# Recent advances in traditional plant drugs and orchids

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## ABSTRACT

The main objective of this paper is to review recent advances in plant drug research and developments in orchid study, in an attempt to provide useful references for plant drug studies. Plants have been used as medicine for millennia. Out of estimated 250 000 to 350 000 plant species identified so far, about 35 000 are used worldwide for medicinal purposes. It has been confirmed by WHO that herbal medicines serve the health needs of about 80 percent of the world's population; especially for millions of people in the vast rural areas of developing countries. Meanwhile, consumers in developed countries are becoming disillusioned with modern healthcare and are seeking alternatives. The recent resurgence of plant remedies results from several factors: 1) the effectiveness of plant medicines; 2) the side effect of most modern drugs; and 3) the development of science and technology. It has been estimated that in the mid-1990s over 200 companies and research organizations worldwide are screening plant and animal compounds for medicinal properties. Actually, several important drugs used in modern medicine have come from medicinal plant studies, eg, taxol/paclitaxel, vinblastine, vincristine, topotecan, irinotecan, etoposide, teniposide, *etc*. As for drugs derived from orchids, some novel discoveries, both in phytochemical and pharmacological properties, were reported by some universities. However, studies on plants are very limited. Only about a third of the million or so species of higher plants have been identified and named by scientists. Of those named, only a tiny fraction has been studied. Nowadays the linking of the indigenous knowledge of medicinal plants to modern research activities provides a new approach, which makes the rate of discovery of drugs much more effective than with random collection.

## INTRODUCTION

Traditional medicine has a long history of serving peoples all over the world. Medicinal plant is an important element of indigenous medical systems in China as well as elsewhere. The enthnobotany and ubiquitous plants provide a rich resource for natural drug research and development. In recent years, the use of traditional medicine information on plant research has again received considerable interest. While the Western use of such information has also come under increasing scrutiny and the national and indigenous rights on these resources have become acknowledged by most academic and industrial researchers. Meanwhile, the need for basic scientific investigations on medicinal plants using indigenous medical systems becomes imminent. In the following, a brief review of the development of traditional plant drugs will be given.

## HISTORY

The use of plants as medicine goes back to early

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man. Evidences of this early association have been found in the grave of a Neanderthal man buried 60 000 years ago. Pollen analysis indicated that the numerous plants buried with the corpse were all of medicinal value. The earliest known medical document is a 4000-year-old Sumerian clay tablet that recorded plant remedies for various illnesses. By the time of the ancient Egyptian civilization, a great wealth of information already existed on medicinal plants. Among the many remedies prescribed were mandrake for pain relief, and garlic for the treatment of heart and circulatory disorders. This information, along with hundreds of other remedies, was preserved in the Ebers papyrus about 3500 years ago.

Ancient China is also a source of information about the early medicinal uses of plants. The Pun-tsao, a pharmacopoeia that was actually published around 1600, contained thousands of herbal cures that are attributed to the works of Shen-nung, China's legendary emperor who lived over 4500 years ago. In India, herbal medicine dates back several thousand years to the Rig-Veda, the collection of Hindu sacred verses. This has led to a system of health care known as Ayurvedic medicine. One useful plant from this body of knowledge is snakeroot, *Rauwolfia serpentina*, used for centuries for its sedative effects. Today the active components in snakeroot are widely used in Western medicine to treat high blood pressure. In all parts of the world, indigenous people discovered and developed the medicinal uses of native plants, but it is from the herbal medicine of ancient Greece that the foundations of Western medicine were established.

Western medicine can be traced back to the Greek physician Hippocrates (460-377 BC), known as the Father of Medicine. Hippocrates believed that a disease had a natural cause and used various herbal remedies in his treatments. Early Roman writing also influenced the development of Western medicine, especially the works of Dioscorides (1st century AD). Although Greek by birth, Dioscorides was a Roman military physician whose travels with the army brought him in contact with many useful plants. He compiled this information in De Materia Medica, which contained an account of over 600 species of plants with medicinal value. It included descriptions and illustrations of the plants, along with directions on the preparation, uses, and side effects of the drugs. After the arrival of Columbus, many New World plants became available to Europeans, and by the time of Henry VIII in England (1491-1547), an entire European or Western medical system that blended plant use and astrology had developed. For centuries, medicine in the West meant herbal medicine.

In the other parts of the world, medicinal plants are also an important element of indigenous medical systems. For example, in the northwestern Amazon, indigenous people use at least 1300 plant species to create *drogas do certão* or "wildness drugs." In Southeast Asia, traditional healers use 6500 different plants to treat malaria, stomach ulcers, syphilis, and other disorders.

During the eighteenth century, as scientific knowledge progressed, a dichotomy in medicine developed between practitioners of herbal medicine and regular physicians. At about this same time a similar split occurred between herbalism and scientific botany, the study of plants above and beyond their medical application.

## MODERN PRESCRIPTION DRUGS

Although herbalism waned in the eighteenth and nineteenth centuries, many of the remedies employed by the herbalists provided effective treatment. Some of these became useful prescriptions as physicians began experimenting with therapeutic agents. William Withering was the first in the medical field to scientifically investigate a folk remedy. His studies (1775-1785) of foxglove as a treatment for dropsy (congestive heart failure) set the standard for pharmaceutical chemistry.

In the nineteenth century, scientists began purifying the active extracts from medicinal plants. One breakthrough in pharmaceutical chemistry came when Friedrich Serturner isolated morphine from the opium poppy (*Papaver somniferum*) in 1806. Continuing this progress, Justus von Liebeg, a German scientist became a leader in pioneering the field of pharmacology. With increased knowledge of active chemical ingredients, the first purely synthetic drugs based on natural products were formulated in the middle of the nineteenth century. In 1839, salicylic acid was identified as the active ingredient in a number of plants known for their pain-relieving qualities and was first synthesized in 1853. This led to the development of asprin, which is the most widely used synthetic drug today.

Although the direct use of plant extracts continued to decrease in the late nineteenth and early twentieth centuries, medicinal plants still contribute significantly to prescription drugs. It is estimated that 25 % of prescriptions written in the United States contain

plant-derived active ingredients (close to 50 % if fungal products are included). An even greater percentage is based on semi-synthetic or wholly synthetic ingredients originally isolated from plants. Today there is a renewed interest in investigating plants for medically useful compounds, with some of the leading pharmaceutical and research institutions involved in this search.

## HERBAL MEDICINE TODAY

While Western medicine strayed away from herbalism, 75 % to 90 % of the rural population in the rest of the world still relies on herbal medicine as their only health care. The long tradition of herbal medicine continues to the present day in China, India, and many countries in Africa and South American. In many village marketplaces, medicinal herbs are sold alongside vegetables and other wares. Practitioners of herbal medicine often undergo a rigorous and extended training to learn the names, uses, and preparation of native plants.

The People's Republic of China is the leading country for incorporating traditional herbal medicine into a modern health care system. The resulting blend of herbal medicine, acupuncture, and Western medicine is China's unique answer to the health care needs of over one billion people. Plantations exist for the cultivation of medicinal plants and the training of doctors. Active research programs also investigate potentially useful specimens. According to a recent survey[1], almost 7300 plants have been used in traditional Chinese medicine. Chinese apothecaries contain a dazzling array of dried plant specimens, and prescriptions are filled, not with prepackaged pills or ointments, but with measured amounts of specific herbs. These colorful apothecaries can also be found in US cities such as San Francisco, with their large Chinese populations.

While China melded traditional practices with Western medicine, in India traditional systems have remained quite separate from Western medicine. At Indian universities, medical students are trained in Western medicine. However, much of the populace puts its belief in the traditional systems. In addition to Ayurvedic medicine, which has a Hindu origin, Unani medicine with its Muslim and Greek roots is another widely practiced herbal tradition. Economics is also a factor in the reliance on indigenous cures, since the cost of manufactured pharmaceuticals is beyond the reach of most of the population.

The renewed interest in medicinal plants has focused on herbal cures among indigenous populations around the world. This is especially true among indigenous peoples in the tropical rain forests. Tropical rainforests cover only 12 % of the land area of the Earth, yet they are home to between 50 % to 90 % of the world's species. They contain 90 % of non-human primates, 40 % of all prey birds and 80 % of the world's insects and, particularly important, over 60 % of all known plants, which have been studied by some of the world's leading ethnobotanists including Richard Schultes, Mark Plotkin, and Walter Lewis, who spent time with local tribes learning their medical lore. Hopefully, these investigations will add new medical plants to the world's pharmacopoeia before they are lost forever.

Tropical rainforests are a vital source of medicines. Today, less than 1 % of the world's tropical forest plants have been tested for pharmaceutical properties, yet at least 25 % of all modern drugs originally came from rainforests. Most were first discovered and used by indigenous peoples. Tropical rainforests are of special concern since the widespread destruction of these ecosystems threatens to eliminate thousands of species that have never been scientifically investigated for medical potential. The potential and fragility of the rainforests as an invaluable source of medicine is clearly illustrated in the following account from the World Rainforest Report No 26:

"Starting with twigs from a Malaysia gum tree, researchers in 1991 isolated a compound that blocks the spread of the AIDS virus in human cells. The team sent biologists racing back to Malaysia for more samples from the tree. But when they got to the swamp, the tree was gone, it had been cut down. And no tree found since it has produced the same compound." No identical trees have been found in the immediate area and samples from the same species found elsewhere did not yield the same compound.

In addition to the destruction of the forests, the erosion of tribal cultures is also a threat to herbal practices. As younger members are drawn away from tribal life-styles, oral traditions are not passed on. Mark Plotkin has compared this loss of knowledge to the burning down of a library containing books that are one of a kind and irreplaceable. One step in preserving this knowledge was recently taken by the government of Belize, which established the Terra Nova Forest Reserve. This Central American Reserve is a 6000-acre sanctu-

ary dedicated to the survival of medicinal plants and the traditional healers that use them.

## THE RECENT DEVELOPMENT OF NATURAL DRUGS

Natural products play an important role in the field of new drugs research and development, but it was not until the 19th century that man began to isolate the active principals of medicinal plants and the landmark discovery of quinine from *Cinchona* bark was made by the French scientists Caventou and Pelletier.

Prior to World War II, a series of natural products isolated from higher plants became clinical agents and a number are still in use today. Quinine from *Cinchona* bark, morphine and codeine from the latex of the opium poppy, digoxin from *Digitalis* leaves, atropine (derived from (-)-hyoscyamine) and hyoscine from species of the *Solanaceae* continue to be in clinical use. Some antibiotics found during and after World War II also continue to be used. These were developed from the antibacterial effects of a whole series of natural products isolated from species of *Penicillium*, *Cephalosporium*, and *Streptomyces*. In the post-war years there were relatively few discoveries of new drugs from higher plants with the notable exception of reserpine from the *Rauwolfia* species heralding the age of tranquillisers and also vinblastine from *Catharanthus roseus* which were effective in cancer chemotherapy. A new trend in new drug development is the emergence of successful clinical agents emerged from the multidisciplinary research of pharmacology and synthesis, eg, atenolol (beta-blocker) and captopril (ACE-inhibitor) for the treatment of hypersion, salbutamol (adrenoceptor stimulant) for asthma and the benzodiazepines (hypnotics and anxiolytics) for insomnia and anxiety attacks.

From the point of view of marketing, Farnsworth and colleagues indicated[2] that globally there were 119 compounds from 90 plants which were used as single entity medicinal agents. Significantly, 77 % of these were obtained as a result of examining the plants based on an ethnomedical use, and are employed in a manner that approximates that use. The number of plants used as medicinal agents in commerce globally is unknown, but is around 7300 in China alone[1]. The analysis of drugs approved by the Food and Drug Administration in the United States in a 10-year period (1983-1992) conducted by Cragg and associates found that 157 of 520 drugs (30 %) approved were natural products or their derivatives[3]. When focused efforts are made to discover natural products for clinical use, the success level rises dramatically, thus in the same period, 61 % of anticancer agents approved were natural products and their derivatives. The Western European phytochemical market in prescriptions was $2.2 billion (70 % in Germany) in 1989 and growing. Figures show that the trade in plants used within Europe for non-conventional medicines is increasing by 15 % to 20 % a year, with an import value of $3.6 billion in 1995[4]. However the exact value of the medicinal/phytochemical drug market is difficult to establish because although some of these products are sold via prescription, others are sold over the counter by a range of different retailers. Today, among the 25 best-selling drugs in the world, 30 % come from natural products. In 1996, six of the top twenty pharmaceutical drugs sold were natural products and more than 50 % of the top twenty were linked directly to natural products.

According a review of the two databases, Pharmaprojects and R & D Focus, Liu Ji-Kai found that among the projects carried out by the 20 highest ranked transnational pharmaceutical corporations from 1990 to 1997[5], more than 80 % of the compounds involved were from microorganisms and natural products. Because projects involving natural products at the clinical test and pre-clinical test stage in the world's 25 leading pharmaceutical corporations account for 46 % and 41 % respectively of the Pharmaprojects and R & D Focus databases, those two databases represent the research trend worldwide. Among them, Bristol-Myers Squibb and Eli Lilly take the leading position. Researchers at Eli Lilly pharmaceuticals investigated this low-growing tropical plant with delicate pink blossoms in 1958, following clues from indigenous medicine men, or shamen, in Madagasar. They found the plant contained two powerful alkaloids: vincristine and vinblastine. The former was found to be effective against Hodgkin's disease, resulting in an 80 % remission in sufferers of this form of lymph cancer. Vincristine achieves a 90 % remission rate against childhood leukemia. Global sales of vincristine and vinblastine earn Eli Lilly about $100 million each year. This is what encourages companies like Merck to mine tropical forests for other drugs. A report concerning the development of Glaxo showed that it had a long history of association with natural products, dating to its origins in New Zealand at the turn of the century. As early as the 1960's, Glaxo grew poppies, *Papaver somniferum* (Papaveraceae) in Tas-

mania from which the powerful analgesic morphine (Kapanol™) is made. Apart from natural products as pharmaceuticals and as industrial intermediates, Glaxo has most recently pursued its interests in the use of Natural Product Source Materials as templates for new lead discovery. At the end of the 1970's the Chairman of Glaxo, Mr Paul Girolami, took the decision that all Glaxo's business should be concentrated on the discovery and development of ethical pharmaceuticals. Today Glaxo still continues to adhere to this policy achieving success in research, development and commercialization.

There have been about 60 new herb-derived drugs developed by Chinese scientists over the past four decades. An illustrative example is the discovery of artemisinin[6]. Chemical studies on many species of *Artemisia* have been carried out in many places since the 1930's, but China was the first to discover its antimalarial activity and this yielded a new antimalarial drug in 1972. Artemisinin is quite different from the old generation of antimalarial drugs because of its novel bioactive peroxide group, which is effective in treating chloroquine-resistant and severe cases without side effects, which is also a common feature of many Chinese herbal medicines. Recently, a study was reported that artemisinin became cytotoxic in the presence of ferrous iron and it could be used to treat human breast cancer[7], also the interaction of biomolecules with artemisinin and its derivatives in the presenceof ferrous ion was investigated[8].

Today, the studies of Chinese traditional medicine and plant drugs has spread to many countries and districts. In the USA, several new drugs originally from Chinese traditional medicine have undergone development in recent years. Huperzine A, an alkaloid from the leaves of a Chinese herb, has the potential to improve memory and learning ability in Alzheimer's patients[9]. Huperzine A is much more potent and less toxic than tacrine and E2020 the drugs approved in the USA for the treatment of Alzheimer's disease. A detailed review on the pharmcological profiles of Huperzine[10] was given by Prof Tang. There still were other studies related the anti-Alzheimer drugs, such as the study of inhibitory effect of Zeatin, which was isolated from *Fiatoua villos*a on acetylcholinesterase activity[11].

Based on clinical data and preclinical tests in China, Interneuron Pharmaceuticals, based in Lexington, Mass, was granted a patent on the composition of Huperzine A and made efforts to develop the drug in 1992. A bitter melon study, based on the fact that it has been used in China as a treatment for tumors, common infections and immune disorders, has been implemented in the attempt to develop an alternative therapy for AIDS. In 1990, a protein, MAP 30, was isolated at the National Cancer Institute, which has multiple functions that are responsible for its anti-HIV activity. In 1995, it was reported that the MAP 30 protein was able to inhibit HIV-1 integrase, an enzyme essential for the gene expression of the virus[12]. This type of activity is novel among anti-HIV agents. Further work is continuing. Another example, is the daidzin, isolated from the root of the vine, Radix pucrariae, which has been used in traditional Chinese medicine for hundreds of years to treat alcohol abuse. It was reported that daidzin could suppress alcohol drinking in animal models[13]. In contrast to current drugs on the market which exhibit a range of side effects, a Harvard study suggests that this compound be a nontoxic drug able to reduce/solve the problems of alcohol abuse.

Cancer and AIDS are the most dangerous diseases to human beings, thus research into these diseases has been prioritized. The National Cancer Institute (NCI) has several ongoing collaborative programs which screen plants for the possibility of new drugs and active plant chemicals for the treatment of cancer and AIDS/HIV.

Plants have been collected from the African countries of Cameroon, the Central African Republic, Gabon, Ghana, Madagascar, and Tanzania. Collections are now being concentrated in Madagascar (one of the most rapidly disappearing rainforest regions in the world), and collaborative programs have been established in South Africa and Zimbabwe.

In Central and South America, samples have been collected from Belize, Bolivia, Colombia, the Dominican Republic, Ecuador, Guatemala, Guyana, Honduras, Martinique, Paraguay, Peru, and Puerto Rico. The National Cancer Institute (NCI) has established collaborative programs in Brazil, Costa Rica, Mexico, and Panama. Southeast Asian collections have been performed in Bangladesh, Indonesia, Laos, Malaysia, Nepal, Pakistan, Papua New Guinea, the Philippines, Taiwan (China), Thailand, and Vietnam. Collaborative programs have been established in Bangladesh, China, Korea, and Pakistan. In each country, NCI contractors work in close collaboration with local botanical institutions.

After a series of long term and painstaking works, seven plant-derived anticancer drugs have received Food and Drug Administration (FDA) approval for commer-

cial production. They are:

1) Taxol/Paclitaxel —A chemical discovered in the Pacific Yew tree (*Taxus brevifolia*) is now the first drug of choice in several tumorous cancers including breast cancer.

2) Vinblastine —A chemical discovered in the Madagascar periwinkle in the 1950s. Vinblastine is the first drug of choice in the treatment of many forms of leukemia and since the 1950's it has increased the survival rate of childhood leukemias by 80 %.

3) Vincristine —Another antileukemic drug discovered in the Madagascar periwinkle.

4) Topotecan —An analog (synthesized chemical) of a plant alkaloid discovered in the Chinese tree species, *Camptotheca acuminata*, for the treatment of ovarian and small cell lung cancers.

5) Irinotecan —Another chemical analog which has been developed from another plant alkaloid discovered in the same tree, *Camptotheca acuminata*, for the treatment of metastatic colorectal cancer.

6) Etoposide —A semisynthetic derivative of a plant chemical, epipodophyllotoxin, discovered in the Mayapple plant family (*Podophyllum peltatum*).

7) Teniposide —Another semisynthetic derivative of a plant chemical discovered in the Mayapple plant family (*Podophyllum peltatum*).

Since 1986, only five chemicals showed significant activity against AIDS among more than 40 000 screened plant samples. The following are plants and chemicals which are still under research for cancer and AIDS:

1) (+)-Calanolide A and (-)-Calanolide B (costatolide) are isolated from *Calophyllum lanigerum* and *Calophyllum teysmanii*, respectively, trees found in Sarawak, Malaysia. (+)-Calanolide A is currently in early clinical trials in the United States.

2) Conocurovone, isolated from the shrub species, *Conospermum incurvum* (saltbush), found in Western Australia.

3) Michellamine B, from the leaves of *Ancistrocladus korupensis*, a vine found in the Korup rainforest region of southwest Cameroon, has undergone extensive preclinical study, but is considered too toxic for advancement to clinical trials.

4) Prostratin, isolated from the wood of *Homolanthus nutans*, a tree found in Western Samoa, has been placed on low priority, largely due to its association with a class of compounds shown to be tumor promoters.

5) A tree native to China -- *Camptotheca acuminata* —is the source of four promising anticancer drugs, two of which have been approved by the FDA and are described above. The other two chemicals still under research include:

· 9AC (9-aminocamptothecin) which is currently in clinical trials for several types of cancer, including ovarian and stomach cancers and T-cell lymphoma.

· Camptothecin: while no clinical trials are being performed in the United States, trials are ongoing in China.

6) Homoharringtonine from the Chinese tree *Cephalotaxus harringtonia* is in early clinical trials.

7) Perillyl alcohol, flavopiridol, a totally synthetic compound based on a flavone isolated from *Dysoxylum binectiferum*, is in early clinical trials.

In 2001, L Taylor gave a list of chemicals/drugs from plants[14], which is useful for plant drug studies.

## COMPLEMENTARY POINT OF VIEW

An aspect of Western herbal remedies that makes their practice very different from the conventional pharmacology of medicine is the fact that it involves not simply a single chemical constituent, but, rather, the entire plant. This "whole plant" philosophy can begin to be better understood by considering the notion that a single plant is greater than the sum of its parts. Because any plant is literally made up of hundreds, if not thousands, of different chemicals that interact in a highly complex manner, an herbal medication cannot be reduced to the simple isolation of a certain plant's active constituent or major ingredient. This phenomenon is known as synergism, which means, in this context, the effect produced by all of a plant's constituent parts working and combining together. Chinese traditional medicine is similar, in which several kinds of plants are usually mixed and interact together.

Prof Varro E TYLER, an internationally recognized expert on herbal medicine at Purdue University's School of Pharmacy, has pointed out that rational phytotherapy need not proceed beyond the determination of phytoequivalence of products prepared from standardized herbal extracts[15]. That is, it is not necessary to isolate the active constituents from an herb and market them in highly purified form. It is necessary to determine the identity of the principal actives so that chemical profiling and the establishment of phytoequivalence can be made precise, but beyond this point phytotherapy sepa-

**Tab 1. Chemicals and drugs from plants.**

| Drug/Chemical | Action/Clinical Use | Plant Source |
|---|---|---|
| Acetyldigoxin | Cardiotonic | *Digitalis lanata* |
| Adoniside | Cardiotonic | *Adonis vernalis* |
| Aescin | Anti-inflammatory | *Aesculus hippocastanum* |
| Aesculetin | Anti-dysentery | *Frazinus rhychophylla* |
| Agrimophol | Anthelmintic | *Agrimonia supatoria* |
| Ajmalicine | Circulatory Disorders | *Rauvolfia sepentina* |
| Allantoin | Vulnerary | *Several plants* |
| Allyl isothiocyanate | Rubefacient | *Brassica nigra* |
| Anabesine | Skeletal muscle relaxant | *Anabasis sphylla* |
| Andrographolide | Baccillary dysentery | *Andrographis paniculata* |
| Anisodamine | Anticholinergic | *Anisodus tanguticus* |
| Anisodine | Anticholinergic | *Anisodus tanguticus* |
| Arecoline | Anthelmintic | *Areca catechu* |
| Asiaticoside | Vulnerary | *Centella asiatica* |
| Atropine | Anticholinergic | *Atropa belladonna* |
| Benzyl benzoate | Scabicide | *Several plants* |
| Berberine | Bacillary dysentery | *Berberis vulgaris* |
| Bergenin | Antitussive | *Ardisia japonica* |
| Betulinic acid | Anticancerous | *Betula alba* |
| Borneol | Antipyretic, analgesic, antiinflammatory | *Several plants* |
| Bromelain | Anti-inflammatory, proteolytic | *Ananas comosus* |
| Caffeine | CNS stimulant | *Camellia sinensis* |
| Camphor | Rubefacient | *Cinnamomum camphora* |
| Camptothecin | Anticancerous | *Camptotheca acuminata* |
| (+)-Catechin | Haemostatic | *Potentilla fragarioides* |
| Chymopapain | Proteolytic, mucolytic | *Carica papaya* |
| Cissampeline | Skeletal muscle relaxant | *Cissampelos pareira* |
| Cocaine | Local anaesthetic | *Erythroxylum coca* |
| Codeine | Analgesic, antitussive | *Papaver somniferum* |
| Colchiceine amide | Antitumor agent | *Colchicum autumnale* |
| Colchicine | Antitumor agent, anti-gout | *Colchicum autumnale* |
| Convallatoxin | Cardiotonic | *Convallaria majalis* |
| Curcumin | Choleretic | *Curcuma longa* |
| Cynarin | Choleretic | *Cynara scolymus* |
| Danthron | Laxative | *Cassia species* |
| Demecolcine | Antitumor agent | *Colchicum autumnale* |
| Deserpidine | Antihypertensive, tranquillizer | *Rauvolfia canescens* |
| Deslanoside | Cardiotonic | *Digitalis lanata* |
| *L*-Dopa | Anti-parkinsonism | *Mucuna sp* |
| Digitalin | Cardiotonic | *Digitalis purpurea* |
| Digitoxin | Cardiotonic | *Digitalis purpurea* |
| Digoxin | Cardiotonic | *Digitalis purpurea* |
| Emetine | Amoebicide, emetic | *Cephaelis ipecacuanha* |
| Ephedrine | Sympathomimetic, antihistamine | *Ephedra sinica* |
| Etoposide | Antitumor agent | *Podophyllum peltatum* |
| Galanthamine | Cholinesterase inhibitor | *Lycoris squamigera* |
| Gitalin | Cardiotonic | *Digitalis purpurea* |
| Glaucarubin | Amoebicide | *Simarouba glauca* |
| Glaucine | Antitussive | *Glaucium flavum* |
| Glasiovine | Antidepressant | *Octea glaziovii* |
| Glycyrrhizin | Sweetener, Addison's disease | *Glycyrrhiza glabra* |

| Drug/Chemical | Action/Clinical Use | Plant Source |
|---|---|---|
| Gossypol | Male contraceptive | *Gossypium species* |
| Hemsleyadin | Bacillary dysentery | *Hemsleya amabilis* |
| Hesperidin | Capillary fragility | *Citrus species* |
| Hydrastine | Hemostatic, astringent | *Hydrastis canadensis* |
| Hyoscyamine | Anticholinergic | *Hyoscyamus niger* |
| Irinote | Anticancer, antitumor agent | *Camptotheca acuminata* |
| Kaibic acud | Ascaricide | *Digenea simplex* |
| Kawain | Tranquillizer | *Piper methysticum* |
| Kheltin | Bronchodilator | *Ammi visaga* |
| Lanatosides A, B, C | Cardiotonic | *Digitalis lanata* |
| Lapachol | Anticancer, antitumor | *Tabebuia sp.* |
| a-Lobeline | Smoking deterrant, respiratory stimulant | *Lobelia inflata* |
| Menthol | Rubefacient | *Mentha species* |
| Methyl salicylate | Rubefacient | *Gaultheria procumbens* |
| Monocrotaline | Antitumor agent (topical) | *Crotalaria sessiliflora* |
| Morphine | Analgesic | *Papaver somniferum* |
| Neoandrographolide | Dysentery | *Andrographis paniculata* |
| Nicotine | Insecticide | *Nicotiana tabacum* |
| Nordihydroguaiaretic acid | Antioxidant | *Larrea divaricata* |
| Noscapine | Antitussive | *Papaver somniferum* |
| Ouabain | Cardiotonic | *Strophanthus gratus* |
| Pachycarpine | Oxytocic | *Sophora pschycarpa* |
| Palmatine | Antipyretic, detoxicant | *Coptis japonica* |
| Papain | Proteolytic, mucolytic | *Carica papaya* |
| Papavarine | Smooth muscle relaxant | *Papaver somniferum* |
| Phyllodulcin | Sweetner | *Hydrangea macrophylla* |
| Physostigmine | Cholinesterase Inhibitor | *Physostigma venenosum* |
| Picrotoxin | Analeptic | *Anamirta cocculus* |
| Pilocarpine | Parasympathomimetic | *Pilocarpus jaborandi* |
| Pinitol | Expectorant | *Several plants* |
| Podophyllotoxin | Antitumor anticancer agent | *Podophyllum peltatum* |
| Protoveratrines A, B | Antihypertensives | *Veratrum album* |
| Pseudoephredrine* | Sympathomimetic | *Ephedra sinica* |
| Pseudoephedrine, nor- | Sympathomimetic | *Ephedra sinica* |
| Quinidine | Antiarrhythmic | *Cinchona ledgeriana* |
| Quinine | Antimalarial, antipyretic | *Cinchona ledgeriana* |
| Qulsqualic acid | Anthelmintic | *Quisqualis indica* |
| Rescinnamine | Antihypertensive, tranquillizer | *Rauvolfia serpentina* |
| Reserpine | Antihypertensive, tranquillizer | *Rauvolfia serpentina* |
| Rhomitoxin | Antihypertensive, tranquillizer | *Rhododendron molle* |
| Rorifone | Antitussive | *Rorippa indica* |
| Rotenone | Piscicide, Insecticide | *Lonchocarpus nicou* |
| Rotundine | Analagesic, sedative, traquillizer | *Stephania sinica* |
| Rutin | Capillary fragility | *Citrus species* |
| Salicin | Analgesic | *Salix alba* |
| Sanguinarine | Dental plaque inhibitor | *Sanguinaria canadensis* |
| Santonin | Ascaricide | *Artemisia maritma* |
| Scillarin A | Cardiotonic | *Urginea maritima* |
| Scopolamine | Sedative | *Datura species* |
| Sennosides A, B | Laxative | *Cassia species* |
| Silymarin | Antihepatotoxic | *Silybum marianum* |
| Sparteine | Oxytocic | *Cytisus scoparius* |

| Drug/Chemical | Action/Clinical use | Plant source |
|---|---|---|
| Stevioside | Sweetner | *Stevia rebaudiana* |
| Strychnine | CNS stimulant | *Strychnos nux-vomica* |
| Toxol | Antitumor agent | *Taxus brevifolia* |
| Teniposide | Antitumor agent | *Podophyllum peltatum* |
| α-Tetrahydrocannabinol (THC) | Antiemetic, decrease occular tension | *Cannabis sativa* |
| Tetrahydropalmatine | Analgesic, sedative, traquillizer | *Corydalis ambigua* |
| Tetrandrine | Antihypertensive | *Stephania tetrandra* |
| Theobromine | Diuretic, vasodilator | *Theobroma cacao* |
| Theophylline | Diuretic, brochodilator | *Theobroma cacao and others* |
| Thymol | Antifungal (topical) | *Thymus vulgaris* |
| Topotecan | Antitumor, anticancer agent | *Camptotheca acuminata* |
| Trichosanthin | Abortifacient | *Trichosanthes kirilowii* |
| Tubocurarine | Skeletal muscle relaxant | *Chondodendron tomentosum* |
| Valapotriates | Sedative | *Valeriana officinalis* |
| Vasicine | Cerebral stimulant | *Vinca minor* |
| Vinblastine | Antitumor, Antileukemic agent | *Catharanthus roseus* |
| Vincristine | Antitumor, Antileukemic agent | *Catharanthus roseus* |
| Yohimbine | Aphrodisiac | *Pausinystalia yohimbe* |
| Yuanhuacine | Abortifacient | *Daphne genkwa* |

rates from non-phytotherapy. The multiplicity of constituents in the former type of product probably renders infeasible their isolation and marketing as purified compounds. It simply is not obligatory to go beyond the establishment of phytoequivalence for herbal product. The stance of the US Food and Drug Administration (FDA) by contrast has been that all drugs, whether they are synthetic chemicals, of herbal origin, or herbal preparations long in use, must meet the same set of strict FDA criteria to be marketed as drugs. Professor Tyler suggested that Europe's experience might be helpful in this respect. Many European countries, including Germany, regulate herbal products as drugs and pharmaceutical companies prepare plant-based drugs simply by extracting the active chemicals from the plant. In UK and France, the traditional use of herbal drugs is usually considered to be sufficient proof of safety and efficacy.

Recently, an initial but important work to compromise the difference of Western medicine and traditional Chinese medicine was done by Lin *et al* in Singapore. A good correlation was observed between the temperature characteristic of *Qi* and the ability of Chinese herbs to produce or scavenge superoxide (Tab 2)[16].

These herbal medicines scavenge the superoxides produced by tissues. Similar observations have been made of orchids used in Chinese medicine. *Dendrobium* nobile and *Bletilla* striata, both considered to be mildly cold, produce a considerable amount of superoxides. The latter also has antimicrobial activity. *Gastrodia* elate, which is 'hot', can scavenge superoxides. Its antiepileptic activity can be attributed to the antioxidant activity of its active components.

**Tab 2. Superoxide production and its scavenging property in three orchids used in Chinese herbal medicine.**

| Orchid | Superoxide Production/ μm·min$^{-1}$·g$^{-1}$ FW | Superoxide Scavenging/% | Remarks |
|---|---|---|---|
| *Bletilla* striata | 9.88±1.58 | | Antimicrobial |
| *Dendrobium* nobile | 0.59±0.17 | | |
| *Gastrodia* elate | | 71±10 | Antioxidant and free radical scavenging |

Some other studies and functions of orchid herbal medicines *Dendrobium* nobile, *Bletilla* striata, and *Gastrodia* elate can also be found[17]. As Singapore lies in the Indo-Malayan rainforest area, where more than

eight thousand species of plants can be found, among them, the largest families are the Orchidaceae with 853 species and because of the importance of *Dendrobium* nobile, *Bletilla* striata, and *Gastrodia* elate in traditional Chinese medicine, in the following part, we will focus on the orchid medicines.

## THE USE OF ORCHIDS AS HERBAL MEDICINES

The *Orchidaceae*, by far the largest family of the plant kingdom, comprises more than 30 000 species in approximately 750 genera, and is one of the most widespread of all plant families, there are terrestial, saprophytic and epiphytic species.

The use of orchids in herbal medicine has a very long history. A total of 365 plants, including several orchids are listed in the earliest known Chinese Materia Medica (Shen Nung Pen-tsao Ching). The following sections describe some of those orchids and their pharmacological effects.

***Bletilla* striata** The orchid currently known as *Bletilla* striata, was also known as *Limodorum* striatum, *Epidendrum* tuberosum, *Bletia* hyacinthina and Jimensia. Its herbal medicinal name in Chinese is Dai Chi (Baiji).

*Bletilla* striata rhizomes are collected from August to November with a non-metal cutting tool, cleaned, and dried. The medicine prepared from these tubers is used to treat tuberculosis, hemoptysis, gastric, and duodenal ulcers, as well as bleeding, and cracked skin on the feet and hands. Other uses in China, Mongolia, and Japan include the introduction of euphoria, purification of blood, strengthening and consolidation of lungs, as well as the treatment of pus, boils, abscesses, malignant swellings, ulcers, and breast cancer. Tubers have also been used as a demulcent, a bechic, and an expectorant. Additional medical applications of the boiled and/or dried tubers include treatment of the flatulence, dispepsia, dysentery, fever, malignant ulcers, gastrointestinal disorders, hemorrhoids, anthrax, malaria, eye diseases, tinea, ringworm, tumors, and necrosis, silicosis, traumatic injuries, coughs, chest pain, tuberculosis, vomiting of blood, gastrorrhagia, enterorrhagia, internal bleeding, inflammation, and chopped skin. The powdered roots mixed with oil have been used as an emollient for burns and skin diseases. Whole plant preparations are tonic and treatment against leucorrhea, hemoptysis, and purulent coughs. Leaves collected in the autumn are reported to cure lung disease. In Japanese folk medicine, the tubers are used for the same purposes as salep.

***Dendrobium Sw* ( Shih-hu )** Shih-hu is a term used to describe all *Dendrobium* and some *Flickingeria* species in China. According to one estimation there are 1400 *Dendrobium* species in China, but only some of them, especially the *Eugenanthe*, provide the drug Shih-hu in its various forms. The frequently used Shih-hu includes such orchids as Chin chai Shih-hu (Golden Hairpin *Dendrobium*), Er Huan Shih-hu (Earring *Dendrobium*), Ma poen Shih-hu (Horse Whip *Dendrobium*), Huan tsao Shih-hu (Yellow Herb *Dendrobium*), and Yu kue Shih-hu (Melon Flickingeria). Among them, the Er Huan Shih-hu (Earring *Dendrobium*), for example, was used as a stomachic in Japan. It was used to treat night sweats in Taiwan, to fortify a person's body, to strengthen the kidneys and to cure impotence. In Korea this species was also employed against impotence, and the entire plant was used as an anti-pyretic, tonic, and peptic. Plants imported into Malaysia by Chinese herbalists were credited as having tonic, stomachic, pectoral, and antiphlogistic properties.

By far the most commonly used species in the preparation of Shih-hu is *Dendrobium* nobile Lindl. This variety of Shih-hu has been valued greatly in China since the Han dynasty (200 BC to 200 AD). It is used as a tonic and a strengthening medicine. It is also reputed to impart longevity and serve as an aphrodisiac. The stems are used to alleviate thirst, calm restlessness, accelerate convalescence, and reduce dryness of the mouth.

Additional properities of Shih-hu are those of a stomachic, pectoral, antiphlogistic, analgesic, and antipyretic medication. It was also used to treat rheumatism, excessive perspiration, weakness brought about by thirst, excessive perspiration, impotence, entropion, insects in the ear, leucorrhea, and menstrual pain.

***Gastrodia elate* Blume (Chih Chien, Tien Ma)** The genus *Gastrodia R* Br is found in Madagascar, tropical Asia, Oceania, Japan, China, and parts of the Soviet Union. It consists of 20 species, five of which are found in China. *Gastrodia elata* Blume (G mairei Schltr) is found in Anhui, Gansu, Guangxi, Guizhou, Hebei, Henan, Hubei, Hunan, Jiangxi, Jilin, Liaoning, Shaanxi, Shangdong, Shanxi, Shichuan, Taiwan, Xizang, and Yunnan. This chlorophyll-free orchid grows in high humus soil in, or at the fringe of broad leaf, coniferous or mixed forests. Being chlorophyll-free, this species is parasitic on its endophyte *Armillaria melea* (Vahl)

Quel. Thus the orchid is a parasite on the fungus which in turn parasitizes another plant. This association is remarkable, especially because the endophyte of *G elate, Armillaria mellea*, is found throughout most of the world and is a very destructive parasite of many plants and yet this orchid controls it.

*Gastrodia* elate tubers were used for food, raw or steamed in China and roasted in Japan, Tibet, and China. This orchid is an important herbal medicine for the control of the internal movement of wind according to the ancient Chinese medicine theory. In China, rhizomes, stalks, and dried tubers (known as Tianma) are used to treat headaches, dizziness, blackouts, numbness of the limbs, hemiplegia, epilepsy, limb cramps, spasms, migraine, expulsion of poisonous effluvia, rheumatism, vertigo, neuralgia, facial paralysis, dysphrasia, infantile convulsions, lumbago, fever, and neverous afflictions. The herb was also used to give strength and virility, improve circulation and enhance memory. The stalks were considered to be aphrodisacs. In Korea, the tubers were used to treat nervous disorders, prevent the common cold and serve as a tonic. This orchid was used in Taiwan as a fortifier, to treat weak nervous systems and headaches. Dried plants were used in Japan to treat vertigo, headaches, and nervous diseases, especially in children.

In North America, orchids also were used as medicine by Indians. The details are described below.

**Dichaea Lindley** There are 40 species of *Dichaea* in the West Indies and tropical Central and South American; all are epiphytic herbs, eg, *Dichaea* muricata (Sw) Lindley, Gen. Et Sp Orch Pl (1833) 209.

A wash prepared from this orchid is valued by the Kofans for treating eye infections, probably conjuctivitis which is very common in the region.

**Elleanthus Presl** The 50 species of this showy orchid are native to tropical America and the West Indies, eg, *Elleanthus sp*. The large purple flowers are crushed and added to chicha for flavoring.

**Epidendrum Linnaeus** The nearly 500 species of *Epidendrum* are native to the area from the South Eastern United States to the American tropics. They are mostly epiphytic. More than 50 species are cultivated as horticultural plants, eg, *Epidendrum sp*. Mucilage from the pseudobulbs is collected for treating sores on the lips.

**Eriopsis Lindley** The half of dozen or so species of this genus are tropical Central and South American epiphytes, eg *Eriopsis sceptrum* Reichenbach fil. Et Warscewicz, Bonpl 2 (1854) 98.

Amongst the Indians of the Rio Apaporis, the basal stems of this clumped epiphyte are boiled in water to extract the copious mucilage which is applied to sores of the gums and mucous membranes of the mouth for relief from discomfort. This orchid is abundantly supplied with mucilage which swells upon uptake of water. The Makuna name means "mouth herb."

**Masdevallia Ruiz et pavon** There are at least 300 species of this genus, all epiphytic, and distributed from Mexico to South America, eg, *Masdevallia sp*. A tea of the entire plant is recommended by the Kamsa medicine men to facilitate urination in pregnant women and to reduce inflammation of the bladder.

**Oncidium Swartz** The 50 species of this genus are either erect or hanging epiphytes or terrestial plants ranging throughout the tropical and subtropical parts of the New World, eg, *Oncidium pusillum* L Reichenbach fil, Walpers, Ann Bot 6 (12863) 714. The Kofans treat lacerations with a wash prepared by boiling the plant in water.

**Phragmipedium Rolfe** This is a tropical South American genus of a dozen terrestial species, eg, *Phragmipedium ecuadorense* Garay, Harling et Spaare, F1. Ecuad, Orch, No 9, pt 1 (1979) 15. Boiled in water this orchid makes a tea used to allay "stomach trouble".

**Pleurothallis R Brown** With more than 1200 species, *Pleurothallis* occurs throughout the American tropical and West Indies, eg *Pleurothallis sp*.

## THE PHYTOCHEMICAL AND PHARMACOLOGICAL STUDIES OF ORCHIDS

As early as 1892, E de Wildeman had already begun investigation of orchid alkaloids in domesticated European orchid species as well as *Dendrobium nobile* and *Phalaenopsis lueddemanniana*. From then until 1896, E de Droog analyzed 104 species in 78 genera. In late 1890s, W Boorsma studied orchid alkaloids at the Bogor Botanical Gardens and detected some in *Paphiopedilum javanicum* and *Liparis parviflora*, among other species.

Other investigations were carried out before World War II in Japan, Europe, the United States, and additional countries. After the war, Björn Lüning and his associates in Sweden, Leonard J LAWLER and Michael B SLAYTOR in Australia, and several scholars in Japan studied the alkaloids in orchids.

Orchids produce 50 or more different flower scents, which attract pollinators. Many of these aromatic compounds have been identified during the past 20 to 30 years. Perhaps the first, and certainly the most influential, scientist to carry on such work was Prof CH DODSON, then at the University of Miami.

Dr C A WILLIAMS together with Prof JB HARBORNE conducted the only major survey of leaf flavonoids at the Plant Science Laboratories of the University of Reading in the UK. They surveyed 142 species in 75 genera and found that the most common constituents were flavone C-glycoside (in 53 % of the species) and flavonols (in 37 %)[18]. Overall, a single familial pattern of flavonoid distribution is not evident in orchids. On the subfamily and trivial levels, a clear correlation does exist with plant geography. Flavone C-glycosides are most common in the tropical and subtropical species of the *Epidendroid* and *Vandoid* subfamily (63 % contain them), whereas flavonol glycosides are found in *Neottioid* orchids (78 % have them). Other flavonoids are less common. Highly methylated or glycosylated derivatives of flavonoids have not been detected in orchid leaves. Several anthocyanins have also been isolated from orchid flowers and leaves and, as in many other plants, they are based primarily on the six most common anthocyanidins. One example is that the 3-(6-malonylglucoside)-3'-glucoside-7-(6-caffeylglucoside) and 3-(6-malonylglucoside)-3'-glucoside-7-(6-ferulylglucoside) were found in one kind of orchid *Sophronitis coccinea*[19]. Recently, a new flavonol was found together with some known flavonols and acylated anthocyanins in the *Dendrobium* Pompadour[20].

The presence of other pigments, metallic ions, the pH of the sap, as well as the position (s) of glycosylation and acylation can affect the color of each anthocyanin. As a result, the six most common anthocyanidins can produce a large number of actual pigments.

Anthocyanins and other pigments determine the visible and ultraviolet light (UV) patterns of orchids. And, as in other plants, visible light and UV images play important roles in the attraction of pollinators, in addition to scents and morphology. Following pollination, anthocyanins may be destroyed in some orchids (eg, *Vanda*) and produced in others (eg, *Cymbidium*). Except for pollination, anthocyanins and other pigments in orchids may have the function of screening ultraviolet light, which can be damaging to tissues because of its high energy content.

Recently, further studies on *Dendrobium* orchids have been carried out. Honda (2000) isolated three phenanthrenes from *Dendrobium* plicatile[21]. Their structures are 2,5-dihydroxy-4,9,10-trimethoxyphenanthrene, 2,5-dihydroxy-4-methoxyphenanthrene and 2,5,9-trihydroxy-4-methoxy-9,10-dihydrophenanthrene. In 1996, seven stilbenoids were isolated from the above *Dendrobium* plicatile[22]. They are 3-methoxy-3',5-dihydroxybibenzyl, 3,3',4'-trimethoxy-5-hydroxybibenzyl, 2-methoxy-4,7-dihydroxy-9,10-dihydrophenanthrene, 2,4-dimethoxy-3,7-dihydroxyphenanthrene, 3,4-dimethoxy-2,7-dihydroxy-9,10-dihydrophenanthrene, ephemeranthoquionone, and 2,2'-dimethoxy-4,4',7,7'-tetrahydroxy-9,9',10,10'-tetrahydro-1,1'-biphenanthrene. In 1994, N Saito *et al* isolated an acylated anthocyanin from the red-purple flower of *Dendrobium* ' Pramot' (*phalaenopsis* type cv). The structure of this pigment was determined to be cyanidin-3-*O*-(6-malonyl) -*D*-glucopyranoside) 7,3'-di-*O*-[6-*O*-(-*D*-glucopyranosyl)oxybenzoyl]-*D*-glucopyranoside)[23]. The *Dendrobium* loddigesii methanol extract analysis found that some principals can inhibit the aggregation of rabbit platelets induced by arachidonic acid and collagen. They are moscatilin, moscatin, and moscatilin diacetate[24]. A report concerning the constituents and effect of *Dendrobium* loddigesii rolfe showed that it contained shihunidine, shihunine and dendrophenol (4,4'-dihydroxy-3,3',5-trimethoxybibenzyl). Chemical reactions showed that shihunidine was derived from shihunine during isolation. Shihunidine and shihunine were shown to be inhibitors of $Na^+$, $K^+$-ATPase in the rat kidney[25]. Majumder and Pal isolated two bibenzyl derivatives cumulatin and tristin, from *Dendrobium cumulatum* and *Bulbophyllum* triste respectively. Cumulatin and tristin were shown to be 3,3'-dihydroxy-4,4',5,5'-tetramethoxybibenzyl and 3,4',5-trihydroxy-3'-methoxybibenzyl, respectively[26]. They also isolated 2,7-dihydroxy-3,4,6-trimethoxy-phenanthrene, 2,7-dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene, nudol, moscatin, batatasin-III and 2,5,9-trihydroxy-4-methoxy-9,10-dihydrophenan-threne[27]. From *Dendrobium crepidatum* and *Dendro-bium moscatum*, Majumder isolated crepidatin and moscatilin (4,4'-dihydroxy-3,3',5-trimethoxybi-benzyl), both are bibenzyl derivatives[28,29]. Denfigenin, a diosgenin derivative with the structure (25*R*)-22-*O*-spirost-5-ene-3,16,17-triol was isolated from the whole plant *Dendrobium* fimbriatum, along with diosgenin and defuscin (*n*-triacontyl-*p*-coumarate)[30], and amoenumin with the structure 9,10-dihydro-5*H*-phenanthro-(4,5-

*b,c,d*)-pyran was isolated from the orchid *Dendrobium* amoenum.

The Chinese traditional medicine Shihu, which belongs to orchid *Dendrobium* has also received attention chemically and medicinally. In 1997, MITSUO Miyazawa *et al* found that the methanol extract from *Dendrobium* nobile, gigantol showed a suppressive effect on the *umu* gene expression of the SOS response in Salmonella typhimurium TA1535/pSK1002 against the mutagen 2-(2-furyl)-3-(5-nitro-2furyl)acrylamide (furylfuramide). Gigantol suppressed the SOS-inducing activity of furylfuramide in the umu test. Gene expression was suppressed 90 % at <0.73 mmol/L, and the $IC_{50}$ value was 0.35 mmol/L. Gigantol was also assayed with the mutagen 3-amino-1,4-dimethyl-5*H*-pyrido(4,3-b)indole (Trp-P-1), which requires liver metabolizing enzymes, and it suppressed the SOS-inducing activity of Trp-P-1 in the umu test. Gene expression was suppressed 91 % at <0.73 mmol/L, and the $IC_{50}$ value was 0.32 mmol/L. In additon, gigantol was assayed for suppressive effect on UV irradiation in the umu test, where it showed suppression of the SOS-inducing activity caused by UV irradiation. Gene expression was suppressed 84 % at <0.36 mmol/L, and the $IC_{50}$ value was 0.17 mmol/L. The antimutagenic activity of gigantol against furylfuramide and Trp-P-1 were assayed by an Ames test using S typhimurium TA 100, which indicated that gigantol suppressed each of the mutagens[31]. Two years later, MITSUO Miyazawa *et al* found that moscatilin, a natural bibenzyl compound isolated from the storage of *Dendrobium* nobile, suppressed the expression of the *umu* gene following the induction of the SOS response in Salmonella typhimurium TA1535/pSK1002 that had been treated with various mutagens. When using 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (furylfuramide) as the mutagen, moscatilin suppressed 85 % of the *umu* gene expression compared to the controls at <0.73 mmol/L, with an $ID_{50}$ value of 0.41 mmol/L. Additionally, moscatilin was tested for its ability to suppress the mutagenic activity of other well-known mutagens such as 4-nitroquinoline-1-oxide (4NQO), *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG), UV irradiation, 3-amino-1,4-dimethyl-5*H*-pyridol[4,3b]indole (Trp-P-1), benzo [a]pyrene (B[a]P), and aflatoxin B(1) [AFB(1)]. With all of the aforementioned chemicals or treatments, moscatilin showed a dramatic reduction in its mutagenic potential. Interestingly, moscatilin almost completely suppressed (97 %) the AFB(1)-induced SOS response at concentrations <0.73 mmol/L, with an $IC_{50}$ value of 0.08 mmol/L. Finally, the antimutagenic activities of moscatilin against furylfuramide and Trp-P-1 were assayed by the Ames test using the S typhimurium TA 100 strain. The results indicated that moscatilin demonstrated a dramatic suppression of the mutagenicity of Trp-P-1, but not furylfuramide[32]. In 1995, two phenanthrenes were isolated from the aerial part of *Dendrobium* nobile Lindl and their structures were identified to be 4,7-dihydroxy-2-methoxy-9,10-dihydrophenanthrene and denbinobin. These two compounds were found to be cytotoxic against A549 (human lung carcinoma), SK-OV-3 (human ovary adenocarcinoma) and HL-60 (human promyelocytic leukemia) cell lines. 4,7-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene also showed antitumor activity on the life span of ICR mice intraperitoneally implanted with $1\times10^6$ cells of sarcoma 180.

The tuber of *Bletilla* striata Reichb Fil, which is called Baiji in China, has been used in traditional medicine to treat pneumonorrhagia and pneumonophthisis. Since 1983 a Japanese research group has conducted continuing studies of this medicine, and a series of results have been reported. They firstly isolated five antibacterial compounds: 3,3'-dihydroxy-2',6'-*bis*(*p*-hydroxybenzyl)-5-methoxybibenzyl;2,6-*bis*(*p*-hydroxybenzyl)-3',5-dimethoxy-3-hydroxybibenzyl; 3,3'-dihydroxy-5-methoxy-2,5',6'-*tris*(*p*-hydroxybenzyl) bibenzyl; 4,7-dihydroxy-2-methoxy-9,10-dihydrophenanthrene; and 4,7-dihydroxy-1-*p*-hydroxybenzyl-2-methoxy-9,10-dihydrophenanthrene. In their later works, they found 4,4'-dimethoxy-9,9',10,10'-tetrahydro-[1,1'-biphenanthrene]-2,2',7,7'-tetrol; 4,4'-dimethoxy-9,10-dihydro-[1,1'-biphenanthrene]-2,2',7,7'-tetrol; and 4,4'-dimethoxy-[1,1'-biphenanthrene]-2,2',7,7'-tetrol. They also found a series of *bis*(dihydrophenanthrene)ethers, benzylphenanthrenes, dihydrophenanthropyrans, phenanthrene with spirolactone ring, and stilbenoids including methylated stilbenoids from *Bletilla* striata[33,34]. More important and more recently, Saito *et al* isolated and elucidated four acylated anthocyanins from the purple-red flowers of *Bletilla* striata[35]. Their structures were determined to be cyanidin 3-*O*-[6-*O*-(malonyl)-β-*D*-glucopyranoside]-7-*O*-[6-*O*-(*trans*-*p*-coumaryl)-β-*D*-glucopyranoside]-3'-*O*-[6-*O*-(*trans*-4-*O*-(6-*O*-(*trans*-4-*O*-(β-*D*-glucopyranosyl)-*p*-coumaryl)-β-*D*-glucopyranosyl)-*p*-coumaryl)-β-*D*-glucopyranoside] and demalonyl cyanidin 3-*O*-[6-*O*-(malonyl)-β-*D*-glucopyranoside]-7-*O*-

[6-*O*-(*trans*-*p*-coumaryl)-β-*D*-glucopyranoside]-3'-*O*-[6-*O*-(*trans*-4-*O*-(6-*O*-(*trans*-4-*O*-(β-*D*-glucopyranosyl)-*p*-coumaryl)-β-*D*-glucopyranosyl)-*p*-coumaryl)-β-*D*-glucopyranoside]; cyanidin 3-*O*-[6-*O*-(malonyl)-β-*D*-glucopyranoside]-7-*O*-[6-*O*-(*trans*-caffeyl)-β-*D*-glucopyranoside]-3'-*O*-[6-*O*-(*trans*-4-*O*-(6-*O*-(*trans*-4-*O*-(β-*D*-glucopyranosyl)-caffeyl)-β-*D*-glucopyranosyl)-caffeyl)-β-*D*-glucopyranoside] and demalonyl cyanidin 3-*O*-[6-*O*-(malonyl)-β-*D*-glucopyranoside]-7-*O*-[6-*O*-(*trans*-caffeyl)-β-*D*-glucopyranoside]-3'-*O*-[6-*O*-(*trans*-4-*O*-(6-*O*-(*trans*-4-*O*-(β-*D*-glucopyranosyl)-caffeyl)-β-*D*-glucopyranosyl)-caffeyl)-β-*D*-glucopyranoside] respectively.

## CONCLUSION

Today, more and more people take plant medicine as an alternative therapy. The resurgence in Western of herbal remedies mainly results from the lack of side effects, its holistic emphasis, respect for the individual and emphasis on self-help. In addition to these factors, the economic advantages also contribute to this resurgence. The role of plants in medicine is expanding beyond their traditional and continuing role as a pharmacopoeia. The basic similarity of all life chemistry has inspired the use of plants as manufactories for tumor-attacking monoclonal antibodies and other biopharmaceuticals. Genes for clinically important proteins are engineered and inserted into the plant cells, which can be coaxed to take up and express the DNA. Large amounts of the expressed protein could then theoretically be harvested and extracted from the seeds of the adult plants. Investigations into traditional plant medicine conducted with modern theories and techniques can enrich Western medicine by absorbing new ideas and concepts from traditional plant medicine from all over the world. Traditional plant medicine will become an area of ever-increasing importance in the health-care system in the future.

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