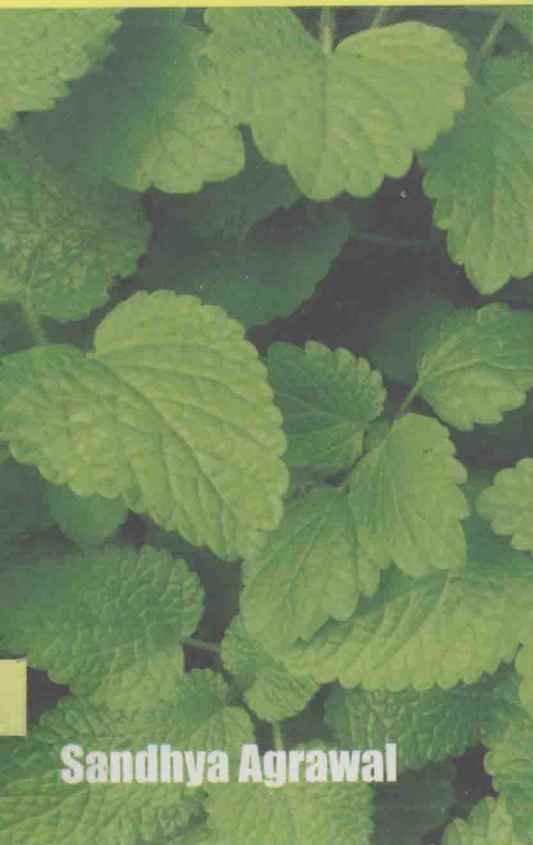


Advances in Medicinal Plants



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Medicinal Plants**

Preface

Primitive humans experimentally sampled many kinds of plants in their search for nourishment. Plants that were palatable were used for food; those with toxic or unpleasant effects were avoided or used against enemies; others that produced physiological effects such as perspiration, defecation, healing or hallucination were saved for medicinal purposes and divination. Over a period of thousands of years, people learned to use a variety of plants for different ailments, with the process continuing to be so even in the age of allopathy, especially through systems as Ayurveda and Unani.

The present text aims to acquaint readers with the advances that have been taking place in the in the field of medicinal plants, particularly within the context of New Age medicine. The book delineates not just conventional practices, techniques and treatments associated with medicinal plants, but also gives space to understand the challenges and issues and how current trends and advances are making progress to address them. In addition, the book brings within its purview the use in history of medicinal plants, its progress and decline, the competition faced from allopathic drug treatment, with an emphasis on its continuity and contemporary revival.

Sandhya Aggarwal

Contents

<i>Preface</i>	<i>v</i>
1. Current Status of Medicinal Plants	1
2. Cultivation of Medicinal Plants	36
3. Bioprospecting of Medicinal Plants	68
4. Medicinal Plants and Health Care	87
5. Wild Harvesting of Medicinal Plants	113
6. Conservation of Medicinal Plants	133
7. Heritage of Indian Medicinal Plants	175
8. Quality Control of Plant-based Medicines	195
9. Industrial Utilisation of Medicinal Plants	217
10. International Trade in Medicinal Plants	228
11. Medicinal Plants and Intellectual Property Rights	258
12. Medicinal Plant Information Databases	277
<i>Bibliography</i>	298
<i>Index</i>	300

Current Status of Medicinal Plants

Traditional medicine is the synthesis of therapeutic experience of generations of practicing physicians of indigenous systems of medicine. Traditional preparation comprises medicinal plants, minerals and organic matters etc. Herbal drug constitutes only those traditional medicines that primarily use medicinal plant preparations for therapy.

The ancient record is evidencing their use by Indian, Chinese, Egyptian, Greek, Roman and Syrian dates back to about 5000 years (Table 1). About 500 plants with medicinal use are mentioned in ancient texts and around 800 plants have been used in indigenous systems of medicine. Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments, which also forms a rich source of knowledge.

The various indigenous systems such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different ailments. In India around 20,000 medicinal plant species have been recorded recently, but more than 500 traditional communities use about 800 plant species for curing different diseases. Currently 80 % of the world population depends on plant-derived medicine for the first line of primary health care for human alleviation because it has no side effects. Plants are important sources of medicines and presently about 25%

of pharmaceutical prescriptions in the United States contain at least one plant-derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources.

Table 1: Plant derived ethnotherapeutics and traditional modern medicine.

S.No.	Drug	Basic investigation
1.	Codeine, morphin	Opium the latex of <i>Papaver somniferum</i> used by ancient Sumarians. Egyptaians and Greeks for the treatment of headaches, arthritis and inducing sleep.
2	Atropine, hyoscyamine	<i>Atropa belladona</i> , <i>Hyascyamus niger</i> etc., were important drugs in Babylonium folklore.
3	Ephedrine	Crude drug (astringent yellow) derived from <i>Ephedra sinica</i> had been used by Chinese for respiratory ailments since 2700 BC.
4	Quinine	<i>Cinchona spp</i> were used by Peruvian Indians for the treatment of fevers
5	Emetine	Brazilian Indians and several others South American tribes used root and rhizomes of <i>Cephaelis spp</i> to induce vomiting and cure dysentery.
6	Colchicine	Use of Colchicum in the treatment of gout has been known in Europe since 78 AD.
7	Digoxin	Digitalis leaves were being used in heart therapy in Europe during the 18th century.

MODERN MEDICINE FROM HIGHER PLANTS

Medicinal plants play a vital role for the development of new drugs. During 1950-1970 approximately 100 plants based new drugs were introduced in the USA drug market including deserpidine, reseinnamine, reserpine,

vinblastine and vincristine which are derived from higher plants. From 1971 to 1990 new drugs such as ectoposide, Eguggulsterone, teniposide, nabilone, plaunotol, Z-guggulsterone, lectinan, artemisinin and ginkgolides appeared all over the world. 2% of drugs were introduced from 1991 to 1995 including pacitaxel, toptecan, gomishin, irinotecan etc.

Plant based drugs provide outstanding contribution to modern therapeutics; for example: serpentine isolated from the root of Indian plant *Rauwolfia serpentina* in 1953, was a revolutionary event in the treatment of hypertension and lowering of blood pressure. Vinblastine isolated from the *Catharanthus rosesus* is used for the treatment of Hodgkins, choriocarcinoma, non-hodgkins lymphomas, leukemia in children, testicular and neck cancer. Vincristine is recommended for acute lymphocytic leukemia in childhood advanced stages of hodgkins, lymphosarcoma, small cell lung, cervical and breast cancer.

Phophyllotoxin is a constituent of *Phodophyllum emodi* currently used against testicular, small cell lung cancer and lymphomas. Indian indigenous tree of *Nothapodytes nimmoniana* (*Mappia foetida*) are mostly used in Japan for the treatment of cervical cancer (Table 2). Plant derived drugs are used to cure mental illness, skin diseases, tuberculosis, diabetes, jaundice, hypertension and cancer. Medicinal plants play an important role in the development of potent therapeutic agents. Plant derived drugs came into use in the modern medicine through the uses of plant material as indigenous cure in folklore or traditional systems of medicine.

More than 64 plants have been found to possess significant antibacterial properties; and more than 24 plants have been found to possess antidiabetic properties, antimicrobial studies of plants, plant for antidotes activity—*Daboia russellii* and *Naja kaouthia* venom

neutralisation by lupeol acetate isolated from the root extract of Indian sarsaparilla *Hemidesmus indicus* R.Br. Which effectively neutralised *Daboia russellii* venom induced pathophysiological changes. The present investigation explores the isolation and purification of another active compound from the methanolic root extract of *Hemidesmus indicus*, which was responsible for snake venom neutralisation.

Table 2: Some of the important medicinal plants used for major modern drugs for cancer.

Plant name/family	Drugs	Treatment
<i>Catharanthus roseus</i> L. (Apocynaceae)	Vinblastine and vincristine	Hodgkins, Lymphosarcomas and children leukemia.
<i>Podophyllum emodi</i> Wall. (<i>Berberidaceae</i>)	Podophyllotoxin,	Testicular cancer, small cell lung cancer and lymphomas.
<i>Taxus brevifolius</i> (Taxaceae)	Pacitaxel, taxotere	Ovarian cancer, lung cancer and malignant melanoma.
<i>Mappia foetida</i> Miers.	Comptothecin, Irenoteccan and topotecan	Lung, ovarian and cervical cancer.
<i>Comptotheca acuminata</i>	Quinoline and comptothecin alkaloids	used in Japan for the treatment of cervical cancer
<i>Juniperus communis</i> L. (Cupressaceae)	Teniposide and etoposie	Lung cancer

Antagonism of both viper and cobra venom and antiserum action potentiation, antioxidant property of the active compound was studied in experimental animals. Recently, Chatterjee et al. from this laboratory reported that an active compound from the *Strychnus nux vomica* seed extract, inhibited viper venom induced lipid peroxidation in experimental animals.

The mechanism of action of the plant derived micromolecules induced venom neutralisation need further attention, for the development of plant-derived therapeutic antagonist against snakebite for the community in need. However, the toxicity of plants has known for a long period of time, and the history of these toxic plants side by side with medicinal ones are very old and popular worldwide, they considered the major natural source of folk medication and toxication even after arising of recent chemical synthesis of the active constituents contained by these plants.

Teniposide and etoposide isolated from *Podophyllum* species are used for testicular and lung cancer. Taxol isolated from *Taxus brevifolius* is used for the treatment of metastatic ovarian cancer and lung cancer. The above drugs came into use through the screening study of medicinal plants because they showed less side effects, were cost effective and possessed better compatibility.

Market Potential of Phytomedicine

The estimation of total phytomedicine sale reported in country wise European Union was about US\$ 6 billion in 1991 and \$ 4 billion in 1996, of which almost half were sold in Germany \$ 3 billion, in France \$ 1.6 billion, in Italy \$ 0.6 billion and in Japan \$ 1.5 billion. The present global market (Table 3) is said to be US 250 billion.

In India the sale of total herbal products is estimated at \$ 1 billion and the export of herbal crude extract is about \$ 80 million, of which 50% is contributed by Ayurvedic classical preparations. Plant derived drugs are important in Germany and Russia. Particularly, herbal drugs are imported by several countries for their usage of traditional medicinal preparation from various parts of the country (Table 4). Some of the important Indian medicinal plants exported to various countries are reported. Important medicinal plants and their parts used for the preparation

in indigenous systems of Indian medicines are reported in table 5.

Table 3. Market size of phytomedicine and their sale in US Dollar.

S.No.	Country	Years	Drugs sales in US \$ (billion)
1	Europe	1991	6
	Germany		3.0
	France		1.6
	Italy		0.6
	Others		0.8
2	Europe	1996	10.0
3	USA	1996	4.0
4	India	1996	1.0
5	Other countries	1996	5.0
6	All countries	1998	30.0 - 60.0

Table 4. Percentage of herbal drugs imported by various countries for drug preparation

Country	Percentage of herbal drugs imported
China	45%
USA	15.6%
Australia	10.5%
India	3.7%
South Korea	1.4%
Taiwan	1.7%
Indonesia	8.1%

Role of WHO in Phytomedicine

In 1991 WHO developed guidelines for the assessment of herbal medicine, and the 6th International Conference of Drug Regulatory Authorities held at Ottawa in the same year ratified the same. The salient features of WHO guidelines are: 1). Quality assessment: Crude plant materials or extract plant preparation and finished product. 2). Stability: Shelf life. 3). Safety assessment:

Documentation of safety based on experience and toxicological studies. 4). Assessment of efficacy: Documented evidence of traditional use and activity determination (Animals and human).

Standardisation of Phytomedicine

In the traditional system of medicine, the drugs are primarily dispensed as aqueous or ethanol extract. Fresh plant juice or crude extract are a rarity rather than a rule. The medicinal plants should be authentic and free from harmful materials like pesticides, heavy metals, and microbial and radioactive contamination. The medicinal plant should be single solvent extraction once or repeatedly or aqueous extract or as described in the ancient texts. The extract should be then checked for biological activity in experimental animal models. The bioactive extract should be standardised on the basis of active compound (Table 5). The bioactive extract should undergo limited safety studies.

Table 5

S.No	Traditional sector <i>pharmas</i>	Modern sector <i>pharmas</i>	Standardisation of <i>phytomedicine (formulation)</i>
1	Himalaya	Ranbaxy	Chromatography techniques
2	Zandu	Lupin	Thin Layer chromatography (TLC)
3	Dabur	Allembic	UV - Spectrophotometer
4	Hamdard	-	High Performance of Liquid Chromatography (HPLC)
5	Maharishi	-	Nuclear Magnetic Resonance spectroscopy (NMR)

New Sources of Tribal Medicine

Tribal healers in most of the countries, where ethnomedical treatment is frequently used to treat cut wounds, skin infection, swelling, aging, mental illness,

cancer, asthma, diabetes, jaundice, scabies, eczema, venereal diseases, snakebite and gastric ulcer, provide instructions to local people as how to prepare medicine from herbal. They keep no records and the information is mainly passed on verbally from generation to generation.

World Health Organisation (WHO) has shown great interest in documenting the use of medicinal plants used by tribals from different parts of the world. Many developing countries have intensified their efforts in documenting the ethnomedical data on medicinal plants. Research to find out scientific evidence for claims by tribal healers on Indian herbs has been intensified. Once these local ethnomedical preparations are scientifically evaluated and disseminated properly, people will be better informed regarding efficacious drug treatment and improved health status.

HERBAL MEDICINE SCENARIO IN INDIA

Herbal medicine is still the mainstay of about 75–80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, the last few years have seen a major increase in their use in the developed world. In Germany and France, many herbs and herbal extracts are used as prescription drugs and their sales in the countries of European Union were around \$ 6 billion in 1991 and may be over \$ 20 billion now.

In USA, herbal drugs are currently sold in health food stores with a turnover of about \$ 4 billion in 1996 which is anticipated to double by the turn of the century. In India, the herbal drug market is about \$ one billion and the export of plant-based crude drugs is around \$ 80 million. Herbal medicines also find market as nutraceuticals (health foods) whose current market is estimated at about \$ 80–250 billion in USA and also in Europe.

India is sitting on a gold mine of well-recorded and wellpracticed knowledge of traditional herbal medicine. But, unlike China, India has not been able to capitalise on this herbal wealth by promoting its use in the developed world despite their renewed interest in herbal medicines. This can be achieved by judicious product identification based on diseases found in the developed world for which no medicine or only palliative therapy is available; such herbal medicines will find speedy access into those countries. Backward integration from market demands will pay rich dividends. Strategically, India should enter through those plant-based medicines which are already well accepted in Europe, USA and Japan. Simultaneously, it should identify those herbs medicinal plants) which are time-tested and dispensed all over in India.

The basic requirements for gaining entry into developed countries include: (i) well-documented traditional use, (ii) singleplant medicines, (iii) medicinal plants free from pesticides, heavy metals, etc., (iv) standardisation based on chemical and activity profile, and (v) safety and stability. However, mode of action studies in animals and efficacy in human will also be supportive. Such scientifically generated data will project herbal medicine in a proper perspective and help in sustained global market.

Herbal Medicine

The World Health Organisation (WHO) has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today. Or say, traditional medicine is the synthesis of therapeutic experience of generations of practising physicians of indigenous systems of medicine. The traditional preparations comprise medicinal plants,

minerals, organic matter, etc. Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy. The earliest recorded evidence of their use in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years. The classical Indian texts include *Rigveda*, *Atharveda*, *Charak Samhita* and *Sushruta Samhita*. The herbal medicines/traditional medicaments have, therefore, been derived from rich traditions of ancient civilisations and scientific heritage.

Nutraceuticals

This is a term of recent origin and comprises nutritionally or medicinally enhanced foods with health benefits. These include engineered grain, cereals supplemented with vitamins or minerals or genetically manipulated soybean and canola oil without trans fatty acids, etc. Many pharma and biotech companies have moved into this area since it does not involve regulatory clearances and offers large markets. These companies have extended the term nutraceutical to include pure compounds of natural origin like lovastatin (a lipid lowering agent from red rice yeast), docosahexaenoic acid (a cardiovascular stimulant from algae), sterols, curcumin (from plants), etc. Likewise herbal preparations are being marketed as nutraceuticals or health foods and even the minimum standards laid down by WHO are not followed. It is pertinent to mention that herbal medicines are therapeutics of the indigenous/traditional systems of medicine and it is unethical to classify them as health foods. The regulatory agencies should, therefore, step in to prevent such misuse of natural products/herbal medicines as was done by US-FDA by banning the dietary supplement cholestin (i.e. lovastatin).

Nutraceuticals are in great demand in the developed world particularly USA and Japan. Nutraceutical market in USA alone is about \$ 80–250 billion, with a similar

market size in Europe and Japanese sales worth \$ 1.5 billion. Such huge markets have arisen because of the Dietary Supplement Health Education Act passed by USA in 1994 which permits unprecedented claims to be made about food or the dietary supplement's ability about health benefits including prevention and treatment of diseases. This act has motivated pharma to include not only compounds isolated from fauna and flora but also herbal medicines as nutraceuticals, which is unfortunate. The developing countries also see this as a good opportunity and are marketing such products.

Herbal Medicine Market

As per available records, the herbal medicine market in 1991 in the countries of the European Union was about \$ 6 billion (may be over \$ 20 billion now), with Germany accounting for \$ 3 billion, France \$ 1.6 billion and Italy \$ 0.6 billion. Incidentally in Germany and France, herbal extracts are sold as prescription drugs and are covered by national health insurance. In 1996, the US herbal medicine market was about \$ 4 billion and with the current growth rate may be more than double by the turn of century. Thus a reasonable guesstimate for current herbal medicine market worldwide may be around \$ 30–60 billion. The Indian herbal drug market is about \$ one billion and the export of herbal crude extracts is about \$ 80 million.

The 10 best-selling herbal medicines in developed countries are given in Table 7. The sales of these drugs account for almost 50% of the herbal medicine market. These drugs have been well standardised and some of them namely echinacea, garlic, ginkgo, ginseng and saw palmeto are supported with mode of action and clinical studies. Amongst the developed countries Germany holds the lead and has published individual monographs on therapeutic benefits of more than 300 herbs. In developing countries, China has compiled/generated data on over