has been used in Ayurvedic medicine to treat arthritis, obesity, and disorders of lipid metabolism. Since the 1960s, the lipid-

lowering activity of guggul preparations has been thoroughly investigated, establishing guggul as a powerful, natural alternative to hypolipidemic pharmaceuticals. Although more research needs to be conducted to confirm guggul's antioxidant properties and ability to inhibit platelet aggregation, the preliminary research in these areas, coupled with its established hypolipidemic activity, warrants its continued use in the management and prevention of cardiovascular disease. The role of guggul in the treatment of obesity and inflammatory conditions is also promising, and deserves further investigation.

4DD

Feverfew

General Description

Feverfew (*Tanecetum parthenium),* a member of the sunflower family, grows in flower gardens throughout Europe and the United States. The round,

leafy, branching stems bear alternate, bipinnate leaves with ovate, dark-green leaflets.

The flowers are small and daisy-like, with yellow disks and from ten to twenty white, toothed rays. The name *feverfew* is a corruption of the Latin word *febrifuge*, used to signify its tonic and fever-dispelling properties.

4EE

Chemical composition

The major active chemicals in the plant are sesquiterpene lactones, principally parthenolide. The flowering herb also contains 0.02-0.07 percent essential oils (L-camphor, L-borneol, turpenes, and miscellaneous esters) (37).

4FF

History and folk use

Feverfew has been used for centuries as a febrifuge (anti-pyretic) and for the treatment of migraines and arthritis. Other historical uses of feverfew have been in the treatment of anemia, earache, dysmenorrhea, dyspepsia, trauma, and intestinal parasites (38). It has also been used as an abortifacient,

and in gardens to control noxious pests (since its pyrethrin component is an effective insecticide and herbicide).

4GG

Pharmacology

Feverfew has demonstrated some remarkable pharmacological effects in experimental studies. Its long history of use in the treatment of inflammatory conditions such as fever, arthritis, and migraine suggests that its mechanism of action may be similar to the more common, nonsteroidal anti-inflammatory prostoglandins, leukotrienes, and thromoboxanes. Unlike aspirin and other NSAIDs, inhibition by feverfew occurs during the initial stages of the inflammatory response and, thus, behaves more like cortisone than NSAIDs (39).

Feverfew also has a favorable effect on the behavior of blood platelets. It inhibits platelet aggregation and inhibits the secretion of inflammatory and allergic mediators such as histamine and serotonin. Parthenolide components also exert a tonic effect on vascular smooth muscle (40). Feverfew's combined action on smooth muscle and platelets is probably why it is effective in the prevention and treatment of migraine headaches.

4HH

Clinical applications

Feverfew has been used for centuries to relieve fever, migraines, and arthritis. The only condition with confirmed scientific documentation at the present time is in the prevention and treatment of migraine headache.

4II

Migraine headache

In his book *The Family Herbal* (1772), physician John Hill noted, “In the worst headache, this herb exceeds whatever else is known.” Recently, interest in feverfew as a treatment for migraine headache has increased tremendously. This renewed interest began in the 1970’s in Great Britain, where increased public awareness of the herb led to scientific investigation.

A 1983 survey found that 70 percent of 270 migraine sufferers who had eaten feverfew daily for prolonged periods claimed that the herb decreased the frequency and/or intensity of their attacks (41). Many of these patients had been unresponsive to traditional medicines. This prompted two clinical investigations of the therapeutic and preventative effects of feverfew in the treatment of migraine.

The first double-blind study was done at the London Migraine Clinic, and involved patients who reported being helped by feverfew. Those patients who received the placebo (and as a result stopped using feverfew) experienced a significant increase in the frequency and severity of headache, nausea, and vomiting during the 6 months of the study, while patients taking feverfew showed no change in the frequency or severity of their symptoms.

Two patients in the placebo group who had been in complete remission during self-treatment with feverfew leaves developed recurrence of incapacitating migraine while on placebo treatment and had to withdraw from the study. The resumption of self-treatment led to renewed remission of symptoms in both patients.

The second double-blind study was performed at the University of Nottingham. The results of the study clearly demonstrated that feverfew was

effective in reducing the number and severity of migraine attacks. In the study, seventy-two patients were randomly allocated to receive either one capsule of dried feverfew leaves (82 mg.) daily or placebo. After 4 months patients were transferred to the other treatment group for another 4 months (42). Treatment with feverfew was associated with a reduction in the mean number and severity of attacks and in the degree of vomiting; while the duration of single attacks was unaltered.

4JJ

Rheumatoid arthritis

Inflammatory compounds released by white blood cells and platelets contribute greatly to the inflammation and cellular damage found in rheumatoid arthritis. The inhibition of the release of inflammatory factors by feverfew is much greater than that achieved by NSAIDs like aspirin. This coupled with many of its other effects indicated that this substance could greatly reduce inflammation in rheumatoid arthritis.

One double-blind, placebo-controlled study demonstrated no apparent benefit from oral feverfew in rheumatoid arthritis. However, the dosage used was extremely small (76 mg.) once per day; the level of parthenolide was not determined in the product; and the patients continued to take NSAIDs, a practice that has been suggested to reduce the efficacy of feverfew (43). Feverfew contains relatively high concentrations of a sesquiterpene lactone called parthenolide. Terpenoids are common in plants and diterpenes and sesquiterpenes are among the active ingredients. A good quality feverfew will contain about 0.2% of parthenolide, and it is this compound that is thought to be responsible for the anti-inflammatory and anti-migraine activities in the leaves of the plant.

Studies in vitro have shown that parthenolide inhibits the release of serotonin in blood platelets. The assumption is that the compound also blocks serotonin release in the brain from platelets. This effect would be beneficial in preventing and treating migraine attacks because platelet release of serotonin is thought to be involved in the dilation of the blood vessels characteristic of a migraine attack. The parthenolide may also help decrease the pain sensation. Furthermore, parthenolide has the ability to inhibit the enzyme cyclooxygenase, shown to be involved in the synthesis of thromboxanes-mediators of inflammation in the body-so there is also potential benefit in the use of feverfew in arthritis.

4KK

Dosage

As discussed, the effectiveness of feverfew depends on adequate levels of parthenolide. Unfortunately, a recent analysis of the parthenolide content of more than thirty-five different commercial preparations indicates a wide variation in the amount of parthenolide. The majority of products contained no parthenolide or only traces of the substance.

The preparations used in successful clinical trials had a parthenolide content of 0.4 to 0.66 percent. To achieve the benefit noted in migraine studies, the dosage of parthenolide must be similar. The dosage of feverfew used in the London Migraine Clinic study was one capsule containing 25 mg. of feverfew, twice daily. In the Nottingham study the dosage was one capsule of 82 mg. twice daily.

Based on this data, the daily dose of parthenolide that may be effective in the prevention of a migraine headache is roughly 0.25 mg to 0.5 mg per day. While these low dosages may be effective in preventing an attack, a higher dose (1-2 grams) is recommended during an acute attack (44).

4LL

Toxicity

The 6-month migraine studies made no report of toxic reactions in patients taking feverfew. Feverfew has been used by large numbers of people for many years without reports of toxicity. Chewing the leaves, however, may result in aphthous ulcerations (painful ulcers that occur in the lining of the mouth), and some sensitive persons will develop an exudative dermatitis from external contact (45).

4MM

Conclusions

Feverfew has been shown, in clinical studies, not only to alleviate the pain of migraines, but help reduce the inflammation of arthritis, ease dizziness and tinnitus, relieve painful periods and sluggish menstrual flow. Successful use in migraines may be a result of inhibition of the initial vasoconstriction which is thought to precede the "rebound" vasodilatation. The subsequent vasodilatation phase is thought to be inhibited by the sesquterpine lactone. In addition, the blocking of serotonin release by the platelets may decreases the migraine effect, thought to be caused, in part, by serotonin. The role of

feverfew in the treatment of other inflammatory related disorders is also promising, and deserves further investigation.

4NN

Summary

Recently, herbal preparations have been appearing on the shelves of mainstream retailers that a few years ago would have been relegated to discretely marked jars in local food co-ops. A major change in the way herbs are marketed has largely occurred after passage of the Dietary Supplement Health and Education Act in 1994, which allowed companies to market herbal products without going through the FDA's costly testing programs. In so doing, the United States Congress acknowledged that millions of consumers not only believed that herbs provided bonafide health benefits but they wished to take some responsibility in the decision of what is healthy and what is not. For millions in this country and around the world, this has been nothing short of a paradigm shift away from traditional Western medicine towards a more holistic, and naturally focused approach.

References

1. Douglas SE ; Turner S Molecular evidence for the origin of plastids from a cyanobacterium-like ancestor. J Mol Evol, 33:267-73 1991

2. Shapiro, Harry L 1975 Peking Man. New York: Simon & Schuster.

3. E. A. Speiser, in Ancient Near Eastern Texts (Princeton, 1950), pp. 60-72

4. Pavlovich N Herbal remedies: the natural approach to combating stress. J Perianesth Nurs, 14:134-8 1999

5. Winslow LC ; Kroll DJ Herbs as medicines. Arch Intern Med, 158:2192-9 1998

6. Planta M ; Gundersen B ; Petitt JC Prevalence of the use of herbal products in a low-income population. Fam Med, 32:252-7 2000

7. Klepser TB ; Doucette WR ; Horton MR ; Buys LM ; Ernst ME ; Ford JK ; Hoehns JD ; Kautzman HA ; Logemann CD ; Swegle JM ; Ritho M ; Klepser ME Assessment of patients' perceptions and beliefs regarding herbal therapies. Pharmacotherapy, 20:83-7 2000

8. Glisson J ; Crawford R ; Street S Review, critique, and guidelines for the use of herbs and homeopathy. Nurse Pract, 24:44-6, 53, 60 passim; quiz 68-9 1999

9. Hr´objartsson A The uncontrollable placebo effect. Eur J Clin Pharmacol, 50:345-8 1996

10. Bostr¨om H Placebo--the forgotten drug. Scand J Work Environ Health: 53-7 1997

11. Margo CE The placebo effect. Surv Ophthalmol, 44:31-44 1999

12. Couch JR Jr Placebo effect and clinical trials in migraine therapy. Neuroepidemiology, 6:178-85 1987

13. Zakharov NA ; Pridantseva NM ; Khokhlova AA ; Nikolaeva VG [Use of a tincture of birch buds for treating suppurative wounds] Vestn Khir Im I I Grek, 124:82-5 1980

14. Bellakhdar J ; Claisse R ; Fleurentin J ; Younos C Repertory of standard herbal drugs in pharmacopoea. J Ethnopharmacol, 35:123-43 1991

15. Zhu YP ; Woerdenbag HJ Traditional Chinese herbal medicine. Pharm World Sci, 17:103-12 1995

16. Bauer BA Herbal therapy: what a clinician needs to know to counsel patients effectively. Mayo Clin Proc, 75:835-41 2000

17. Kanba S ; Yamada K ; Mizushima H ; Asai M Use of herbal medicine for treating psychiatric disorders in Japan. Psychiatry Clin Neurosci, 52 Suppl:S331-3 1998

18. Nordstrom CR Exploring pluralism--the many faces of Ayurveda. Soc Sci Med, 27:479-89 1988

19. Harrison DD ; Colloca CJ ; Troyanovich SJ ; Harrison DE Torque: an appraisal of misuse of terminology in chiropractic literature and technique. J Manipulative Physiol Ther, 19:454-62 1996

20. B¨uhring M [Special therapeutic practices from the viewpoint of naturopathy] Z Arztl Fortbild Qualitatssich, 91:674-81 1997

21. Nityanand S ; Srivastava JS ; Asthana OP Clinical trials with gugulipid. A new hypolipidaemic agent J Assoc Physicians India, 37:323-8 1989

22. Dalvi SS ; Nayak VK ; Pohujani SM ; Desai NK ; Kshirsagar NA ; Gupta KC Effect of gugulipid on bioavailability of diltiazem and propranolol. J Assoc Physicians India, 42:454-5 1994

23. Sheela CG ; Augusti KT Effects of S-allyl cysteine sulfoxide isolated from Allium sativum Linn and gugulipid on some enzymes and fecal excretions of bile acids and sterols in cholesterol fed rats. Indian J Exp Biol, 33:749-51 1995

24. Sheela CG Antiperoxide effects of cysteine sulphoxide isolated from gugulipid. Indian J Exp Biol, 33:337-41 1995

25. Svoboda RE Ayurveda's role in preventing disease. Indian J Med Sci, 52:70-7 1998

26. Agarwal RC ; Singh SP ; Saran RK ; Das SK ; Sinha N ; Asthana OP ; Gupta PP ; Nityanand S ; Dhawan BN ; Agarwal SS Clinical trial of gugulipid--a new hypolipidemic agent of plant origin in primary hyperlipidemia. Indian J Med Res, 84:626-34 1986

27. Gopal K ; Saran RK ; Nityanand S ; Gupta PP ; Hasan M ; Das SK ; Sinha N ; Agarwal SS Clinical trial of ethyl acetate extract of gum gugulu (gugulipid) in primary hyperlipidemia. J Assoc Physicians India, 34:249-51 1986

28. Das Gupta R [letter; comment] J Assoc Physicians India, 38(2):186 1990 Feb

29. Gupta RD Gugulipid: pro-lipaemic effect [letter] J Assoc Physicians India, 38:598 1990

30. Kendler BS Recent nutritional approaches to the prevention and therapy of cardiovascular disease. Prog Cardiovasc Nurs, 12:3-23 1997

31. Rothhut B ; Russo-Marie F Novel concepts in the mode of action of anti-inflammatory steroids. Agents Actions Suppl, 14:171-80

32. Nityanand S ; Srivastava JS ; Asthana OP Clinical trials with gugulipid. A new hypolipidaemic agent J Assoc Physicians India, 55:764-1 1996

33. Sheela CG ; Augusti KT Antiperoxide effects of S-allyl cysteine sulphoxide isolated from Allium sativum Linn and gugulipid in cholesterol diet fed rats. Indian J Exp Biol, 33:337-41 1995

34. Agarwal RC ; Singh SP ; Saran RK ; Das SK ; Sinha N ; Asthana OP ; Gupta PP ; Nityanand S ; Dhawan BN ; Agarwal SS
Clinical trial of gugulipid--a new hypolipidemic agent of plant origin in primary hyperlipidemia. Indian J Med Res, 84:626-34 1986

35. Sheela CG ; Augusti KT Effects of S-allyl cysteine sulfoxide isolated from Allium sativum Linn and gugulipid on some enzymes and fecal excretions of bile acids and sterols in cholesterol fed rats. Indian J Exp Biol, 33:749-51 1995

36. Svoboda RE Ayurveda's role in preventing disease. Indian J Med Sci, 52:70-7 1998

37. Heptinstall S ; Awang DV ; Dawson BA ; Kindack D ; Knight DW ; May J Parthenolide content and bioactivity of feverfew (Tanacetum parthenium (L.) Schultz-Bip.). Estimation of commercial and authenticated feverfew products. J Pharm Pharmacol, 44:391-5 1992

38. Groenewegen WA ; Heptinstall S A comparison of the effects of an extract of feverfew and parthenolide, a component of feverfew, on human platelet activity in-vitro. J Pharm Pharmacol, 42:553-7 1990

39. Heptinstall S ; Groenewegen WA ; Spangenberg P ; Loesche W Extracts of feverfew may inhibit platelet behaviour via neutralization of sulphydryl groups. J Pharm Pharmacol, 39:459-65 1987

40. Barsby RW ; Knight DW ; McFadzean I A chloroform extract of the herb feverfew blocks voltage-dependent potassium currents recorded from single smooth muscle cells. J Pharm Pharmacol, 45:641-5 1993

41. Hayes NA ; Foreman JC The activity of compounds extracted from feverfew on histamine release from rat mast cells. J Pharm Pharmacol, 39:466-70 1987

42. Murphy JJ ; Heptinstall S ; Mitchell JR Randomised double-blind placebo-controlled trial of feverfew in migraine prevention. Randomised double-blind placebo-controlled trial of feverfew in migraine prevention.

43. Johnson ES ; Kadam NP ; Hylands DM ; Hylands PJ Efficacy of feverfew as prophylactic treatment of migraine. Br Med J (Clin Res Ed), 291:569-73 1985

44. Pattrick M ; Heptinstall S ; Doherty M Feverfew in rheumatoid arthritis: a double blind, placebo controlled study. Ann Rheum Dis, 48:547-9 1989

45. Jain NK ; Kulkarni SK Antinociceptive and anti-inflammatory effects of Tanacetum parthenium L. extract in mice and rats. J Ethnopharmacol, 68:251-9 1999