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Origins of Plant Derived Medicines

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Abstract

This review article describes the origins of plant derived medicines that have been developed as a result of traditional knowledge being handed down from one generation to the next. Various industries are now searching into sources of alternative, more natural and environmentally friendly antimicrobials, antibiotics, diabetics, antioxidants and crop protection agents. Medicinal plants have provided a good source of a wide variety of compounds, such as phenolic compounds, nitrogen compounds, vitamins, terpenoids and some other secondary metabolites, which are rich in valuable bioactivities, e.g., antioxidant, anti-inflammatory, antitumor, antimutagenic, anti-carcinogenic, antibacterial, or antiviral activities. Medicinal plants have become the main object of chemists, biochemist, and pharmaceutics. Their research plays an important role for discovering and developing new drugs that hopefully have more effectiveness and no side actions like most modern drugs.

Origin of Medicine

Fossil records revealed that the human use of plants as traditional medicine date back to middle Paleolithic age, approximately 60,000 years ago (Solecki *et al.*, 1975). The plants were used as flavors, foods, insect deterrents, ornamentals, fumigants, spices, and cosmetics (Kunin *et al.*, 1996; Pieroni *et al.*, 2004). Generally, the medicinally useful plants are sold as commodities in the market, and those that are sold for medicinal purposes dominate the market (Runner *et al.*, 2001). At present, natural products (and their derivatives and analogs) represent over 50% of all drugs in clinical use, in which natural products derived from higher plants represent *ca.* 25% of the total (Alandrin *et al.*, 1998). The World Health Organization estimated that over 80% of the people in developing countries rely on traditional remedies such as herbs for their daily needs (Tripathi *et al.*, 2003), and about 855 traditional medicines include used crude plant extracts. This means that about 3.5 to 4 billion of the global population rely on plants resources for drugs (Farnsworth, 1988).

Many infectious diseases are known to be treated with herbal remedies throughout the history of mankind. The maximum therapeutic and minimum side effects of herbal remedies have demonstrated or verified in numerous scientific investigations. Even today, plant materials continue to play a major role in primary health care as therapeutic remedies in many developing countries (Czygan, 1993; Ody, 1993).

Market Demands of Medicinal Plants

Nearly 95 percentage of plants used in traditional medicines are collected from forests and other natural sources. The plants collected from different sources show wide disparity in therapeutic values and also much variation in market rates. In the recent years there has been greater expansion of indigenous drug industry in India. Consequently the demand for the new material (medicinal plants) has enormously increased. According to latest estimate, there are about eight thousand licensed pharmacies of ISM in the country, engaged in the manufacture of bulk drugs to meet the requirement of people. The total annual requirement of the raw materials of these pharmacies was estimated to be thousands of quintals. This is presently met by cutting trees in the forest or uprooting herbs and shrubs either on nominal payment or unauthorized. Further, there is prime need to provide authentic or genuine drugs to manufacture standard medicine, as emphasized by earlier worker (Singh and Ghouse, 1993). The annual demand of the global market is \$32 million of medicinal plants from developing countries. The herbal drug production in our country has been estimated to be rupees 4000 crores in the year 2000. Out of 15,000 - 20,000 medicinal plants, our rural communities use 7,000 - 7,500 medicinal plants. About 130 pure compounds, which are extracted from 100 species of higher plants of Indian origin, are used throughout the world. India can play a major role for supplying the raw herbs, standardized extracted materials and pure compounds isolated from natural resources (Mitra, 2002).

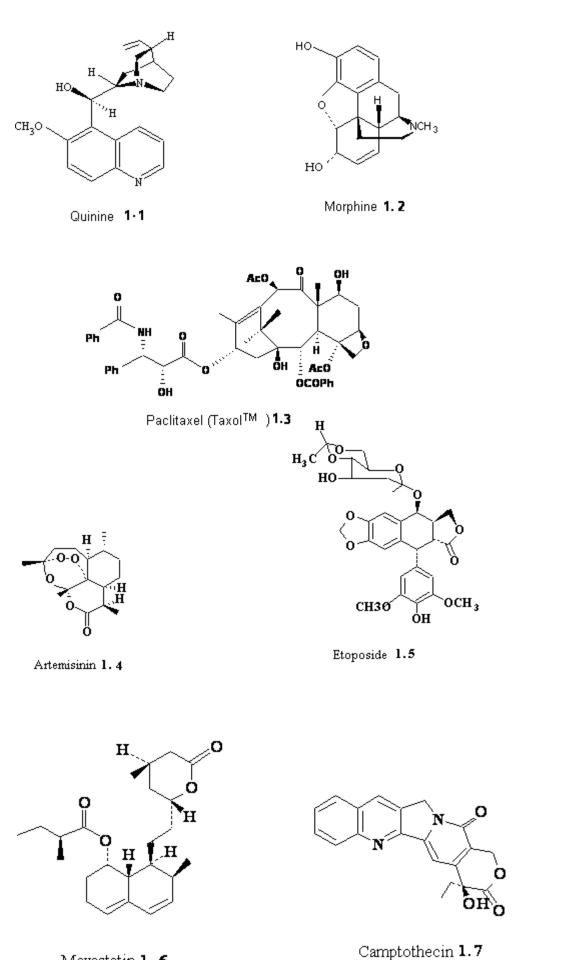
New medicines have been discovered with traditional, empirical and molecular approaches (Harvey, 1999). The traditional approach makes use of material that has been found by trial and error over many years in different cultures and systems of medicine (Cotton, 1996).

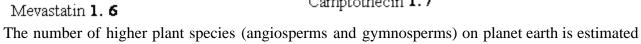
Plant Name	Family	Used Drugs
Ammi majus	Umbelliferae	Xanthotoxin ^a
Ananas comosus	Bromeliaceae	Bromelain
Atropa belladonna	Solanaceae	Belladonna Extract
Avena sativa	Gramineae	Oatmeal Concentrate
Capsicum species	Solanaceae	Capsicum Oleoresin
Carica papaya	Caricaceae	Papain
Cassia acutifolia	Leguminosae	Sennosides A + B
Cassia angustifolia	Leguminosae	Sennosides A + B
Catharanthus roseus	Apocynaceae	Leurocristine (vincristine)
		Vincaleukoblastine
		(vinblastine)
Cinchona species	Rubiaceae	Quinine
Citrus limon	Rutaceae	Pectin
Colchicum autumnale	Liliacae	Colchicine
Digitalis lanata	Scrophulariaceae	Digoxin,Lanatoside C,
		Acetyligitoxin
Digitalis purpurea	Scrophulariaceae	Digitoxin
		Digitalis whole leaf
Dioscorea species	Dioscoreaceae	Diosgenin
Duboisia myoporoides	Solanaceae	Atropine, Hyoscyamine
		Scopolamine

Table 1. Currently used Drugs in the United States that are obtained from flowering Plants.

Ephedra sinica	Ephedraceae	Ephedrine, Pseudoephedrine
Glycine max	Leguminosae	Sitosterols
Papaver somniferum	Papaveraceae	Opium,Codeine,Morphine
	_	Noscapine, Papaverine
Physostigma venenosum	Leguminosae	Physostigmine (Eserine)
Pilocarpus jaborandi	Rutaceae	Pilocarpine
Plantago species	Plantaginaceae	Psyllium husks
Podophyllum peltatum	Berberidaceae	Podophyllin
Prunus domestica	Rosaceae	Prune Concentrate
Rauvolfia serpentine	Apocynaceae	Reserpine, Alseroxylon
		Fraction
		Powdered whole root
		Rauwolfia
Rauvolfia vomitoria	Apocynaceae	Deserpidine, Reserpine
-		Rescinnamine
Rhamnus purshiana	Rhamnacee	Casanthranol
Rheum species	Polygonaceae	Rhubarb Root
Ricinus communis	Euphorbiaceae	Castor Oil, Ricinoleic Acid
Veratrum viride	Liliaceae	Veratrum viride
		Cryptennamine

Natural products have provided many effective drugs. These include a wide range of older drugs such as quinine (Kremsner *et al.*, 1994) and morphine (Benyhe *et al.*, 1994) and newer drugs such as paclitaxel (TaxolTM) (Wani *et al.*, 1971), camptothecin (Wall *et al.*, 1966), etoposide (Endo *et al.*, 1976), mevastatin (Keller-Juslén, *et al.*, 1971), and artemisinin (Klayman, 1985). Further evidence of the importance of natural products is provided by the fact that almost half of the world's 25 bestselling pharmaceuticals in 1991 were either natural product or their derivatives (O'Neill, 1993).





around 250,000 (Ayensu *et al.*, 1978), with a lower level at 215,000 (Cronquist, 1981) and an upper level high as 500,000 (Tippo *et al.*, 1977; Schultes, 1972). Of these, only about 6% have been screened for biological activity, and only 15% have been pharmacologically screened. Moreover, plant extracts contain up to several thousands of secondary metabolites. The major types of compounds identified in Indian medicinal herbs include alkaloids, saponin, flavonoids, anthroquinones, terpenoids, coumarins, lignans, polysaccharides, polypeptides and proteins. Efficient detection and rapid characterization of these components on a molecular basis offer better understanding of the pharmacological application of Indian herbal medicines.

Plant-Derived Drugs from Traditional Systems of Medicine

For thousands of years, plant-derived (herbal) remedies have remained a vital part of traditional Chinese medicine, and even today it constitute about a 30% to 50% proportion of the total drug therapy for a fifth of the world's population who live in the People's Republic of China (PRC). Out of 5500 medicinal plants used in traditional Chinese medicine, between 300 and 500 are commonly used in regular prescriptions (Han *et al.*, 1988). A drug that has been in use in China for at least 5000 years is *Ephedra sinica* (*Ma huang*), from which the potent sympathomimetic amine ephedrine was isolated and pharmacologically tested in the early years of this century, and is now used in western medicine in the form of various salts to combat bronchial asthma (Tyler *et al.*, 1988). Recently phytochemical investigation on plants used in Chinese traditional medicine, both in the PRC and elsewhere, have led to the discovery of several hundred pharmacologically active substances, and about 60 new drugs being derived from such compounds. (Xiao and Fu, 1987).

The drugs commonly used in People's Republic of China PRC include tropane alkaloids anisodamine and anisodine from *Scopolia tangutica*, which are employed as a mild, naturally acting *anticholinergic* agent for septic shock in cases of bacillary dysentery, and in the treatment of migrane headache. An isoquinoline alkaloid, racemic tetrahydropalmatine, from *Corydalis ambigua* is used as an analgesic and tranquilizer, and indirubrin, a nitrogen-containing metabolite produced by *Indigofera tinctoria*, is effective in the treatment of chronic myelocytic leukemia (Xiao and Fu, 1987; Han *et al.*, 1988).

Plant-Derived Antibacterial Chemotherapeutants

Infectious disease is the number one cause of death accounting for approximately one-half of all deaths in tropical countries. Death from infectious diseases, ranked 5th in 1981, has become the 3rd leading cause of death in 1992, with an increase of 58% (Pinner *et al.*, 1996).

More than hundreds of plants world wide are used in traditional medicine as treatments for bacterial infection (Martin *et al.*, 2003). Although many have been treated by conventional pharmaceutical approaches, there is a growing interest in the use of natural products by the general public. In addition the pharmaceutical industry continues to examine their potential as sources novel growth factor, immunomodulatory and antimicrobial activity (Ghose *et al.*, 2003).

Plant-Derived Wound Healing Agents

Wound healing occupies an important field of research in modern biomedical sciences. Wound

healing involves cellular, physiological, biochemical and molecular processes which result ultimately in connective tissue repair and the formation of a fibrous scar (Peacock, 1988). Wound healing process uses a combination of three mechanisms. Contraction is the major method by which wound healing occurs at an amputation site, such as the tip of a finger. Epithelisation predominates in the healing of abrasions and connective tissue deposition occurs when lacerations are sutured and closed (Cockbill *et al.*, 2000).

Healing of wound is an important part of the reparative process. A detailed pathophysiology of wound was better understood following the establishment of the theory of a cell signal cascade system involved in the formation of new tissues repairing the wound. Like the alchemist's dream of turning base metal into gold, efforts aimed at achieving a perfect wound healing has inspired many researchers in trying various therapeutic options which were thought to aid or accelerate the wound healing process. The cheaper and more effective the agent, may be better for the patient. Durodola (1977) demonstrated

the effectiveness of crude extract of Ageratum conyzoides in inhibiting the growth of Staphylococcus

aureus, a major wound pathogen in *in-vitro* cultures of the organism. Much work has recently been done on the wound healing effect of several medicinal plants (Oladejo *et al.*, 2003; Biswas *et al.*, 2003; Abo *et al.*, 2004; Biswas *et al.*, 2004).

Plant-Derived Anti-Diarrhoeal Agents

Diarrhoea is a major health problem especially for children under the age of 5 years and up to 17% of all death in the indoor pediatric patients is related to diarrhoea. Worldwide incidence of diarrhoeal death account for more than 5-8 million each year in infants and small children less than 5 year especially in developing countries (Fauci *et al.*, 1998). According to WHO estimate for the year 1998, there were about 7.1 million deaths due to diarrhoea (Park*et al.*, 2000). A range of medicinal plants with anti-diarrhoeal properties has been widely used by the traditional healers; however, the effectiveness of many of these anti-diarrhoeal traditional medicines have not been scientifically evaluated (Chitme *et al.*, 2004).

Plant-Derived Anti-Diabetic Agents

There are 143 million people worldwide suffering from diabetes, almost five times more than the estimates ten years ago. This number may probably double by the year 2030. Therefore, the global human population appears to be in the midst of an epidemic of diabetes. Reports from the World Health Organization (WHO) indicate that diabetes mellitus is one of the major killers of our time, with people in Southeast Asia and Western Pacific being most at risk.

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia. It may be secondary to a deficiency or disturbance in the secretion of insulin or to an abnormal response of peripheral tissues to insulin. The resulting metabolic derangement of the intermediary metabolism of carbohydrate, lipid, and protein affects all organ systems but most prominent in the arteries, arterioles, and capillaries (Damjanov *et al.*, 1996). There are two main categories of this disease. Type 1 diabetes mellitus also

called insulin-dependent *diabetes mellitus* (IDDM) and Type 2, the non-insulin-dependent *diabetes mellitus* (NIDDM). IDDM represents a heterogenous and polygenic disorder, with a number of non-HLA loci (about 20) contributing to the disease susceptibility. Though this form of diabetes accounts for 5 to 10% of all cases, the incidence is rapidly increasing in specific regions. It is estimated that incidence of Type 1 diabetes will be about 40% higher in the year 2010 than in 1997, and yet there is no identified agent substantially capable of preventing this type of disease. NIDDM is far more common and results from a combination of defects in insulin secretion and action. This type of disease accounts for 90 to 95% of all diabetic patients. Treatment of type 2 diabetes is complicated by several factors inherent to the disease process, typically, insulin resistance, hyperinsulinemia, impaired insulin secretion, and reduced insulin-mediated glucose uptake and utilization (Tiwari and Madhusudana Rao, 2002).

The recommended use of plants in the treatment for diabetes needs to be evaluated. Plants are important not only for the control of type 2DM but also for its prevention, especially for people with elevated levels of blood glucose and blood intolerance who have a greater risk of developing diabetes (Anderson *et al.*, 2004). Botanical products can improve glucose metabolism and the overall condition of individuals with diabetes not only by hypoglycemic effects but also by improving lipid metabolism, antioxidant status, and capillary function (Bailey *et al.*, 1989). A number of medicinal/culinary herbs have been reported to yield hypoglycemic effects in subjects with diabetes. These include cinnamon, cloves, bay leaves, turmeric (Khan *et al.*, 1990), bitter melon (Srivastava *et al.*, 1993; Raman and Lau,

1996), gurmar (Basakaran et al., 1990; Shanmugasundaram et al., 1990; Bishayee and Chatterjee, 1994),

Korean ginseng (Sotaniemi et al., 1995), onions and garlic (Koch and Lawson, 1996), holy basil (Rai et al., 1997).

Drugs	Chemical Action/Clinical Use	Plant Source
Acetyldigoxin	Cardiotonic	Digitalis lanata
Adoniside	Cardiotonic	Adonis vernalis
Aescin	Anti-inflammatory	Aesculus hippocastanum
Aes culetin	Anti-dysentery	Frazinus rhychophylla
Agrimophol	Anthelmintic	Agrimonia supatoria
Ajmalicine	Circulatory disorders	Rauvolfia sepentina
Allantoin	Vulnerary	Several plants
Allyl isothiocyanate	Rubefacient	Brassica nigra

Table 2. Chemical drugs and drugs from medicinal plants.

Anabesine	Skeletal muscle relaxant
Andrographolide	Baccillary dysentery
Anisodamine	Anticholinergic
Anisodine	Anticholinergic
Arecoline	Anthelmintic
Asiaticos ide	Vulnerary
Atropine	Anticholinergic
Benzyl benzoate	Scabicide
Berberine	Bacillary dysentery
Bergenin	Antitussive
Betulinic acid	Anticancerous
Borneol	Antipyretic, analges ic, antiinflammatory
Bromelain	Anti-inflammatory, proteolytic
Caffeine	CNS stimulant
Camphor	Rubefacient
Camptothecin	Anticancerous
(+)-Catechin	Haemos tatic
Chymopapain	Proteolytic, mucolytic
Cis sampeline	Skeletal muscle relaxant
Cocaine coca	Local anaesthetic
Codeine	Analgesic, antitus sive
Colchiceine amide	Antitumor agent
Colchicine	Antitumor agent, anti-gout

Anabasis sphylla Andrographis paniculata Anisodus tanguticus Anisodus tanguticus Areca catechu Centella asiatica Atropa belladonna Several plants Berberis vulgaris Ardisia japonica Betula alba Several plants Ananas cosmosus Camellia sinensis Cinnamomum camphora Camptotheca acuminate Potentilla fragar ioides *Carica papaya* Cissampelos pareira Erythroxylum Papaver somniferum Colchicum autumnale Colchicum autumnale

Convallatoxin	Cardiotonic	Convallaria majalis
Curcumin	Choleretic	Curcuma longa
Cynarin	Choleretic	Cynara s colymus
Danthron	Laxative	Cassia species
Demecolcine	Antitumor agent	Colchicum autumnale
Des erpidine	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 ipecacuanh
Ephedrine	Sympathomimetic, antihis tamine	Ephedra sinica
Etoposide	Antitumor agent	Podophyllum peltatur
Galanthamine	Cholinesterase inhibitor	Lycor is squamigera
Gitalin	Cardiotonic	Digitalis purpurea
Glaucarubin	Amoebicide	Simarouba glauca
Glaucine	Antitussive	Glaucium flavum
Glasiovine	Antidepressant	Octea glaziovii
Glycyrrhizin	Sweetener, Addison's disease	Glycyrrhiza glabra
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	Anti cancer, antitumour agent	Camptotheca acumina
Kaibic acud	Ascaricide	Digenea simplex
Kawain	Tranquillizer	Piper methysticum
Kheltin	Bronchodilator	Ammi visage
Lanatosides A, B, C	Cardiotonic	Digitalis lanata
Lapachol	Anticancer, antitumor	Tabebuia sp.
a-Lobeline	Smoking deterrant, respiratory stimulant	Lobelia inflate
Menthol	Rubefacient	Mentha species
Methyl salicylate	Rubefacient	Gaultheria procumbe
Monocrotaline	Antitumor agent (topical)	Crotalaria sessiliflora
Morphine	Analgesic	Papaver somniferum
Neoandrographolide	Dysentery	Andrographis panicu

longa colymus ecies n autumnale canescens lanata ppurpurea purpurea purpurea ipecacuanha sinica lum peltatum quamigera purpurea a glauca flavum ziovii za glabra m species amabilis cies Canadensis us niger eca acuminate simplex thysticum ige lanata sp. ıflate

pecies a procumbens a sessiliflora somniferum phis paniculata

Nicotine Nordihydroguaiaretic acid Nos capine Ouabain Pachycarpine Palmatine Papain Papavarine Phyllodulcin Physostigmine Picrotoxin Pilocarpine Pinitol Podophyllotoxin Protoveratrines A, B Pseudoephredrine Pseudoephedrine, Quinidine Quinine **Qulsqualic** acid Rescinnamine Res erpine Rhomitoxin Rorifone Rotenone Rotundine Rutin Salicin Sanguinarine Santonin Scillarin A Scopolamine Sennosides A, B Silymarin Sparteine Stevioside Strychnine Toxol Teniposide a- ntiemetic Tetrahydropalmatine Tetrandrine Theobromine Theophylline Thymol Topotecan Trichos anthin Tubocurarine Valapotriates

Ins ecticide Antioxidant

Antitussive Cardiotonic Oxytocic Antipyretic, detoxicant Proteolytic, mucolytic Smooth muscle relaxant Sweetner Cholinesterase Inhibitor Analeptic Parasympathomimetic Expectorant Antitumor anticancer agent Antihypertens ives * Sympathomimetic nor- Sympathomimetic Antiarrhythmic Antimalarial, antipyretic Anthelmintic Antihypertensive, tranquillizer Antihypertensive, tranquillizer Antihypertensive, tranquillizer Antitussive Piscicide, Insecticide Analagesic, sedative, traquillizer Capillary fragility Analgesic Dental plaque inhibitor Ascaricide Cardiotonic Sedative Laxative Antihepatotoxic Oxytocic Sweetner CNS stimulant Antitumor agent Antitumor agent occular tens ion decrease sic, sedative, traquillizer Antihypertensive Diuretic, vasodilator Diuretic, bronchodilator Antifungal (topical) Antitumor, anticancer agent Abortifacient Skeletal muscle relaxant Sedative

Nicotiana tabacum Lar rea divaricata

Papaver somniferum Strophanthus gratus Sophora pschycarpa Coptis japonica *Carica papaya* Papaver somniferum Hydrangea macrophylla Physostigma venenosum Anamirta cocculus Pilocarpus jaborandi Several plants *Podophyllum peltatum* Veratrum album Ephedra sinica Ephedra sinica Cinchona ledgeriana *Cinchona ledgeriana* Quisqualis indica *Rauvolfia serpentine Rauvolfia serpentine* Rhododendron molle *Rorippa indica* Lonchocarpus nicou Stephania sinica Citrus species Salix alba Sanguinaria Canadensis Artemisia mar itma *Urginea* maritime Datura species Cassia species Silybum marianum Cytisus scoparius Stevia rebaudiana Strychnos nux-vomica Taxus brevifolia *Podophyllum peltatum* Cannabis sativa Corydalis ambigua *Stephania tetrandra* Theobroma cacao Theobroma cacao and others Thymus vulgaris *Camptotheca acuminate* Trichosanthes kirilowii Chondodendron tomentosum Valeriana officinalis

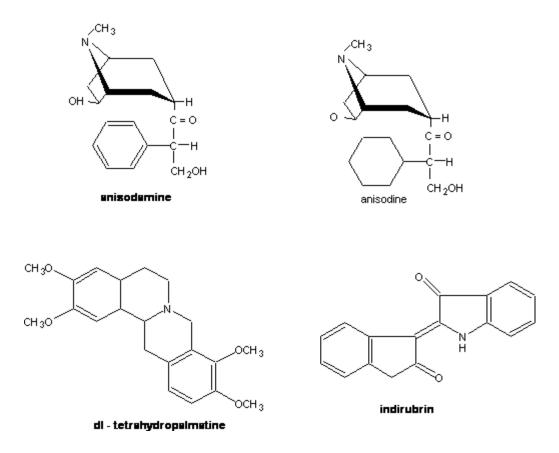
Vasicine	Cerebral stimulant	Vinca minor
Vinblastine	Antitumor, Antileukemic agent	Catharanthus roseus
Vincristine	Antitumor, Antileukemic agent	Catharanthus roseus
Yohimbine	Aphrodis iac	Pausinystalia yohimbe
Yuanhuacine	Abortifacient	Daphne genkwa

Plant-Derived Drugs from Chinese Herbal Remedies and Other Systems of Traditional Medicine

During the past decade, traditional systems of medicine have become a topic of global importance. Current estimates suggest that, in many developing countries, a large proportion of populations relies heavily on traditional practices and medicinal plants may be available in these countries, herbal medicines (phytomedicines) have often maintained popularity for historical and cultural reasons. Concurrently, many people in developed countries have begun to turn to alternative or complementary therapies, including medicinal herbs.

Chinese Traditional Medicine

Traditions of plant-collecting and plant based medications have been handed down from generation to generation. For thousands of years, plant-derived (herbal) remedies have remained a vital part of traditional Chinese medicine, and even today constitute about a 30% to 50% proportion of the total drug therapy for a fifth of the world's population who live in the People's Republic of China (PRC). Of about 5500 medicinal plants used in traditional Chinese medicine, between 300 and 500 are commonly used in regular prescriptions. One drug that has been in use in China for at least 5000 years in *Ephedra sinica (Ma huang)*, from which the potent sympathomimetic amine ephedrine was isolated and pharmacologically tested in the early years of this century, and is now used in western medicine in the form of various salts to combat bronchial asthma. Recently phytochemical investigation on plants used in Chinese traditional medicine, both in the PRC and elsewhere, have led to the discovery of several hundred pharmacologically active substances, with about 60 new drugs being derived from such compounds (**Xiao** and **Fu**, 1987).



Examples of plant drugs that are of use in the PRC include the tropane alkaloids anisodamine and anisodine from *Scopolia tangutica*, which are employed as a mild, naturally acting *antichol inergic* agent for septic shock in cases of bacillary dysentery, and as a migraine treatment, respectively. An isoquinoline alkaloid, racemic tetrahydropalmatine, from *Corydalis ambigua* is used as an analgesic and tranquilizer, and indirubrin , a nitrogen-containing metabolite produced by *Indigofera tinctoria*, is effective in the treatment of chronic myelocytic leukemia.

Conclusion of our research article reported that traditional knowledge on medicinal plants plays a vital role in the primary health care and has potential of the discovery of new herbal drugs, new sources of pharmaceuticals, contraceptives and for sustainable utilization of medicinal plants genetic resources and their conservation.

REFERENCES

- Abo, A., Olugbuiro, J.A.O., and Famakinde, S.A., 2004. Anti-infective and wound healing properties of *Flebellaria aniculata*. *African Journal of Biomedical Research*, **7**(2): 85 87.
- Anderson, R., Broadhurst, C.L., Polansky, M.M., Schmidt, W.F., Khan, A., Flanagan, V.P., Schoene,
 N.W., and Graves, D.J., 2004. Isolation and characterization of polyphenol type-A polymers from *Cinnamom* with insulin like biological activity. *Journal of Agricultural and Food Chemistry*, 52: 65-70.
- Ayensu, E.S., and DeFilipps, R.A., 1978. Endangered and threatened plants of the United States. Washington, DC: Smithsonian Institution.
- Bailey, C.J., and Day, C., 1989. Traditional plant medicines as treatments for diabetes. *Diabetes Care*, **12**:553-564.

- Basakaran, K., Ahmath, B. K., Shanmugasundaram, K. R., and Shanmugasundaram, E.R.B., 1990. Antidiabetic effects of a leaf extract from *Gymnema sylvestre* in non-insulin dependent diabetes mellitus patients. *Journal of Ethnopharmacology*, **30**: 295-305.
- Bishayee, A., and Chatterjee, M., 1994. Hypolipidaemic and antiastherosclerotic effects of oral *Gymnema sylvestre* R.Br. leaf extract in albino rats fed a high fat diet. *Phytotherapy Research*, 8: 118-120.
- Biswas, T.K., and Mukherjee, B., 2003. Plant medicines of Indian Origin for wound healing activity: A review. *Lower Extremity Wounds*, **2**(1): 25-39.
- Chitme, H.C., Chandra, R, and Kaushik, S., 2004. Studies on anti-diarrhoeal activity of *Calotropis gigantea* R.BR. in experimental animals. *Journal of Pharmacy and Pharmaceutical Sciences*, 7(1): 70-75.
- Cockbill, S., and Frpharms, F.C.P.P., 2000. Wound the healing process. *Hospital Pharmacist*, **9**: 255-260.
- Cotton, C.M., 1996. Ethnobotany Principles and Applications, John Wiley & Sons Ltd., Chichester, UK.
- Cronquist, A., 1981. An integrated system of classification of flowering plants. New York, Columbia University press.
- Czygan, F.C., 1993. Kulturgeschichte and Mystic des Johanniskrautes, Zeitschrift fur *Phytotherapie*, **5**: 276 282.
- Damjanov, I., and McCue, P.A., 1996. Histopathology: A color Atlas and Text Book, Williams and Wilkins, A Waverly Company, Baltimore, USA.
- dependent diabetes mellitus. J. Nutr. Environ. Med., 7: 113-118.
- Durodola, J.J., 1977. Antibacterial properties of crude extracts from a herbal wound healing remedy *Ageratum conyzoides*. *Planta Medica*, **32**: 388-390.
- Endo, A., Kuroda, M., and Tsujita, Y., 1976. Y.ML-236A, MI-236B, and ML-236C New Inhibitors of Cholesterogenesis produced by *Penicillium citrinum. Journal of Antibiotics*, **29**: 1346-1348.
- Farnsworth, N.R., 1998. In: Human Medicinal Agents from Plants. (Editors Kinghorn, A.D., Balandrin, M.F.), ACS Symposium Series, 534: 2-12.
- Fauci, A.S., Bravnwold, E., Isselpacher, K., Wilson, J.D., Martin, J.B., Kasper, D.L, Hauser, S.L, and Longo, D.L., 1998. Harrison's Principles of Internal Medicine. Volume I. New York, McGraw Hill Company, 236-242.
- Ghose, S., and Playford, R.J., 2003. Bioactive natural compounds for the treatment of gastrointestinal disorder. *Clinical Science*, **104**: 547-556.
- Harvey, A. L., 1999. Medicines from nature: are natural products still relevant to drug discovery. *Trends Pharmacology Science*, **20**: 196-198.
- Keller-Juslén, C., Kuhn, M., Von Wartburg, A.,and Stähelin, H., 1971. Synthesis and antibiotic activity of glycisidic lignan derivatives related to Podophyllotoxin. *Journal of Medical Chemistry*, 14: 936-940.
- Khan, A., Bryden, N.A., Polansky, M.M., and Anderson, R.A., 1990. Insulin potentiating factor and chromium content of selected foods and spices. *Bio. Trace. Element Res.*, **24**: 183-188.

- Klayman, D.L., 1985. Qinghaosu (Artemisinin): An Antimalarial Drug from China. *Science*, **228**: 1049-1055.
- Koch, H.P., and Lawson, L.D., 1996. Garlic: The Science and Therapeutic Application of *Allium sativum* L. related species; Williams and Wilkins: Baltimore, M.D.
- Kremsner, P.G., Winkler, S., Brandts, C., Neifer, S., Bienzle, U., and Graninger, W., 1994. Clindamycin in combination with chloroquine or quinine is an effective therapy for uncomplicated *Plasmodium falciparum* Malaria in children from Gabon. *Journal Infectious Diseases*, **169**: 467-470.
- Kunin, W.E., and Lawton, J.H., 1996. Does biodiversity matter? Evaluating the case for conserving species. In: Biodiversity, (Editor Gaston, K.J.), Blackwell Science LTD, UK. pp. 283-308.
- Martin, K.W., and Ernst, E., 2003. Herbal medicines for treatment of bacterial infections: a review of controlled clinical trials. *Journal of Antimicrobial chemotheraphy*, **51**: 241-246.
- Mitra, R. 1980. Silent pharmacognostical characters of Varuna, important drugs of Ayurveda. *Bull.Med. Etheno. Bot. Res.*, **1**: 80-98.
- O'Neill, M.J., and Levis, J.A., 1993. In Human medicinal agents from Plants. (Editors Kinghorn, A.D., and Balandrin, M.), ACS, Symposium series, **534**: 48-55.
- Oladejo, O.W., Imosemi, I.O., Osuagwu, F.C., Oluwadara, O.O., Aiku, A., Adewoyin, O., Ekpo, O.E., Oyedele, O.O., and Akanj, E.E.U., 2003. Enhancement of cutaneous wound healing by methanolic extracts of *Agratum conyzoides* in the wistar rat, *African Journal of Biomedical Research*, 6(1): 27-31.
- Park, H.J., and Cha, H.C., 2003. Flavonoids from leaves and exocarps of the grape Kyoho. *Korean Journal of Biological Sciences*, 7: 327-330.
- Peacock, E.E., 1988. Wound repair. Philadelphia, PA; WB Saunders Company, pp 38-55.
- Pieroni, A., Quare, C.L., Villanelli, M.L., Mangino, P., Sabbatini, G., Santini, L., Boccetti, T., Profili, M., Ciccioli, T., Rampa, L.G., Antonini, G., Girolamini, C., Cecchi, M, and Tomasi, M., 2004. Ethnopharmacognostic survey on the natural ingredients used in folk cosmetics, cosmeceuticals and remedies for healing sting diseases in the inland Marches, Central-Eastern Italy. *Journal of Ethnopharmacology*, 9: 331- 344.
- Pinner, R., Teutsch, Simonsen, L., Klug, L., Graber, J., Pinner, R., Clark, M., and Berkelman, R., 1996. Trends in infections diseases mortality in the United States. *Journal of American Medical Association*, 275: 189-193.
- Rai, V., Mani, U.V., and Iyer, U.M., 1997. Effect of *Ocimum sanctum* leaf powder on blood lipoproteins, glycated proteins, and total amino acids in patients with noninsulin
- Raman, A., and Lau, C., 1996. Antidiabetic properties and phytochemistry of *Momordica chantaria* L. (Cucurbitaceae). *Phytomedicine*, **2**: 349-362.
- Runner, R.T., Majindai, Berhanu, M., Abegaz Bezabih, M., Bonaventure, T., Ngadjui Cornelius, C.W., Wanjala, Ladislaus, K., Bojase, G., Silayo, A., Masesange, I., Samuel, O., and Yeboah, 2001.
 Recent results from natural product research at the University of Botswana, *Pure Applied Chemistry*, **73**(7): 1197-1208.
- Schultes, R.E., 1972. The future of plants as source of new biodyanamic compounds. In : Plants in the development of modern medicine.(Editor,Swin,T.),Cambridge,MA,Harvard University

press,pp.103-124.

- Shanmugasundaram, E.R., Rageswari, B.G., Baskaran, K., Rajesh Kumar, K.K., and Ahmath, B.K., 1990. Use of *Gymnema sylvestre* leaf extract in the control of blood glucose in insulin dependent diabetes mellitus. *Journal of Ethnopharmarmacology*, **30**: 281-294.
- Singh, V.K., and Ghouse, A.K.K., 1993. Plantation of medicinal plants is the need of the day in India. Glimpses in Plant Research X: 203-207. (Editors Govil, J.N., Singh, V.K., and Hasmi, S.) Today and Tomorrow's printers, New Delhi.
- Solecki, R., and Shanidar, I.V., 1975. A Neanderthal flower burial in northern Iraq. *Science*, **190**: 880 881.
- Sotaniemi, E.A., Haapakoski, E., and Rautio, A., 1995. Ginseng therapy in non-insulin dependent diabetic patients. *Diabetes Care*, **18**: 1373-1375.
- Srivastava, S., 1996. Wound healing activity of latex of *Euphorbia nerifolia* Linn. *Indian Journal of Pharmacology*, **28**(2): 107-109.
- Tippo, O., and Stern, W.L., 1977. Humanistic Botany. New York, W.W, Norton.
- Tiwari, K.A., and Madhusudana Rao, J., 2002. Diabetes mellitus and multiple therapeutic approaches of phytochemicals: Present status and future prospects. *Current Science*,**83**(1):30-38.
- Tyler, V.E., Brady, L.R., and Robbers, J.E., 1988. *Pharmacognosy* 9th ed., Lea and Febiger, Philadelphia.
- Wall, M.E., Wani, M.C., Cook, C.E., Palmer, K.H., Mcphail, A.T., and Sim, G.A., 1966. Plant Antitumor Agents I. The Isolation and structure of camptothecin, a novel alkaloidal leukemia and tumor inhibitor from *Camtotheca acuminata*. *Journal of American Chemical Society*, 88: 3888-3890.
- Wani, M.C., Taylor, H.L., Wall, M.E., Coggon, P., and McPhail, A.T., 1971. Plant Antitumor Agents VI. The Isolation and Structure of Taxol, a Novel Antileukemic and Antitumor agent from *Taxus brevifolia*. *Journal of American Chemical Society*, **93**: 2325-2327.
- Xiao, P.G., and Fu, S.L., 1987. In: Herbs, Spices and Medicinal Plants: Recent Advances in Botany, Horticulture, and Pharmacology, Vol. 2, (Editors Craker, L.E. and Simon, J.E.), pp. 1-55. Oryx Press, Phoenix, AZ.