Pt. Govind Ballabh Pant Memorial Lecture - XI

Medicinal Plants for Health Care

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Pandit Govind Ballabh Pant Memorial Lecture

ABSTRACT

The economic value and future potential of the biological resources of a country are getting redefined in the wake of the newly emerging international trade regulations from a system, held over countries, where these resources were viewed as global heritages, they are now being treated as invaluable reserves for the future of the country with an untapped economic potential. Unlike that for physical resources, we do not have yet a system of defining 'biological resource holdings' of a country and consequently there is a greater chance of these resources leaking out to other countries even before their potentiality is realized by the host countries. Thus there is an urgent need for developing inventory systems (qualitative and quantitative) that help defining the biological holdings of a country. Databases and documenting systems of biological resources of a country are useful in conservation, commercialization and in establishing the patent rights. The Government of India has taken timely initiatives in establishing National Bioresource Development Board (NBDB) which is taking requisite measures to take care of our bioresources and GB Pant Institute of Himalayan Environment and Development has been playing a very active role with respect to MAPs by not only maintaining gene banks but making appropriate selection of rich strains for commercial exploitation. I therefore,
greatly appreciate the efforts of all the members of the institute and on this gracious occasion I congratulate them for their contributions in the national endeavour.

Our country is among 12 leading biodiversity centres of the world with 45,000 plant species in 16 agroclimatic and 10 vegetative zones. We have 18,000 flowering plants, 44% of which are of medicinal significance. These medicinal plants are the richest resource of our traditional medicines, phytopharmaceuticals, modern allopathic drugs, household remedies and nutraceuticals. The use of phytopharmaceuticals is increasing at the rate of 15 percent annually. Global market is booming for MAPs and their products. Our contributions in the world market are not significant. Therefore, we need to look seriously on various issues, problems and technologies. The problems include

Quality parameters not being followed, unregulated trade, nearly 90 percent dependence on natural resources, agro-practices, post-harvest and post gathering practices are not appropriate, storage conditions deplorable leading to inconsistency in quality. The issues which need to be addressed include regulatory especially registration of herbal products, non-existent nutraceutical regulations, unregulated medicinal plant extract industry, safety aspects etc. We need to strengthen agro, post harvest, grinding, extraction of plants, isolation of phytoconstituents, formulation technologies. Extensive use of qualitative and quantitative techniques for quality assurance. Some of the leads obtained in medicinal plants by Indian scientists will be highlighted and certain current needs and developments in medicinal plant based products shall be discussed. Some of these would include Phytosome herbal drug delivery, raw material for synthetic drug tamif1u (birdf1u H_5N_1 virus), polysaccharides as safer therapeutics and for other industrial uses, promoting Indian gums through scientific inputs, sugar substitutes having least caloric values, improving quality of plant purgatives, chemotypes of medicinal significance, organic farming for Pharma products, enzymes such as phytases, systems biology, roadmap to safe, efficacious, quality assured and scientifically validated herbal drugs and plant derived allopathic drugs. Aromatic plants for global volatile oil production will be also discussed. Some of the priority disease areas such as protozoal diseases (like malaria, filarial, leishmania), cancer, rheumatic diseases, diabetes, bronchial asthma, viral diseases, liver disorders and mental disorders where medicinal plants can play a crucial role have been discussed.

1. Tribute

It is indeed an honour and privilege to be asked to deliver the Pandit Govind Ballabh Pant memorial lecture. On this occasion I would like to pay my homage to revered Pandit Govind Ballabh Pant, a great son of India, an enlightened, visionary and inspiring leader, statesman par excellence and freedom fighter of our country. Bharat Ratna Shri Govind Ballabh Pant's contributions to the nation are immense and monumental. Being one of the chief architects of free India, he held many prestigious positions including those of the Chief ministership of Uttar Pradesh and Home Ministership of the country. He hailed from Himalayan region and the Government of India has very rightly established an institute, in his cherished memory, on the occasion of his birth centenary year (1987-88), called the Govind Ballabh Pant Institute of Himalayan Environment and Development at Almora. All his life, Pandit Pant was in close contact with people and had great concern for their well being.

2. Glimpse of Himalayan Drug Plants

As Himalayan region is one of the richest repositories of medicinal and aromatic plants which contribute immensely to the drug-armamentarium of all the traditional systems of medicines and modern therapeutics, it is with this background that I have chosen the topic "medicinal plants for health care".

The Himalaya has been fountain head of yogic wisdom and spirituality of millions of Indians, not withstanding their differing religious beliefs. The mountain chain has influenced the life, culture and history of India. The holy epics like Ramayana and Mahabharata carry excellent descriptions of 2800 km long Himalayan belt occupying an area of about 591,000 sq. km (18% of India) inhibited by nearly 52 million people covering 12 states including union territories.

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To save the life of Lakshman, the younger brother of Lord Rama, Hanuman travelled to the Himalaya in search of S*anjiwani booti* (life saving herb). Thus the Himalaya is well known for a whole range of medicinal and aromatic plants some of which have gone into commerce and have their centre of origin in the Himalaya. Among the important ones are *Asparagus racemosus (g*alactagogue of Indian origin), *Atropa belladonna* (source of antispasmodic atropine), *Aconitum heterophyllum* (high value bitter tonic), *Berberis* species (one of the richest source of pharmacologically active alkaloid berberine), *Colchicum-luteum* (containing antigout colchicine), *Coptis teeta* (another source of berberine), *Cymbopogon* species (citral source for production α-ionone & β-ionone), *Curcuma zedoaria* (well established anti-inflammatory drug and wonderful wound healer), *Digitalis purpurea, Digitalis lanata* (both producing cardiotonic glycosides), *Dioscorea deltoidea*, *D. prazeri, D. floribunda* (very first and rich source of diosgenin used for the synthesis of cortocosteroidal drugs), *Ephedra geradiana* (contains bronchodilatory ephedrine used for the treatment of bronchial asthma), *Gentiana kurrooa* (hepatoprotective drug), *Heracleum spp* (source of xanthotoxin), *Hyoscyamus niger* (source of hyoscyamine and hyoscine), *Inula racemosa* (pushkarmool of Ayurveda for bronchitis), *Mentha arvensis* (commercial source of menthol), *Nardostachys jatamansi* (tranquilizer and sedative), *Orchis latifolia* (for unspecified diarrhea in children),

Papaver somniferum (source of analgesic morphine and antitussive codeine), *Physochlaina praelta* (commercial rich source of atropine and hyoscyamine), *podophyllum hexandrum* (source of podophyllotoxin for producing anticancer drugs etoposide & tenoposide), *Picrorhiza kurrooa* (drug for liver protection), *Saussurea lappa* (antidiarrheal, antiemetic & digestive*), Swertia* species (bitter tonic), *Valeriana wallichii* (sedative and tranquilizer), *Voila adorata* (expectorant).

3. Medicinal plants: well spring of Traditional and Modern drugs

The use of plants as source of medicinal agents lies deep in the roots of autiquity. No one will ever know what led primitive man emerging from his ancestral, origin, to select certain plant material for the treatment of various ailments and diseases though it may be assumed that during the long transition from instinctive behaviour to more rational action, there was a conscious realization that certain roots, leaves, bark, fruits and even plant exudations had some beneficial action. This knowledge and the characteristics of the plant material, or even the entire plant itself, would be remembered for future occasions and the information passed on to others by word of mouth. Later, as different civilizations developed, man was able to communicate his knowledge and ideas, first by carving into stones or clay and later by writing on parchment or paper with the result that his knowledge became known to the coming generations. Reverence may be made to the clay writings from the library of the Assyrian king, to the Ebers Papyrus and to the writings of Dioscorides to indicate sources of our knowledge today about the crude drugs by Arabians, Babylonians, Chinese, Egyptians, Greeks, Indians, Persians, Romans and Sumarians thousands of years ago. The oldest treatises dealing with Ayurveda are *Susruta samhita* and *Charaka samhita* both compiled between 500-300 B.C. The development of the Ayurvedic system of medicine was based on scientific approach and methodology. Many of the drugs used in the traditional systems have stood the test of time.

With the advent of European scientific methods, many of the reputed medicinal plants came under chemical scrutiny, leading to the isolation of active principles. Beginning with A.D. 1800 there was continuous activity in this area and many of the well known medicinal plants were chemically analysed and their active principles characterized. Soon after their isolation and characterization, these compounds either in pure state or in the form of well characterized extracts, became part of pharmacopoeias of several countries. To cite well known examples reference can be made to ephedrine, morphine, quinine and emetine which still occupy an honourable place in pharmacies. The Chinese crude drug Ma Huang has been in use in China for over 5000 years for the treatment of fevers and respiratory ailments. Its active component ephedrine was isolated in 1887 by Nagi and Hari in Japan. Detailed pharmacological work follwed and the compound was introduced in western medicine in 1925 by Chen of Eli Lilly company. Morphine was isolated from opium poppy (*Papaver somniferum*) in 1804 by Sertuner and was introduced in medicine in 1818. Quinine isolated by Pelletier in 1820 from a Peruvian tree. Cinchona, was introduced as an antimalarial drug in 1825. From a Brazilian medicinal plant *Cephaelis ipecacuanha* an active principle emetine was isolated in 1894 and introduced in medicine in 1912. Thus pharmacists in pharmaceutical industry started paying attention to the chemical constituents of drugs, especially aconite, belladonna, cinchona, digitalis, ergot and opium. Morphine has given the organic chemists an interesting lead on which to base a large number of opioid analgesic drugs and the same may be said for the natural drug quinine for numerous antimalarial drugs. Many new and useful drugs based upon these natural products are now available but they have not been able to replace effectively till today these two alkaloids in medical practice.

It has been estimated that from 250,000 to 750,000 species of higher (flowering plants) exist on earth; some of these have not yet been botanically described. Although there is no way to determine accurately how many of these species have been used in traditional medicine, a reasonable estimate would be about 10% or from 25,000 to

75,000 species. However, perhaps only about 1% of these are acknowledged through scientific studies to have real therapeutic value when used in extract form by humans. Virtually all such plants have been discovered and put to wide spread use in traditional medical systems through information derived from their use in folk medicine, ethnomedicine or traditional medicine.

World population is 5 billion today and with this rate of growth it is likely to touch 7.5 billion by the year 2020. Global estimates indicate that over 3/4th of the five billion world population cannot afford the products of the western pharmaceutical industry and have to rely upon the use of traditional medicines, which are mainly derived from plants. This fact is well compiled by W.H.O. in an inventory of medicinal plants list in over 20,000 species. As a part. of strategy to reduce financial burden on developing countries which spend 40-50% of their total health budget on drugs, W.H.O. currently encourages, recommends and promotes the inclusion of herbal drugs in national health care programmes because such drugs are easily available at a price within the reach of a common man and as such are time tested and thus considered to be much safer than the modern synthetic drugs. Resurgence of interest in herbal drugs in the western European countries is evident from the fact that two volumes of British Herbal Pharmacopoeia have been published and $ 33 million worth literature on herbal products was sold in the USA in 1990. The "green wave" in the utilization of medicinal plants resulted in higher consumption. Only recently British Pharmacopoeia Commission and European Pharmacopoeia Commission both have decided to include atleast 20 Ayurvedic Indian medicinal plants and 20 Chinese medicinal plants in their respective Pharmacopoeias. International agencies like W.H.O., UNIDO and FAO are promoting the industrial use of medicinal plants in National Health care programmes of all countries. The current world trade in medicinal plants is nearly US$ 60 billion and as per world Bank estimates by the year 2050 this figure will touch US$ 5 trillion for medicinal plants trade in the world.

4. Medicinal Plants Based Drug Industries

Business opportunities in the medicinal and aromatic plants sector are exponentially expanding due to diversified uses of the plant derived molecules in pharma, cosmetics, nutraceuticals and agri-chemical industries. A shift from the present mind set of collection and consumption to cultivation for utilization will automatically ensure purity, authenticity and availability of MAPs for various end-user industries.

Medicinal plant based drug industry has four major segments, viz. (i) plant drugs for Indian systems of medicine covering Ayurvedic, Unani and Siddha systems, (ii) over the counter, non-prescription items involving plant parts, extracts and galenicals (iii) essential oils and (iv) phytopharmaceuticals. Medicinal plants as resource of drugs (see figure 1)

4.1 Medicinal plants based drug industries in Indian Systems of Medicine

There are at present 8000 manufacturers of drugs for Indian Systems of Medicine. Besides, there are many small manufacturing units using medicinal plants and thousands of Vaidyas preparing their own drugs from various plants. Annual herbal drug production has been estimated at around Rs.5,500 crores. Various bottlenecks in the Indian herbal drug industry have been discussed elsewhere [2].

4.2 Plant parts extract and galenicals

The direct utilization of plant material is a feature of traditional medicines not only in the developing world but also in Europe and the U.S.A. e.g. herbal formulations on health food shops. Preparations of decoctions, tinctures, galencials and total extracts of plants also form a part of many pharmacopoeias of the world. The current trend of medicinal plants based drug industry is to procure standardized extracts of plants as raw material.
At present, there are nearly twenty herbal extract manufacturers in the country (out of which 50% are very small manufacturers) with an annual turnover of less than Rs. 4 crores. Major herbal extract manufacturers are given below with their annual turnover in brackets:

a. Alchem International, New Delhi (80 crores)
b. Sami Labs, Bangalore (65 crores)
c. Chemilloids, Vijayawada (60 crores)
d. Indfrag, Hosur (22 rores)
e. Arjuna extracts, Alwaye, Kerala (20 crores)
f. Sanat Products, Ghaziabad (17 crores)
g. Amsar, Indore (12 crores)
h. Dhanwantri, Bangalore (12 crores)
i. Natural Remediies, Bangalore (10 crores)
j. Phytotech (5 crores)

4.3 Essential oils from plants

The essential oil industry was traditionally a cottage industry in India. Since 1947, a number of industrial companies have been established for large scale production of essential oils, oleoresins and perfumes. The essential oils from plants being produced in India include ajowain oil, cedarwood oil, celery oil, citronella oil, davana oil, eucalyptus oil, geranium oil, lavender oil, lemongrass oil, *Mentha* oil, palmarosa oil, patchouli oil, rose oil, sandalwood oil, turpentine oil and vetiver oil (see figures 2-5). The manufacture of turpentine oil, and resin form pines is a sizable and well established industry in India having 10,000-25,000 tonnes annual production of the oil. α-pinene and δ-3 carene are the two vital components produced from the oil. α-Ionone from lemongrass oil for perfumery and β-ionone for Vitamin A synthesis are produced in India. Before, 1960, menthol was not produced in India but the introduction of Japanese mint, *Mentha arvensis* and subsequent improvements thereupon enabled India to produce over 500 tonnes of menthol and now tops the world market in export of natural menthol.

Annual world production of limonene is 50,000 tonnes and Brazil is the biggest producer in the world market. It is a by-product of citrus industry. Though turpentine oil and eucalyptus oil also yield limonene but the best economically cheap raw material is the discarded orange and lemon peel which is being used by Brazilian phytochemcial industry. India has not yet tapped this source for limonene production. During the last five decades, the Indian essential oil industry has made excellent progress. India today is the largest producer of menthol in the world and other aromatic plants such as *Mentha piperita, M. citrate*, Himalayan cedarwood, Jamrosa, basil etc have become commercial essential oil yielding crops. Like wise Indian flower extracts from Jasmine, Jasmine Sambac and tuberose have become internationally established. The Indian oleoresin and spice oils have also made excellent progress in global market. The world production of essential oil is estimated around 1.2 lakh tones per year valued around US$ 1 billion.

4.4 Phytopharmaceuticals

Before 1947, the production of plant based modern drugs in India was confined to quinine from *Cinchona* in three state owned factories and the very first phytochemical industry for quinine was established by the then British Government at Mungpoo in Darjeeling. During the past three and half decades' bulk production of plant-based modern drugs has become an important segment of Indian pharmaceutical industry. Some of the phytopharmaceuticals which are produced in India at present include morphine, codeine, papaverine, thebaine, emetine, quinine, quinidine, digoxin, caffeine, hyoscine, hyoscyamine, xanthotoxin, psoralen, colchicine, rutin, berberine, vinblastine, vincristine, nicotine, strychnine, brucine, ergot, alkaloids, senna glycosides, pyrethroids and podophyllotoxin resin. Table 1 gives some important therapeutically used constituents isolated from medicinal plants and used in modern medicine. There are 130 such phytoconstituents used in modern medicine.

Phytopharmaceuticals for which technology has been developed for undertaking large scale production include L-dopa from *Mucuna* beans, ajmaline and ajmalicine from *Rauvolfia serpentina* and *Catharanthus* roots, respectively, and 18 β-acetyl glycyrrhetic acid from *Glycyrrhiza glabra.*

Indian Institute of Chemical Technology (I.I.C.T.), Hyderabad has developed methods for etoposide and tenoposide production and CIPLA is now producing it on commercial basis. At present 100 mg of etoposide is sold at Rs. 400/- per vial. National Chemical Laboratory, Pune, developed the method of vincristine (VCR) and vinblastine (VLB) production. CIPLA have further improved the process and now they are the third largest manufacturer of VCR and VLB in the world.

Medicinal plants based drug industry is progressing very fast in India, but it is beset with a number of problems. Most alarming problem the industry has started facing and will face in future is the dwindling supply of plant material from natural resources. A national policy on medicinal plants with a view to preserve endangered species and promoting cultivation of plants which are being extensively used by industry will help in solving the major problem of the industry. Special attention is required on medicinal plants on which significant research leads have been obtained (Table 2) and the overexploited medicinal plants are given in Table 3.

Trade in medicinal plants is largely unorganised and uncertain, both in demand and price structure. There is a need to have Marketing & Development Board for Medicinal and Aromatic Plants and Phytopharmaceuticals. Such a Board could interact, with the growers and user industry to bring stability in their production, demand, price, quality and also to help in fostering international trade

Table 1

Important Active Constituents of Plants Used in Modern Medicine

Active Constituents	**Plant Source**	***Pharmacological Activity***
Ajmalicine	*Catharanthus roseus*	Vasodilator
Berberine	*Berberis* species	Antidiarrlw.:al
Caffeine	*Camellia sinensis*	CNS stimulant
Capsaicin	*Capsicum annum*	Topical analgesic
Cocaine	*Erythroxylum coca*	Local anaesthetic
Codeine	*Papaver somn!ferum*	AntItussive
Curcumin	*Curcuma longa*	Antiinflammatory
Colchicine	*Colchicum alllUfnnale*	Gout; Antiinflammatory
Conessine	*Holarrhena antidyse,r?ferica*	Antidysenteric
Digoxin	*Digitalis lanata*	Cardiotonic
Deserpidine	*Rauwolfia vamitoria*	Vasodilator
Ephedrine and pseudoephedrine	*Ephedra sinica*	Bronchodilator, sympatho-Mimetic, decongestant
Emetine	*Cephaelis ipecacuanha*	Antiamoebic
Ergometrine	*Claviceps purpurea*	Oxytocic
Ergotamine	*Claviceps purpurea*	Vasoconstrictor for headache
Glycyrrhizin	*Glyyrrhiza, glabra*	Antiinflmmatory
Hyoscine	*Hyoscyamusmuticus*	Parasympatholytic
Hyoscyamine	*Atr.opa belladonna*	Parasympatholytic
Lanatosides	*Digitalis lanata*	Cardiotonic
Morphine	*Papaver somniferum*	Analgesic
Papaverine	*Papaver somniferum*	Smooth muscle relaxant
Pilocarpine	*Pilocarpus jaborandi*	Parasympathomimetic
Podophyllotoxin	*Podophyllum peltatum*	Anticancer
Quinine	*Cinchona* species	Antimalarial
Quinidine	*Cinchona* species	Antiarrhythmic
Reserpine	*Rauwolfia serpemina*	Hypotensive
Rescinnamme	*Rauwolfia ca/lescens*	Vasodilator
Sennosides	*Cassia acutifolia*	Purgative
Taxo!	*Taxus baccata*	Anticancer
Vasicine	*Adhatoda zeylanica*	Bronchodilator
Vincamine	*Vinca minor*	Vasodilator
Vincristine and Vinblastine	*Catharanthus roseus*	Anticancer
Warfarin	*Melilotus officinalis*	Blood thinner for clots
Yohimbine	*Pausinystalia johimbe*	Treatment of impotence

Table 2

Medicinal Plants on which significant research leads have been obtained

Commphora mukul	Antihypercholesterlaemic
Boswellia serrata	Antiarthiritic
Picrorrhiza kurroa	Antihepatotoxic
Phyllanthus amarus	antihepatotoxic
Centella asiatica	Brain tonic
Curcuma longa	Antiinflammatory
Andrographis paniculata	Antihepatotoxic
Withania somnifera	Adaptogen
Coleus forskholi	Cardiotonic
Acorus calamus	Tranquilizer
Sida rhombifolia	Anabolic
Albizzia lebeck	Immunomodulator
Valeriana wallichii	Tranquilizer

Tab1e 3
Overexploited medicinal plants of Himalaya

i. Critically endangered species

Name of the species	Plant part used
Aconitum balfourii	Root
Aconitum deinorrhizum	Root
Aconitum falconeri	Root
Aconitum heterophyllum	Root
Aconitum violaceum	Root
Angelica glauca	Root
Arnebia benthami	Root/leaf/flowers
Atropa acuminate	Root/leaf
Berberis kashmiriana	Root
Dactylorhiza hatagirea	Root
Delphinium denudatum	Root
Dioscorea deltoidea	Rhizome
Fritillaria roylei	Root
Gentiana kurroa	Root
Inula racemosa	Root
Nardostachys jatamansi	Root
Podophyllum hexandrum	Root/fruit
Saussurea costus	Root
Swertia chirayita	Root
Taxus wallichiana	Stem bark/leaf
Valeriana jatamansi	Root

ii. Endangered species

Name of the species	**Part used**
Berberis aristata	Root
Berberis chitria	Root
Berberis lyceum	Root
Bunium persicum	Root
Heracleum candicans	Root
Picrorhiza kurroa	Root
Polygonatum verticillatum	Root/leaf
Rheum emodi	*Whole herb*
Saussurea obovallata	*Whole herb*

(iii) Vulnerable Species

Name of the species	**Part used**
Artemisia absinthium	*Aerial part*
Artemisia maritime	*Aerial herb*
Bergenia ligulata	*Root*
Hedychium spicatum	*Root*
Jurinea dolomiaea	*Root*
Lavatera cashmiriana	*Root*
Paeonia emodi	*Root*
Rheum australe	*Root*
Thalictrum foliolosum	*Root*
Tribulus terrestris	*Fruit*

5. India's strength in Medicinal Plant Wealth

If we dwell for a moment on our glorious past, *Rigveda,* one of the oldest repositories of human knowledge written between 4500-1500 BC mentions the use of 67 plants for therapeutic use and *Yajurveda* enlists 81 plants whereas *Atharveda* written during 1200 BC describes 290 plants of medicinal values, "*Chakra Samhita*" (900 BC) describes 341 medicinal plants and the next land mark in Ayurveda "*Sushruta Samhita*" (600 BC) mentions 395 medicinal plants[3.] India unquestionably occupies the top position in the use of herbal drugs, It is one of the, foremost countries exporting plant drugs and their derivatives, and excels in home-consumption too and this is not all surprising because

of the following:

- great biodiversity and abundance of flora
- variety of geographical climatic conditions most exotic medicinal plants can be grown here
- Indian systems of medicine dwell heavily on medicinal plants

- long tradition of phytochemical research and scientific cultivation of medicinal plants
- well developed pharmaceutical industry
- rapidly growing phytochemical and herbal drug industry

India is thus in a vantage position to exploit this source both for meeting the domestic demand for drugs as also for export.

Medicinal plants continue to be an important resource material for therapeutic agents both in developed and developing countries[4-7]. The Figure A shows the medicinal plants resource and better utilization of traditional systems of medicine. India is among the twelve leading biodiversity centres of the world, harbouring nearly 45,000 plant species in 16 agroclimatic and ten vegetative zones. The Indian population is known to have used plants in health care regimens for over 5000 years. Nearly 70% of our population is dependent on traditional plant based medicines. Over 53 million tribal people of 550 tribal communities inhabit the Indian subcontinent and are reported to use around 7500 species of plants for medicinal purposes.

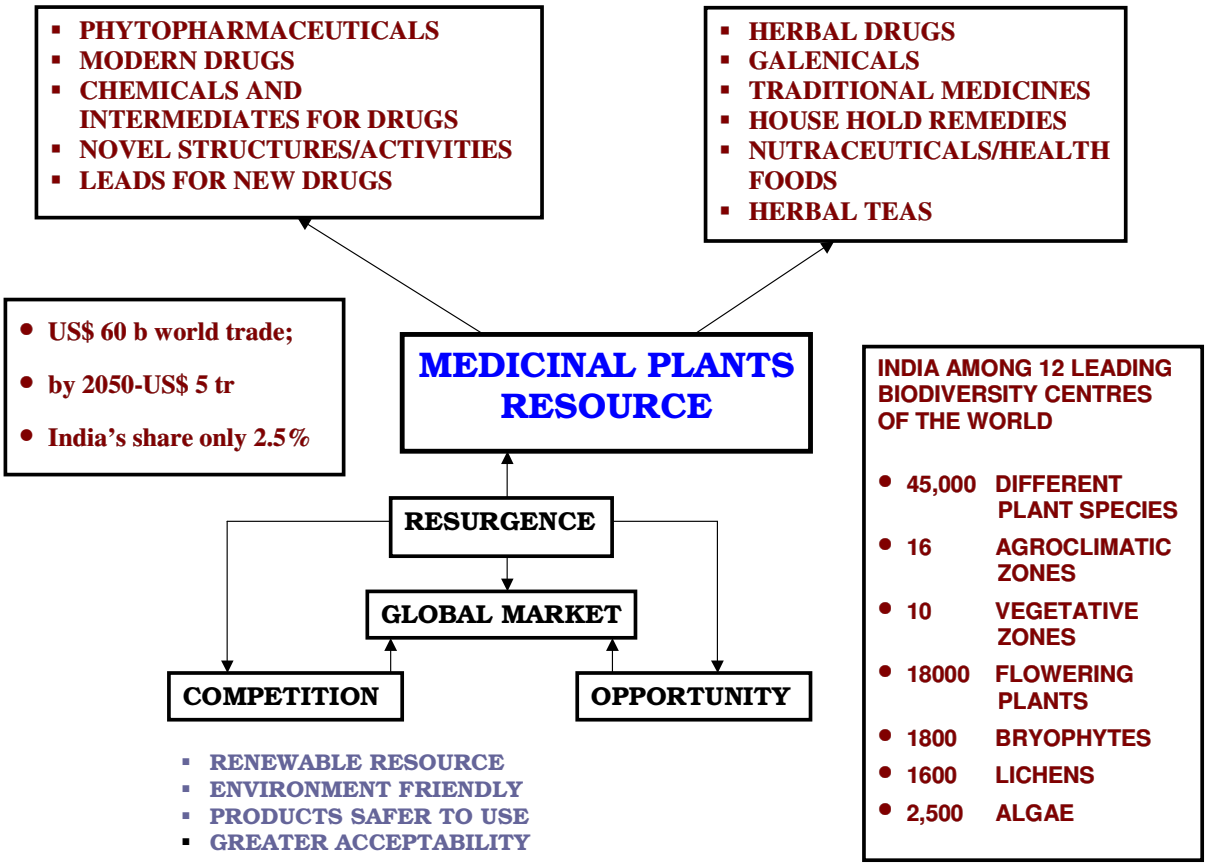

Figure 1: An integrated approach to use medicinal plant resource for drugs

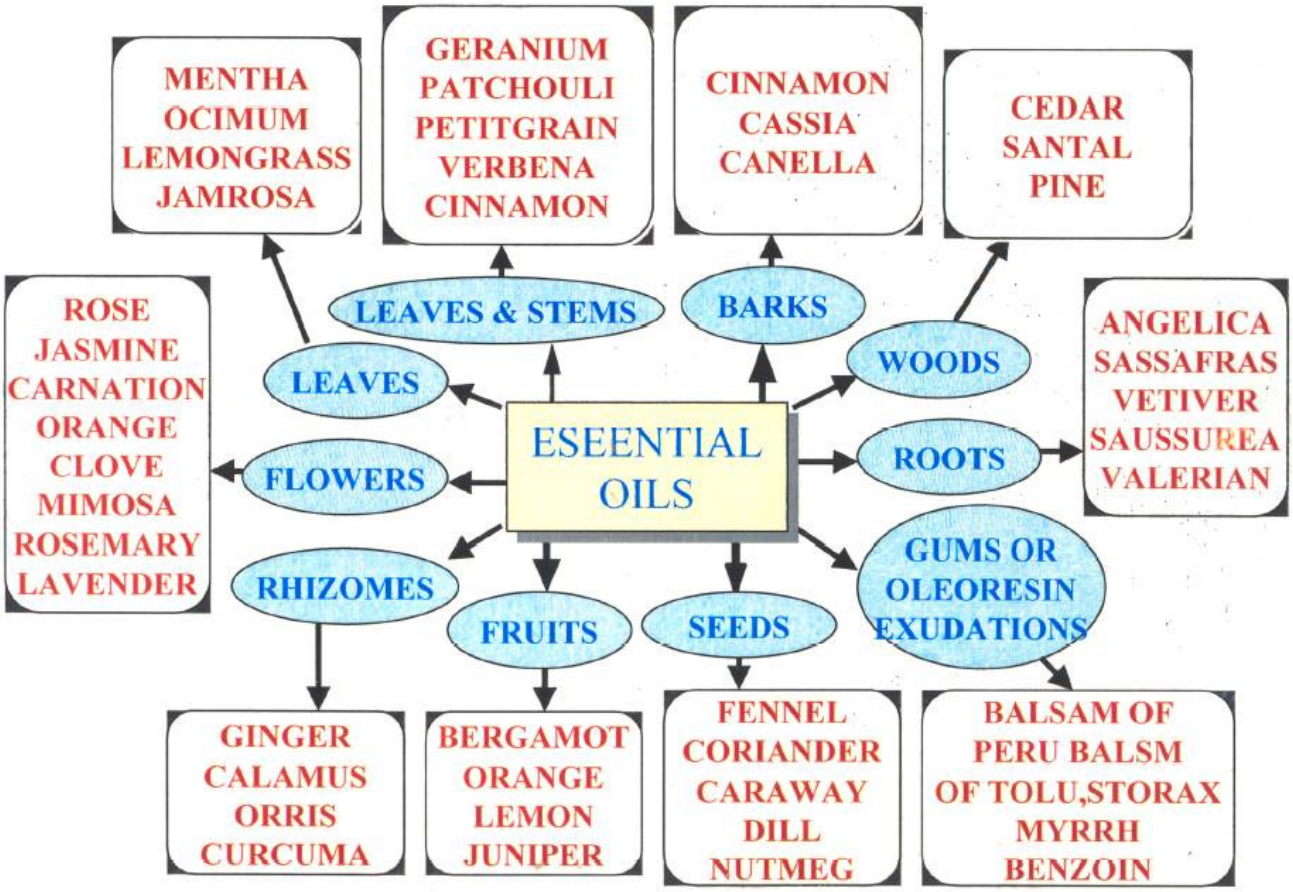
ESEENTIAL OILS
LEAVES & STEMS
BARKS
LEAVES
WOODS
FLOWERS
ROOTS
RHIZOMES
FRUITS
SEEDS
GUMS OR OLEORESIN EXUDATIONS
MENTHA OCIMUM LEMONGRASS JAMROSA
GERANIUM PATCHOULI PETITGRAIN VERBENA CINNAMON
CINNAMON CASSIA CANELLA
CEDAR SANTAL PINE
ROSE JASMINE CARNATION ORANGE CLOVE MIMOSA ROSEMARY LAVENDER
ANGELICA SASSAFRAS VETIVER SAUSSUREA VALERIAN
GINGER CALAMUS ORRIS CURCUMA
BERGAMOT ORANGE LEMON JUNIPER
FENNEL CORIANDER CARAWAY DILL NUTMEG
BALSAM OF PERU BALSM OF TOLU,STORAX MYRRH BENZOIN

Figure 2

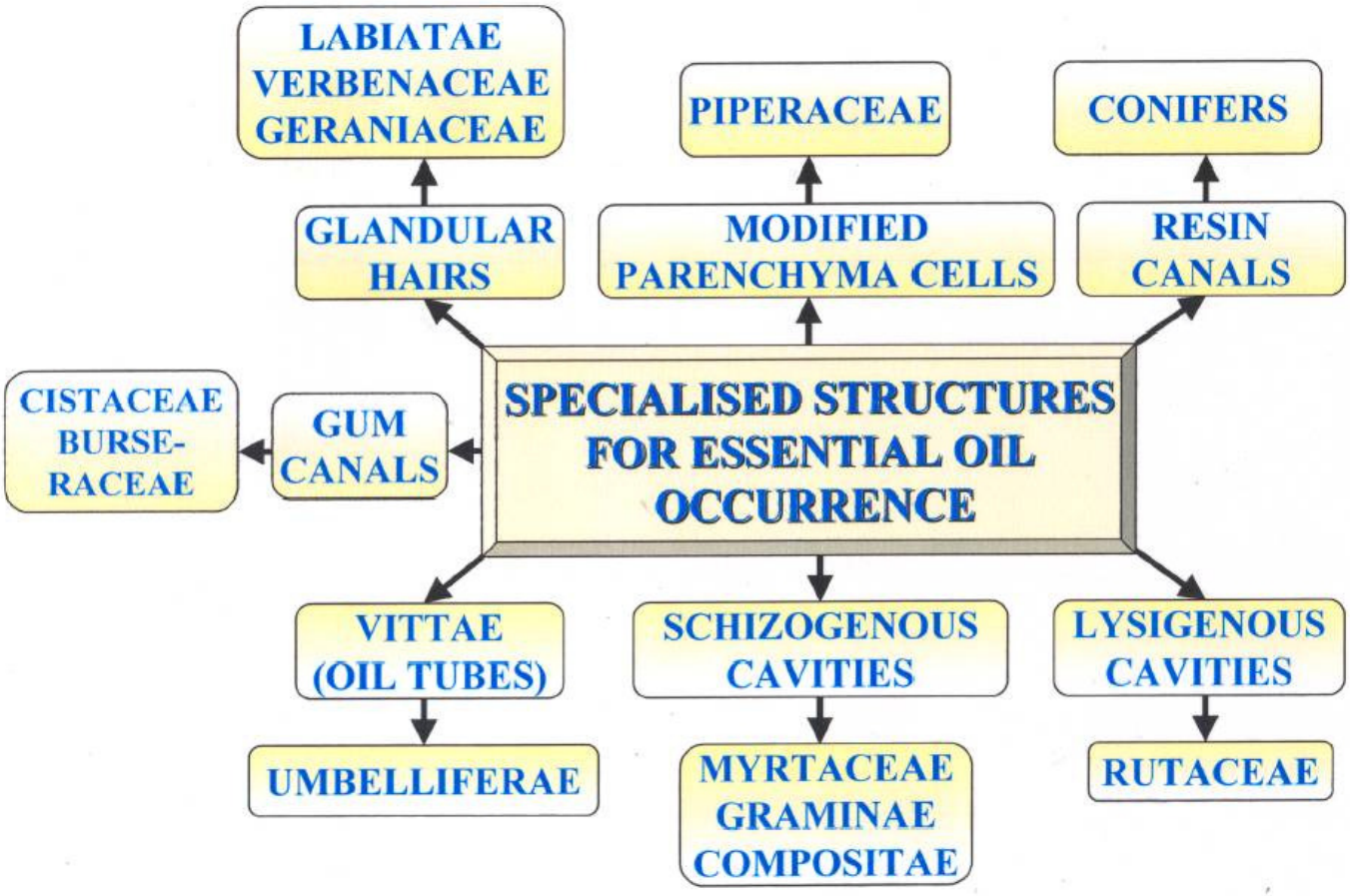
LABIATAE
VERBENACEAE
GERANIACEAE
PIPERACEAE
CONIFERS
GLANDULAR HAIRS
MODIFIED PARENCHYMA CELLS
RESIN CANALS
CISTACEAE
BURSE-
RACEAE
GUM CANALS
SPECIALISED STRUCTURES FOR ESSENTIAL OIL OCCURRENCE
VITTAE (OIL TUBES)
SCHIZOGENOUS CAVITIES
LYSIGENOUS CAVITIES
UMBELLIFERAE
MYRTACEAE
GRAMINAE
COMPOSITAE
RUTACEAE

Figure 3

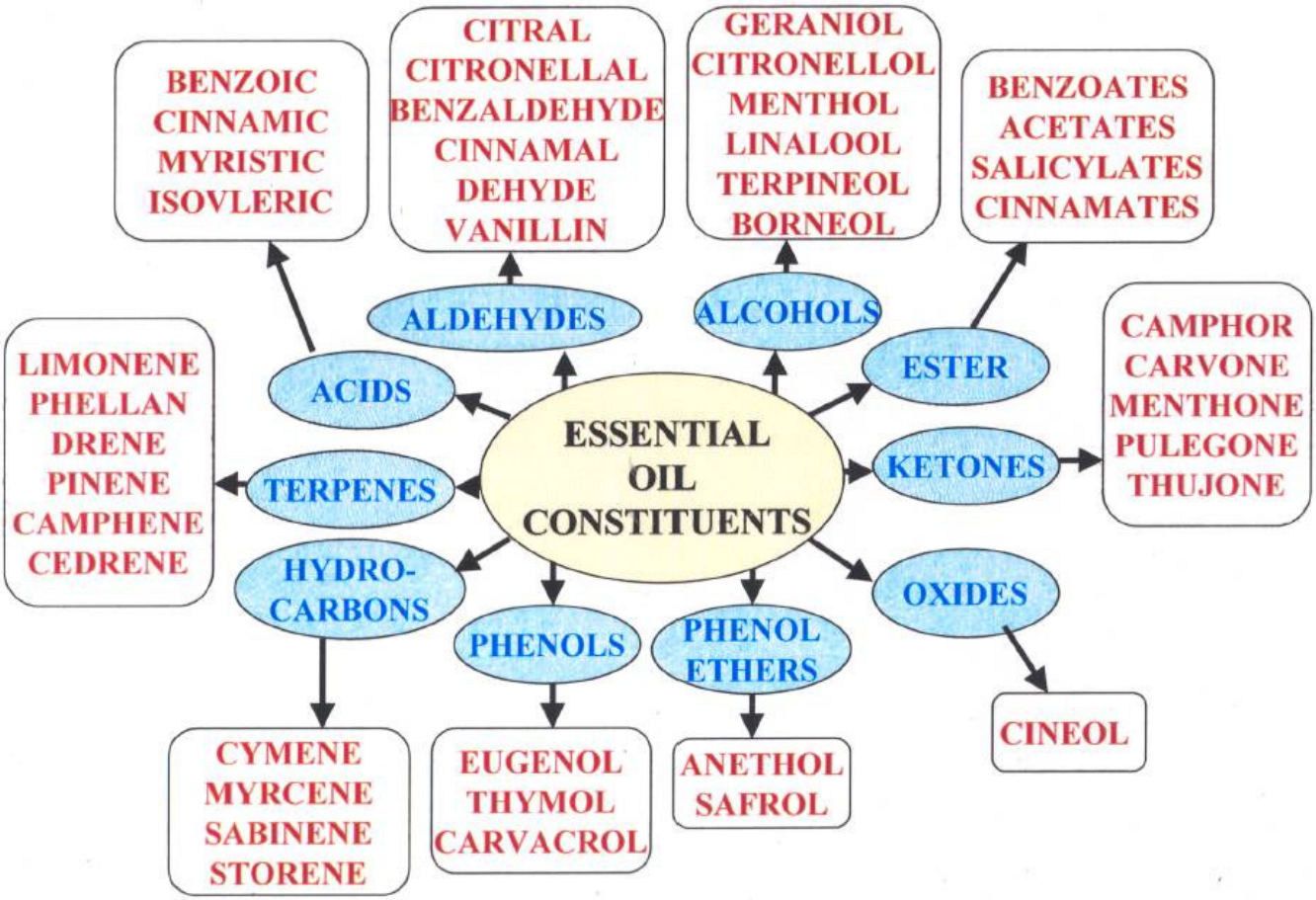
ESSENTIAL OIL CONSTITUENTS
ACIDS
BENZOIC
CINNAMIC
MYRISTIC
ISOVLERIC
ALDEHYDES
CITRAL
CITRONELLAL
BENZALDEHYDE
CINNAMAL
DEHYDE
VANILLIN
ALCOHOLS
GERANIOL
CITRONELLOL
MENTHOL
LINALOOL
TERPINEOL
BORNEOL
ESTER
BENZOATES
ACETATES
SALICYLATES
CINNAMATES
KETONES
CAMPHOR
CARVONE
MENTHONE
PULEGONE
THUJONE
TERPENES
LIMONENE
PHELLAN
DRENE
PINENE
CAMPHENE
CEDRENE
HYDRO-
CARBONS
CYMENE
MYRCENE
SABINENE
STORENE
PHENOLS
EUGENOL
THYMOL
CARVACROL
PHENOL
ETHERS
ANETHOL
SAFROL
OXIDES
CINEOL

Figure 4

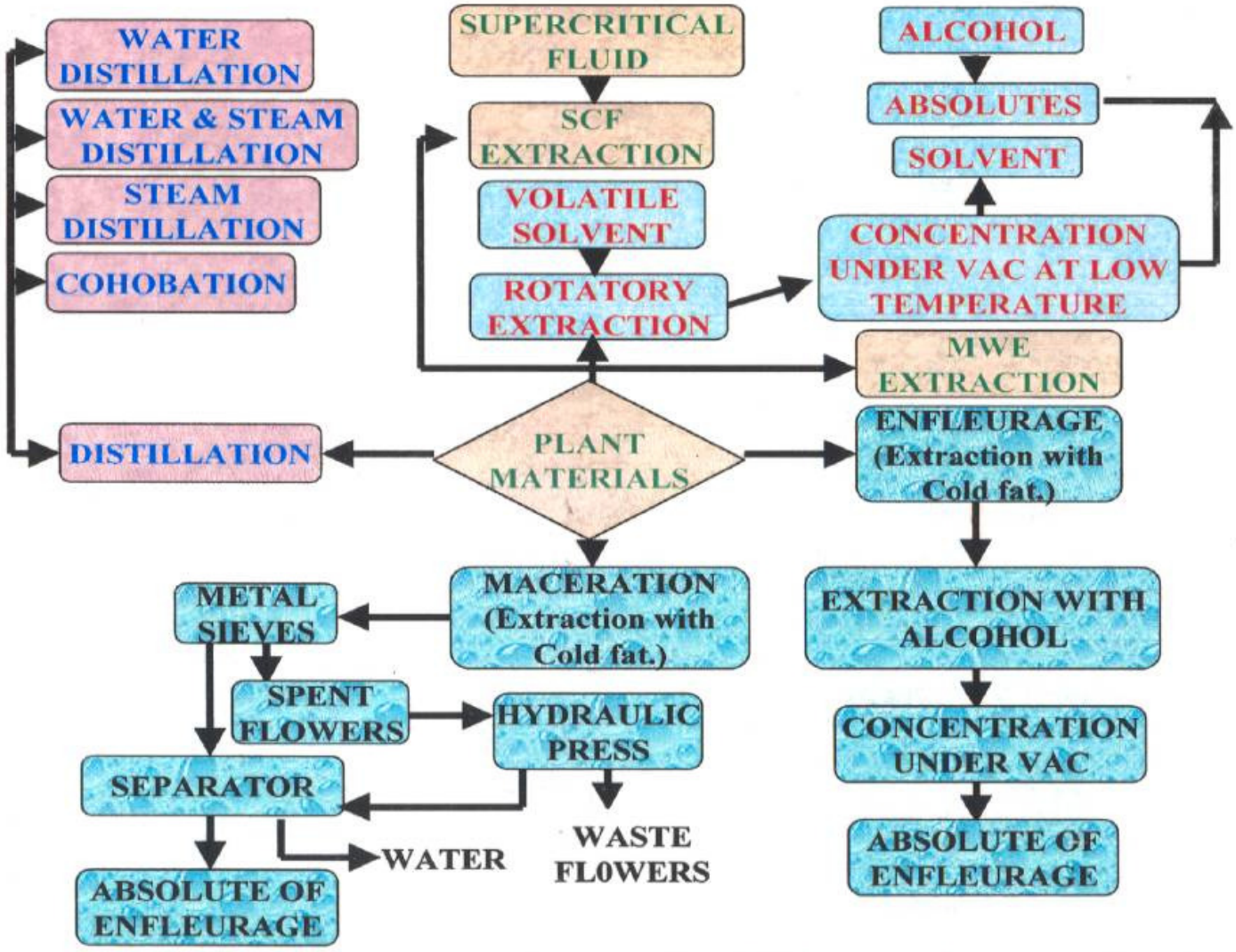
WATER DISTILLATION
WATER & STEAM DISTILLATION
STEAM DISTILLATION
COHOBATION
DISTILLATION
SUPERCRITICAL FLUID
SCF EXTRACTION
VOLATILE SOLVENT
ROTATORY EXTRACTION
ALCOHOL
ABSOLUTES
SOLVENT
CONCENTRATION UNDER VAC AT LOW TEMPERATURE
MWE EXTRACTION
PLANT MATERIALS
ENFLEURAGE (Extraction with Cold fat.)
MACERATION (Extraction with Cold fat.)
METAL SIEVES
SPENT FLOWERS
HYDRAULIC PRESS
SEPARATOR
WATER
WASTE FL0WERS
ABSOLUTE OF ENFLEURAGE
EXTRACTION WITH ALCOHOL
CONCENTRATION UNDER VAC
ABSOLUTE OF ENFLEURAGE
Production methods of essential oils from plant materials

Figure 5

5.1: Domestic demand for 20 major medicinal plants

Data for top 20 medicinal plants (quantity) is given in the table 4. It is observed that top 20 plants account for 66.2 percent of the total demand for 162 medicinal plants and account for 73.1 percent of total value[7a].

Table 4

Estimated domestic demand for selected medicinal plants
Top 20 medicinal plant quantity-wise

Botanical name	Common name	1999-2000 Qty. (Tonnes)	1999-2000 Percent Share (%)
Emblica officinalis Gaertn.	Amala	15146.7	12.5.
Asparagus racemosus Willd.	Shatawar/Satawar	8246.3	6.8
Withania somnifera Dunal.	Aswagandha/Asgandh	5905.1	4.9
Terminalia chebula Retz.	HararlHalela Zard	5413.4	4.5
Saraca asoca [Roxb.]	Ashoka	5331.8.	4.4
Aegle marmelos Carr.	[1] Bael [Bark] [2] Belgiri	4479.8	3.7
Cassia angustifolia Vahl.	Sonapatri/Sana	4356.2	3.6
Adhatoda vasica Nees	Adusa/Arusa	4211.9	3.5
Piper longun Linn.	Pippali	2951.8	2.4
Bacopa monnieri [Linn.]	Brahmi	2650.1	2.2
Sida cordi folia Linn.		2677.8	2.2
Ocimum sanctum Linn.	Tulsi	2371.7	2.0
Bambusa bambos Druce.	Vansalochan	2153.5	1.8
Boerhaavia diffllsa Linn.	Punarnava	2182.3	1.8
Azadirachta indica A. Juss.	Neem	2039.3	1.7
Solanum nigrum Linn.	Mokoya [Mako]	2005.1	1.7
Woodfordia fruticosa Kurz.	Dhataki, Dhai	2014.3	1.7
Andrographis paniculata	Kalmegh	1886.2	1.6
Syzygium aromaticum	Long/lavang.	1967.8	1.6
Tinospora cordifolia [Wild]	Giloe, Guudchi	1897.3	1.6
Total		**79888.4**	**66.2**
Others		**40928.4**	**33.8**
Total		**120816.8**	**100.0**

5.2 Medicinal plants with higher industrial potential

Policy makers have also suggested that with some degree of R&D efforts following plants have considerable potential for increased production. The states in which increased potential may be realized are also indicated for each of the plant.

Table 5
Plants with potential for increased production

Botanical name	Common name	States
Aconitum heterophyllum	Ativisha/Atis	Mizoram, Goa, Himachal Pradesh, Gujrat, Uttar Pradesh
Acorus calamus Linn.	Vacha/Waj-e-Turki	Arunachal Pradesh
Adhatoda vasica Nees	Adusa/Arusa	Goa, Maharashtra, Dadra & NH, Mizoram
Aegle marmelos Corr.	Bael	Imphal,Tripura,Dadra & Nagar Haveli, Gujarat, Uttar Pardesh,
Albizzia lebbeck Benth	Shirisa/Siras	Dadra & NH, Gujarat, Daman & Diu
Anacyclus pyrethrum DC.	aquarqarha	Himachal Pradesh
Andrographis paniculata	Kalmegh	Mizoram, Maharashtra
Aquilaria agallocha Roxb.	Agaru/Agar	Nagaland, Saman
Aralia racemosa Linn.	American spikenard	nagaland
Asparagus racemosus Wind.	ShatawarlSatawar	Goa, Maharast)tra, Arunachal Pradesh, Guiarat, Himachal Padesh, Rajasthan, Uttar Pradesh
Azadirachta indica A. Juss.	Neem	Imphal, Jaipur, Goa, Maharashtra, Dadra & NH, Guiarat, Daman & Diu, Uttar Pradesh
*Bacopa monnieri (*Linn.)	Brahmi	Goa, Gujarat, Andhra Pradesh
Boerhaavia diffuse Linn.	Punarnava	Maharashtra
Bryonia alba Linn	Wild hops	Maharashtra
Carum carvi Linn.	Krishnaiirak-Kalaiira	West Bengal
Cassia fistula Linn.	Amaltas/Khivarshamber	Bihar
Centella asiatica (Linn.) *Urban*	Manduk parni	Mizoram
Cinnamomum zeylanicurn	TwaklDalchini	Imphal, Mizoram, Bihar
Commiphora wightii [Arn.]	Guggal	Uttar Pardesh,Goa ,Guirat, Maharashtra
Crataeva nurvala BuchHam.	Varun	Maharashtra, Gujarat
Curcuma zedoaria Rose.	Kachor/Zarambat	Mizoram, Naaaland, Meahalaya

Desmodium gangeticum	Salparni	Rajasthan
Embelia ribes Burm.f.	VayavidanaalBaobarana	Mizoram
Emblica officinalis Gaertn.	Amala	Uttar Pradesh, Tripura, Goa, Maharashtra. Guiarat
Ephedra gerardiana Wall	Somlata	Himachal Pradesh
Gentiana kurroo Rovle.	kuru	Himachal Pradesh
Gloriosa superba Linn.	Langali	Maharashtra
Hemidesmus indicus R.Br.	sariva	Mizoram
Ipomoea petaloidea Choisy	VidharalKali Nishoth	Bihar
Lavandula stoechas Linn.	Ustukhuddus	Himachal Pradesh
Mallotus phillippinensis	KamilalQimbeel/Kampillak	Mizoram
Mesua terrae Linn.	Nagkesara/Narmushk	Mizoram, Maharashtra, Dadar & NH,
Mucuna prurita Hook	Kawanch	Maharashtra
Nardostachvs jatamansi DC	Jatamansi/Sumbul ut Teeb	Himachal Pradesh
Ocimum sanctum Linn.	Tulsi	Imphal, Tripura, Goa, Dadar & NH, West Bengal, Gujarat, Andhra Pradesh, Daman & Diu
Oroxylum indicum Vent.	shayonak	Mizoram, ArunachalPradesh
Paeonia officinalis Linn.	Ood saleeb	Bihar
Picrorhiza kurroa	Kulaki	Arunachal Pradesh, West Bengal, Bihar, Himachal Pradesh
Piper chaba Hunter	Chab, Peepal chab	Imphal, Tripura, Gujarat, Uttar Pradesh
Piper longum Linn.	Pippali, Filfildaraz	Imphal, Arunachal Pradesh, Karnataka, Gujarat
PlumbaQo zeylanica Linn.	Chitrak/Sheetrai Hindi	Raiasthan
Polygonatum cirrhitolium	Mahameda, Meda	Himachal Pradesh
Rosa damasena Mill	Gulab phool	Dadra, Uttar Pradesh
Salmalia malabarica	Semal/Mocharas	Bihar
Saraca asoca (Roxb.)	Ashoka	Maharashtra, Gujarat, Uttar Pradesh
Sida cordifolia Linn.	Kanghi	Meghalaya, Bihar
Strychnos nux-vomica Linn.	Kuchla/Azaraqi	Maharashtra
Swertia Chirata Buch. Ham.	Chirayata	Himachal Pradesh, Meghalaya
Terminalia arjuna W. & A.	Arjuna	Maharashtra, Andhra Pradesh
Terminalia chebula Retz.	Harar/Halela Zard	Meghalaya
Thuja occidentalis Linn.	Arbor Vitae	Maharashtra
Tinospora cordifolia (Wild)	Giloe, Guddchi	Imphal, Maharashtra, Gujarat
Trachtysperumum ammi	Ajwaien	West Bengal
Trichosanthes dioica Roxb.	Parval	Maharashtra
Trigonella foenum-graecum Linn.	Methi/Hulba	Uttar Pradesh
Urtica urens Linn.	Stinging nettle	Meghalaya
Vitex negundo Linn.	Nirgundi/Sambhalu	Meghalaya

Withania somnifera Dunal.	Aswagandha/Asgandh	Gujarat, Imphal, Tripura, Maharashtra, Arunachal Pradesh, Rajasthan, Himachal Pradesh, Karnataka, West Bengal, Bihar

6. Priorities of Drugs from Plants during 21st century

It is extremely important and desirable to have "need based" approach for drug development from medicinal plants- this was the major objective of a W.H.O. regional group which met in 1980. Efforts thus should be directed to a number of diseases for which suitable or satisfactory drugs are not available in the modern system of medicine and where plant based drugs have a possibility of offering drugs for the ailing humanity, some such areas are delineated and where medicinal plants have already provided promising leads.

6.1 Antiprotozoal drugs from plants

Tropical diseases including malaria where tissue schizontocidal drugs are needed and drugs for multi-drug resistant blood schizonts are required. It has been estimated that one third of the world's population is exposed to the risk of malarial infections[8,9]. Most hard hit areas include Africa, India, China and East Asia. For Malaria, Quinine from *Cinchora* bark, the first antimalarial drug used gave birth to many synthetic antimalarials like primaquin, pamaquuin, chloroquin etc none of which nowdays work against resistant strains of malaria parasite. Artemisinin, a unique novel molecule from *Artemisia annua* gave birth to new antimalarial drugs like Artether which works against resistant strains of the parasite and has been approved by the WHO. Other promising antimalarial plants include *Alstonia scholaris, Ceasalpinia bonducella*, *Picrorhiza kurrooa*, *Swertia chirayata, Berberis* species, *Triclisia patens, Tilicora triandra*. Amoebiasis caused by *Entamoeba histolytica* is the major cause of dysentery in the. developing world where an estimated 42 million cases occur annually and untreated disease may progress to hepatic amoebiasis and other complications which are responsible for 75,000 deaths each year[10]. Filaria and leishmania are two other protozoal diseases affecting our population, Many plants like *Peganum harmala. Celastrus paniculata, Artemisia annua, Berberis aristat.a, Tilicora triandra* have been reported[11,12] to have activities against various species of protozoa and a variety of such plants have been well illustrated in several recent reviews[13-16]. For amoebicidal drugs plants like *Holarrhena antidysenterica, Berberis aristata*[17], *Allium sativum*[18] and *Terminalia belerica*[19] need serious attention. Worldwide it has been estimated that 20 million people are infected with *Leishmania* species and that 400,000new cases occur each year[20]. The plants which have given leads include *Plumbago zeylanica*[21], *Diospyros Montana*[22], *Ricinus communis* and *Pytolacca*[23] species.

6.2 Antiulcer drugs from plants

Important plants for the treatment of gastrointestinal ulcers that have promising prospectus as useful drugs include *Prosopis glandulosa*, *Calendula* species. *Arto carpus integra*, *Musa ferrea* (pulp) and deglycyrrhizinated *Glycyrrhiza glabra* and many others which have been reviewed by Lewis & Hanson[24].

6.3 Antirheumatic plants

Inflammatory diseases including different types of rheumatic diseases are very common throughout the world. Although rheumatism is one of the oldest known diseases of mankind and affects a large population of the world, no substantial progress has been so far achieved for permanent cure. Our review reveals that plant species of ninety six genera belonging to fifty six families have exhibited antiinflammatory activity[25]. Most significant plants include *Aesculus hippocastanum, Azadirachta indica, Boswellia serrata, Commiphora mukul, Curcuma longa, Ochrocarpus longifolia, Pluchea lanceolata and Vitex negundo*[26-28].

6.4 Medicinal plants for diabetes

The world over there are 150 million people suffer from diabetes. In India during 2001 thirty million people were diabetic. In ten years time, India will be world capital in diabetes as per WHO. Over one hundred plants used in Prameha (diabetes) where as several plants have been reported hypoglycemic[29a].

About 148 plants of 50 families reported to have hypoglycaemic activity have been reviewed by us[29]. The most important hypoglycaemic plants which need serious clinical trials include *Pterocarpus marsupium, Momordica charantia, Trigonella foenum-graecum, Salacia prinoides, Gymnema sylvestris and Cyamompis tetragonolobus.*

Each region of the world has developed a material medica of antidiabetic remedies based on the local flora. It is apparent that diversity as well as similarity can be found in the use of plants across the world. The extent to which various antibeietic plants have been studied differ widely. For some (fenu greek, bitter melon or *Gymnema sylvestre*) detailed studies in humans, animals and in-vitro have resulted in the isolation of active compounds with recognizable modes of action. An interesting finding is that plants typically have more than one active compound often associated with more than one mode of action. Additive or synergistic effects between compounds undoubtedly occur, conforming to the view of traditional medicine practitioners that the activity of a medicinal plant cannot be reproduced by the isolation of single active component. Nevertheless, identification of actives and mode of action are important for drug development and for the validation, standardization and rational use of the herbal drugs[29a].

6.5 Antiasthamatic plants

In the lack of any permanent cure in the modern system of medicine for bronchial asthma, plants like *Albizzia lebeck* which have immunomodulatory action need serious attention. Other polyherbal ayurvedic formulations like Yastiadivati and Shereeshadi Kashaya may prove to be efficacious[30]. Other plants include *Acalypha indica, Adhatoda zeylanica, Boswellia serrata, Inula racemosa, Tinospora cordifolia.*

6.6 Antiviral plants

A global dengue pandemic that started during world war II has progressively spread to involve nearly all tropical countries resulting cumulatively in 5 million hospitalized children and causing 70,000 deaths from DHF/dengue shock syndrome (DSS)[30a,30b]. Currently about 2.5 billion people in over 100 tropical and subtropical countries, representing 50% of world population are at risk from dengue W.H.O. estimates 100 million cases of dengue infection worldwide every year[30a,30b]. Experimental work on a number of plants having antiviral activity has been done[31-34]. A lyophilized infusion from flowers of *Sambucus nigra,* aerial parts of *Hypericum perforatum* and roots of *Saponaria officinalis* exhibited antiviral effect inhibiting reproduction of different strains of influenza virus types A & B, both *in vitro* and *invivo* and herpes simplex virus type 1 *in vitro*[35]. These plants need to be carefully examined.

6.7 Iimmunomodulators and adaptogenic plants

The notion of "resistance" to disease and the idea that such resistance can be modified by life experience and by emotional states, forms one of the basic tenets of Ayurveda thus avoiding the Cartesian dichotomization of mind and body[36]. Concept of Rasayana and Rasaayan plants have been reviewed by the author[37-38]. Plant of interest in this area include *Withania somnifera, Ocimum sanctum, Picrorhiza kurroa, Asparagus racemosus, Pueraria tuberose, Sida cordifolia, Desmodium gangeticum, Boerhaavia diffusa and Cissampelos*. We need to develop suitable models for testing such vital plants of Ayurveda. Immunomodulatory plants have been recently reviewed [38a].

6.8 Hepatoprotective Plants

A global estimate indicates that there are about 18,000 deaths every year because of the liver cirrhosis mainly caused by hepatitis. Hepatocellular carcinoma is one of the ten most common tumours in the world with over 2,50,000 new cases each year. Although viruses are the main cause of liver diseases, the liver lesions arising from xenobiotics, excessive drug therapy, environmental pollution and alcoholic intoxication are not uncommon. Modern drugs have very little to offer for alleviation of hepatic ailments, whereas, most important representatives of phytoconstituents used for liver diseases, chiefly on regional basis, include drugs like silymarin *(Si/ybum marianum),* catechin *(Anacardium occidentalis* and others) in Europe, glycyrrhizin (*Glycyrrhiza glabra*)

in Japan and schizandrins *(Schizandra chinensis)* in China[39]. In India, we have 140 polyherbal commercial formulations reputed to have hepatoprotective action. A review published on the subject from our laboratory indicates that 160 phytoconstituents from 101 plants belonging to 52 families have antihepatotoxic activity[40-41]. Our laboratory has worked extensively on *Andrographis paniculata*[42] and hepatoprotective activity has been established due to the presence of andrographolide. Kutkoside from *Picrorhiza kurroa* is a potential hepatoprotectant reported by CDRI [43-47]. *Phyllanthus amarus* is another most important plant selected for clinical trials[48]. Our future work in this area is bound to give fruitful dividends. Antihepatotoxic activity of *Boerhavia diffusa* and *B.repanda* has been also reported from our laboratory[49]. Kolaviron, a mixture of *Garcinia kola* (Guttiferae) biflavonoids at a dose of 100 mg/kg i.p. prevented thioacetamide induced hepatotoxicity[50]. *Withania fruitescens* (Solanaceae) leaves exhibited protective and curative action against carbontetrachloride induced liver toxicity[51]. Plant kingdom appears to be a fruitful ground for the discovery of effective hepatoprotective drugs, which we currently lack in the modern system of medicine.

6.9 Anti-cancer Drugs from Plants

Cancer is an insidious disease affecting mankind in every country. Work on periwinkle plant. *Catharanthus roseus* (L >) G. Don was independently taken up in two different laboratories for its alleged hypoglycaemic activity as per Jamaican folklore. Though none of the groups could substantiate hypoglycaemic activity, the Canadian group of Nobel Beer and Cutts succeeded in isolating vinblastine while Eli Lilly group headed by Svoboda could isolate vinblastine and vincristine along with two other active dimeric alkaloids. These alkaloids are present in exceedingly low concentrations in a complex mixture of 50 alkaloids[53]. Vinblastine was introduced (Velban, Eli Lilly) in 1961 and vincristine (Oncovin, Eli Lilly) in 1963 as anticancer drugs. CIPLA has improved upon the process of isolating vinblastine and vincristine from *Catharanthus roseus* as developed by NCL Pune. Today we are the third largest manufacturer of vinblastine and vincristine in the world and we are exporting these alkaloids to European countries and the demand is steadily increasing[54].

Screening of plant extracts for anticancer activity started in 1961 by National Cancer Institute of the U.S.A., and up to 1981 (20 years) about 1,14,045 plants had been screened, of which only 3.4% (representing about 3.400 different species) have been observed to be active in one or more bioassay systems. The promising phytoconstitutents which are likely candidates for drug uevelopment include indicine N-oxide (a pyrrolizidine alkaloid) from *Heliotropium illdicum.* ellipticine (a monomeric indole alkaloid) from several *Ochrosia* species, homoharringtonine (a cephalotaxine alkaloid) from *Cephalotaxus* species, taxol[55] from *Taxus* species and camptothecine (quinoline alkaloid) from *Camptotheca acuminata* a Chinese tree)[56]. The author has been successful in discovering a number of anticancer agents from plants like *Ostodes paniculata*[57], *Peddiea*

fischeri[58], *Soulamea soulameoides*[59], *Dirca occidelltalis*[60] and *Passerina vulgaris*[61]. The anticancer principles of podophyllum are contained in the resin, podophyllum resin or podophyllin. American podophyllum yields 2-8% and Indian podophyllum about 6-12% of the resin. It is not only the higher amount of the resin present in Indian podophyllum *(P. emodi* var. *hexandrum)* but there are no peltatins present in contrast to American podophyllum *(P.peltatum)* which contains (α and β- peltatins. Thus, the Indian podophyllum has higher amount of podophyllotoxin. In certain cases Indian podophyllum has yielded 20% resin. The highest amount is in May when the plant produces flowers. Thus the Indian podophyllum, when collected at the proper season not only contains 2 ½ times or even more of the resin compared to American podophyllum, but this resin has double the amount of podophyllotoxin which is the active principle used by pharmaceutical industry for structural modifications to produce anticancer drugs tenoposide and etoposide being marketed by Sandoz. Major problem with the cultivation of this plant is that the seeds take very long time to germinate. We need to concentrate on cultivation of this plant either by propagation or by reducing the period of seed germination. Use of Taxol from *Taxus brevifolia* or *Taxus baccata* is the latest addition of anticancer drug especially in ovarian cancer[62].

6.10 Plants for Urinary Stones

The very first mention of 'Pashanbhed' in Ayurvedic literature is in Charak Samhita, and is recommended for painful micturition and for breaking calcui. Sushrut Samhita mentions the drug under various synonyms - Pashanbhed for uric acid calculi and Ashnibhed for biliary calculi. Sushrut Samhita mentions decoction of Pashanbhed, Astimantaka, Satvari, Vrihati, Bhalluka, Varuna *(Crataevanervula),* Kultha *(Dolichos bijlorus),* kola and katak seeds for patients of Vataja Ashmari while Kusa, Ashmabhed, Patala, Trikanthaka, Sirisha, Punarnava (Boerhavia diffusa) and shilajit are for Pittaja Ashmari. About 4000 plants have been mentioned to be useful for dissolving stones in the urinary system in a review published seven years ago[63]. Cystone of Himalaya Drug Co. and Calcury of Charak Pharmaceuticals are already in the market. *Crataeva nervula* bark and *Tribulus terrestris* fruits have been put under clinical trials by Indian Council of Medical Research, *Cucumis trigonus* (curcurbitaceae) has been investigated for its diuretic activity[64.]

6.11 Plants as Sedatives/Tranquillizers

Indian valerian *(Valeriana waltlchii)* contains 2% valepotriates and is thus four times more potent than European valerian *(V. officinalis)* which contains 0.5% valepotriates. These are triesters of polyhydroxy cyclopentanop,Yran esterified with isovaleric, acetic and β-acetoxy valeric acid. Compared to known iridoids, valtrats (valepotriates) are neither glycosides nor lectones and are considered original or primary products present in the drug responsible for activity. Valtrates

are used as tranquillizers and sedatives, and the action is comparable to meprobmate. Additional advantage is that these can be prescribed to alcoholic patients. Valerian also contains valernic acid having spasmolytic action. Valeranone is found in jatamansi *(Nardostachys jatamansi)* possessing sedative property. It will be worthwhile to produce valepotriates in India. A peruvian plant *Valeriana thalictroides* has been found to contain 14.5% total valepotriate content in the roots and thus yields the highest known concentration of valepotriates in plants to date[65]. The high yield of valepotriates in *V. thalictroides* roots. cannot be directly used to overcome shortage of valepotraites for therapeutic use, as the roots have very small diameter (2 cm) and a length of about 5 cm. *V. edu/is* ssp. procera (HBK) F.G. Mey, although having a smaller valepotriate content (7%), is a much better source for valepotriates because of its higher drug yield. However, such high yielding plants could be used to establish high yielding tissue culture for the *in vitro* production of valepotriates. Relation between valepotriate content and differentiation level in various tissues from valerianaceae has been studied[66]. Isolation and evaluation of valepotriates from Indian valerian are well known[67].

6.12 Plants for mental health

For psychomimetic and/or euphoria inducing effects, 217 plant species representing 146 genera belonging to 59 families have been used at one time or another at various mental disorders. The substances of plant origin such as extracts of *Gingko biloba*, papaverine from *Papaver somniferum* fruit latex, theophylline commonly occurring purine base in tea leaves, vincamine indole alkaloid from V*inca minor* hydrated semisynthetic ergot alkolids have been experimentally evaluated with regard to their cerebrovascular activity in patients. Medhya rasayana plants such as Bacopa monniera, centella asiatica, convolvulus pluricaulis, nardostaychs jatamansi and acorus calamus have been reported useful for mental disorders[67a].

6.13 Plant Laxatives

Constipation is a common problem of Western and European countries because of protein rich diet. In the U.S.A., 1000 patents of vegetable origin are there which involves an annual trade of $ 500 million. On an average we export 15,000 tonnes of plantago, 7000 tonnes of senna and 1000 tonnes of rhubarb annually. Trade in plant laxatives increases by over 10% every year. India is the sole supplier of *Plantago ovata* seeds and husk (psyllium) in the international market. India's export of Psyllium seeds in 1980-81 were to the extent of 25,743 metric ttonnes valued at Rs.85.93 million. Indian Institute of Management, Ahmedabad has published recently a survey report on the psyllium production and marketing in India[68].

6. 14 Antihyperlipidemic (lipid lowering) plants

Obesity and high lipid content constitute a serious life style problem in the developed countries and in the affluent class of the developing countries. In the year 2000 the world statin market size was US$ 16 billion with three products viz. Merck's Zocor (Simvastatin), Pfizer's Lipitor (Atorvastatin) and Bristol Meyers Squib/Sankyo's Pravachol (Pravastatin) accounting for 89

percent of sales. The world market of Statins has gone up over $ 25 billion (11 percent annual growth). *Commiphora wightii,* Oleogumresin (Guggul) has scientifically proven lipid lowergin property and 'Guggulip' developed by CDRI, Lucknow commercially transformed to CIPLA has great market value but the raw material is a serious problem as not many trees ae left and new tree if cultivated takes over 10 years before it yields guggul.

Other plants mentioned in Ayurveda as 'Lekhanaya' have great potential for developing lipid lowering drugs. Potential 'Lekhanaya' plant mentioned in Ayurveda are as follows:

Lekhaniya Gana

As per Chakrapani Sutrasthan

Musta	*Cyprus rotundus*
Kushta	*Saussures lappa*
Haridra	*Curcuma longa*
Daruharidra	*Berberis aristata*
Kutki	*Picrorhiza kurroa*
Ativisha	*Aconitum heterophyllum*
Karnaj	*Pongamia pinnata*
Chitrak	*Plumbago zeylanica*
Vacha	*Acorus calamus*

6.15 Plants drugs for cardiovascular system

Cardiovascular diseases are most prevalent of all diseases. Two thirds of the deaths result from cardiovascular diseases and number one killer in the world. Cardiovascular drug market is US$ 50 billion per year. Most important cardiotonic, antiarrhythmic and antihypertensive plants are given below[68a].

Cardiotonics

Terminalia arjuna bark
Nerium oleander
Thevetia nerrifobia } Asclepiadaceae
Carrisa edulis
Asclepias curassavica

Antiarrhythmics

Cinchona sps. (Rubiaceae) (quinine)
Fagara zanthoxyloids (α-fagarine)
Rauwolfia serpentine (Raunavine, ajmaline)
Cytissus scoparius (sparteine)

Antihypertensive

Rauwolfia serpendina (reserpine, rescinnamine deserpidine)
Uncaria rhynchophylla (rohynachophylline)
Nardostachy jatamansi (valeranone)
Inula helenium (alanto lactone)
Arnica Montana (helenalin)

Coleus forskohlii (forskoline, coleonol)
Veratrum & Fritillaria sps (veratrum alkaloids)

...

7. Pitfalls in Plant-drug Research and Implications

Medicinal pant research is beset with a number of problems and the major stumbling blocks encountered in plant drug research are listed below:

(a) Medicinal plants being used by traditional practitioners in India not only bear different names in different geographical areas and in different languages, but it is also not uncommon that different plants are known by the same name which add to the confusion and has resulted in controversial identity of many plants[69].

(b) Major causes of inconsistancy in plant drugs include ontogenetic, ecotypic, genotypic and chemo typic besides variations due to harvesting period, method of drying and storage conditions.

(c) Ayurvedic, unani practitioners invariably use polyherbal formulations, whereas, for obvious reasons, it is easier for the modern scientists to investigate single plant drug.

(d) Appropriate experimental models are not available for validating claims of some very important and useful plant drugs like "Rasaayana" enjoying esteemed repute in Ayurveda and termed in modern terminology as vitalizers, rejuvenators, adaptogens, immunomodulators etc.

(e) Major national laboratories resorted to more broad based screening of plants[70] 70 by including, apart from plants which are well known and time tested by traditional systems of medicine, those which are not mentioned by these systems. Others undertook studies largely on individual initiatives. Inspite of all these efforts, however, the ultimate goal of producing inexpensive, safe and efficaceous drugs for most diseases encountered in our country remains to be achieved.

(f) The major bottleneck, however, is the lack of scientifically planned clinical trials on traditionally used medicinal plants. Though research work on medicinal plants has been carried out in Indian research establishments since long but not much has been achieved. The beneficial phase of a multidisciplinary integrated approach to the evaluation of plants initiated by the Composite Drug Research Scheme seems to have be almost lost in the pages of history. Recently, however, Indian Council of Medical Research has adopted new strategy of disease oriented approach of carrying out clinical trials on medicinal plants selecting certain 'refractory diseases' i.e. those for which modern medicine has

not been able to offer, so far, a satisfactory or a lasting remedy.

(g) The novelty and popular trend on the part of the phytochemists and pharmacologists to continue efforts to find out an "active principle" responsible for the pharmacological action and therapeutic efficacy of a plant, in many instances, has also led to frustrating results. Pharmacologists and phytochemists engaged in medicinal plant research may have to change their approach to wholistic plant material or with semi pure principles or even crude extracts. Gum guggul *(Commiphora wightii)* is a classic example.

(h) Except for Central Drug Research Institute, Lucknow, little facilities exist elsewhere in India for carrying out pre-clinical evaluation including toxicity tests on medicinal plants.

(i) Clinical evaluation of plant drugs is an area which is handicapped with lack of facilities and proper orientation of scientists of different disciplines. At present, for lack of such facilities even the leads obtained so far are being lost to follow-up.

8. Herbal Drug/Intellectual Property Rights (IPR)

Medicinal plant research has been and continues to be considered as a fruitful approach for the search of new drugs[71]. The highly respected magazine *Science* calls attention in its editorial of February, 1990 to the potential of medicinal plant in the search of new drugs and expresses concern about the consequences that loss of biodiversity might have in this context. Since most of the chemically unknown flora and associated medicinal lore exist in the developing and underdeveloped countries, especially those which still possess extensive tropical forests, the rapid loss of biodiversity does indeed become an issue for the future of medicinal plant research. The traditional role of developing countries in plant drug production has been as suppliers of raw material. Most of the pharmacological and chemical studies reported in several journals start by quoting the traditional use of a given plant species promising enough to stimulate further research. It is, therefore, reasonable to assume that the indigenous knowledge did play an important role in medicinal plant research and will continue to do so. Posey[72] calls for legislation to secure Intellectual Property Right for indigenous people.

9. Herbal Drug Trade

The extent of herbal drug usage is hard to quantify for traditional systems of medicine in India as by tradition many of the practitioner manufacture and formulate their own prescription, although there are now about ten well organised large scale herbal drug manufacturers whose individual annual production is of about $ 112 million (June 1988). Their total annual turnover is about $ 350 million[73]. In U.K. there are about 5,500 herbal products involving 1,600 herbal ingredients. It is estimated that some 6,000-7,000 tons of herbs are extracted annually for the ingredients in U.K. medicine[74]. Like India, China is another country which is noted for its adherence to herbal medicines for a number of

therapies like in the treatment of abdominal conditions (appendicitis, perforated ulcers, pancreatitis), arthritic disease and some neurological disease. There are about 248 herbal drugs used for a number of reasons e.g., analgesic sedative, diuretic, anti-tussive, antirehumatic and antiasthmatics[75].

Herbs and the literature about them are big business in America. In 1985 the sales of all forms of herbs exceeded $ 190 million. Unfortunately, most of the literature prepared with a single purpose in mind-to sell a product, since to do so most effectively, it is necessary to promote or advocate all of the good features of the herb while minimizing, or even omitting, any negative aspects, such writings are generally referred to as advocacy literature[76].

Current federal laws do not permit the sale of herbs as drugs, that is, with claims of efficacy appearing on their labels. If such claims are made, the efficacy must be proven to the satisfaction of the Federal Food & Drug Administration, a process as much as $ 100 million per drug. Since no one is willing to spend this amount of money on a product for which patent protection is not available, herbs are sold labelled only with the name of the product, primarily in 'health food' stores. Literature purporting to explain the uses of herbs is also available in such establishments. Because the laws and regulations applied to food naturally do not require any proof of efficacy prior to sale, some manufacturers attempt to market herbal products as nutrients or food supplements, by combining a variety of herbs with standard multivitamin mineral preparation and often make extravagant claim for the products based-on their herbal contents.

10. Herbal Medicines - Medicinal Marvel or Money Spinning Malarkey

Ayurveda, with many centuries of experience and cultural support has strengths which should be used only through the experts and vaidyas in Ayurveda or by modern physicians, who have undergone practical training and experience in Ayurveda. But gross and rampant commercialization of Ayurvedic herbal remedies, by all and sundry, has to be criticized and even condemned. With the onslaught of m'edia television, radio and press several herbal formulations are promoted, often indiscriminately. Consumer associations are very quick and rightly so, when unscientific claims are made by ethical modern drugs. Should they not take up issue with very tall claims by the so-called herbal drugs by commercial interests? There is an urgent need to create an ethical code for advertising and promotion of Ayurvedic drugs.

11. Sociopolitical, Economical & Ethical Issues in Medicinal Plants Research

Due to enormous difference of wealth generated by supplying crude medicinal plant material versus the purified isolated phytoconstituent, the developing countries remain the worst sufferers. It therefore, calls for legislation to Secure Intellectual

Property Right (IPR) for indigenous people. What are the ethics behind utilizing traditional knowledge without adequate compensation to the societies from which it originates.

12. Herbal Drug Development

One may propose a development procedure tailor made for herbal drugs. Traditional medicine usually consists of if mixture of herbal drugs.

In the first step the therapeutic efficacy of the traditional medicine has to be confirmed. Of course, the composition of the recipe has to be affirmed and authenticated by Pharmacognostic methods which means that we have got to be sure which plant, identified by botanical nomenclature, and which part of the plant to which percentage is used. Only in the country where the recipe has been used traditionally clinical trials can be performed. These trials have to be carried out as scientifically as possible. Well defined clinical parameters have to be evaluated in a population of patients with well defined diagnosis. In India such clinical trials on traditional medicines have been initiated by the Indian Council of Medical Research adopting disease oriented approach.

In the positive outcome of such studies we proceed to the second step. We have to select one, perhaps in some cases two or three plants as the active ingredients. This can be done by animal pharmacology or clinical pharmacology. At this stage we have to attempt standardization employing all possible means like finger printing, TLC, HPLC or other related techniques. The clinical trials are performed against a placebo. In each case we have to use as much well defined clinical parameters as possible in order to establish the efficacy of the drug. If the results are positive, we can proceed to the next step where we use purified extract being standardized for the reprocessed extract, we can establish mode of action and also carry out toxicological studies in animals which become mandatory since we now use much higher concentration of the drug than used in the original recipe. With this standardized extract we can perform placebo controlled clinical trials, which still should be performed in the country of origin. Nevertheless, we make our first attempt to submit something like Investigational New Drug (IND) in order to be allowed to perform phase I or even phase II clinical studies outside the country of origin. If the results are positive we can proceed to internationalization of the product. There are some countries in the world where the health authorities have a positive attitude to herbal drugs. In these countries facilitated approval may be possible. They can be fore runners for other countries where the developmental requirement would be the same as the synthetic compounds[77].

13. Quality control and standardization of Herbal Drugs

The single and most important factor which stands in the way of wider acceptance of traditional herbal medicines is the non-availability or inadequacy of standards for checking their quality by chemical or bioassay methods. This also prevents

modernization or modification of the methods of their preparation or production. as there is no way to establish the equivalence of the product made by the modified method with the original product. Thus standardized drugs of well defined consistent quality are needed for reliable clinical trials and therapeutic use. The major reason advanced for the difficulty in developing quality control standards is that these products use whole plant or parts of plants or their total extracts, and in some cases even a mixture of a number of plants, it is thus challenging to develop suitable standards because a vegetable drug or a preparation thereof is regarded as one active ingredient in its entity, whether or not the constituents with therapeutic activity are known. Standardization, of a herbal drug and of a preparation thereof is not just an analytical operation, it does not end with the identification and assay of an active principle rather it embodies total information and controls which are necessary to guarantee constancy of composition. Standardization of plant drugs has been stressed by the World Health Organization[78].

14. Concluding remarks

The following four slides exhibiting road map to development from medicinal plants and growth of the essential oil area fives a message to this institute for potentiating its endeavours in the development of medicinal and aromatic plants with in its mandate especially in the economic mapping of MAPs, development of agrotechnologies, post harvest technologies, quality control and biodiversity conservation for sustainable industrial utilization of medicinal and aromatic plants.

ROAD-MAP TO DEVELOPMENT OF SAFE, EFFICACIOUS, QUALITY ASSURED SCIENTIFICALLY VALIDATED TRADITIONAL DRUGS AND MODERN DRUGS FROM PLANTS: A → "TRADITIONAL HERBAL DRUG"

1

Resort to cultivation of MAPs following **GAP** and organic farming. **Agrotechnology**

2

Taking care of post-harvest technology to ensure quality of raw material
GGP

3

Adopting appropriate ext. technology, percolation, soxhlet extn, steam distillation, S-CO_2 extn, Phytonic extn.
GEP

4

Use appropriate drying technology e.g. Spray drying, tray drying, vacuum drying, freeze drying
GDP

5

Choose an appropriate Formulation Technology e.g. powders, liquid orals tablets, capsules using right excipients and following
GMP

6

Ensure quality specifications confirming identity, purity, quality including stability studies, chromatogrphic finger printing with marker ensure assay, adopt
GLP

7

Generate safety data including general toxicity, cytotoxicity, genotoxicity herbal drug: modern drug interaction through CYP450 study
GLP

8

Well designed statistically valid human clinical trials

GCP

9

Pharmacovigilence studies

(Period 3 yrs; cost US$ 10 Mn.)

MODERN DRUG FROM TRADITIONAL HERBAL SOURCE

- Plant selection – basis: traditional, folklore, scientific knowledge
- Appropriate extraction technology – Activity of each extract
- Bioactive extract fractionated directed by bioactivity
- Fractionation by Sepbox – Activity of each fraction (MTS, HTS)
- Isolation of bioactive molecule – confirm structural and molecular purity
- Reconfirmation of bioactivity by *in-vivo* model
- Examine drugability of the molecule
- IPR protection
- Scale-up isolation of the bioactive
- Bioavailability/pharmacokinetic, ADME studies of the molecule
- Safety evaluation
- Clinical studies phase I, II, III

(Period 10-12 yrs; cost US $ 1 Bn)

ESSENTIAL OILS

- **WORLD PRODUCTION:** (Vol) BRAZIL (40%), USA (20%) INDIA (15%)
  (Value) USA (26%), INDIA (21%), BRAZIL (8%)

- **TRADE/COMMERCIAL ADVANTAGE**: EXPLOIT LOW VOLUME, HIGH VALUE DERIVATIVES

  INDIAN'S SHARE IN WORLD EXPORT OF ESSENTIAL OIL AND PERFUMERY MATERIAL } 0.4%

- **OUR WEAKNESS** : VERY LITTLE VALUE ADDITION

- **IMPROVING & PROMOTING** : EXTRACTION AND FRACTIONATION PROCESSES **AND TECHNOLOGIES**

- AROMATIC PLANTS OFFERING EVIDENCE OF LARGEST NUMBER OF CHEMICAL RACES : LET US EXPLOIT HIGH VALUE PHYTOCONSTITUTENT CHEMOTYPES

ESSENTIAL OIL

MENTHA OIL & MENTHOL PROD. → India today world leader

EUCALYPTUS
50,000 tonnes
total India only
200 tonnes

E. Globulus (Cineolrich >70%
E. macrorrhincha (Rutin 8%)

ORANGE/LEMON OIL : biproduct of juice industry
(lemonene) 80,000 tonnes 2000 tonnes : USA, Brazil, & South America

Citronella oil : CHINA, INDONESIA, INDIA
4000 TONNES FOCUS ON HGIH
GERANIZOL, CITRONELLOL
CONTENT

LAVENDER & LAVANDIN OILS **:** BULGARIA MAJOR PRODUCER
1500 TONNES (NATURAL ONLY 33%) KASHMIR VALLEY CAN COMPETE.

RESINOIDS GUMBENZOIN, GUMLABDANUM, BALSAMTOLU

We need to introduce plants yielding these products

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