

Prospect of Herbal Drugs in the Age of Globalization—Indian Scenario

A Goswami, P K Barooah* and J S Sandhu

Regional Research Laboratory, Jorhat, Assam

There are 2,50,000 known species of higher plants on the Earth and some more may be discovered. Of these, only six per cent have been analysed chemically and only a small fraction pharmacologically. According to pharmacopoeia of the world, at least 119 distinct chemical substances derived from plants are important drugs currently—used within 62 therapeutic categories, and 91 species are the source of these drugs. India has a vast reservoir of 400, 000 Ayurvedic, Siddha, Uninani or Homoeopathic practitioners, hardly used adequately in the health care delivery system. Nearly 80 per cent of drugs used in Indian system of medicine and homoeopathy are derived from plants. With 46, 000 licensed pharmacies manufacturing and satisfying the needs of traditional remedies, large-scale cultivation of medicinal plants must be planned. A number of CSIR laboratories, University departments and hospitals, other scientific institutions are participating in the further evaluation and finetuning of such drugs through use of modern methods and tools. With pooled resources, efforts are being made to reach the goal of development of new drugs, herbal preparations, pest management agents, bio-enhancers, and drug delivery systems. A few examples have been presented in the face of globalisation and WTO.

Introduction

Since independence, the Indian pharmaceutical companies have contributed significantly towards the growth and development of health sector. They have launched several generic drugs in the segment of antibiotics, anti-inflammatory, anti-diabetics, tuberculosis, anxiolytics and anti-migraines. However, due to the fast changing trend in the world scenario in Intellectual Property Right (IPR), about \$30 billion worth of drug will go off-patent globally by 2005 and will reach \$80 billion worth of drug by the year 2010. Although, this might be a rewarding situation to many Indian Multi National Companies (MNC's), however, the small and medium drug manufacturers will encounter a stiff competition. Consequently, the Indian pharmaceutical companies, which have been contributing to Indian drug market, are facing great threats for their co-existence in the global market. The situation has become more alarming due to India's participation in GATT agreement, which allows 100 per cent direct investment of foreign MNCs in pharmaceutical sector of India from 2002.

Pharmaceutical R&D for new drugs has been carried out for almost five decades in India, in the government, academic and industrial sectors. Indian medicinal chemists, pharmacologists, analysts, toxicologists and clinical investigators are of world class.

The Government of India has allocated Rs 150 crore for R&D in the pharmaceutical sector. But the cost of development of a single drug in the US is reported to be \$110 million, which will be Rs 52.8 crore at the present dollar to rupee parity¹. Due to this, the drug price is going higher and unaffordable for the common people. In spite of these problems, some of the pharmaceutical R&D units of MNCs in India, like CIBA-GEIGY, Hoechst, Reddy's Laboratory and CSIR Laboratories have done commendable work and have developed and marketed some very important drugs. So, it is of crucial importance for our pharmaceutical industry's healthy survival and robust progress in the future to ensure continuous free availability of essential drugs. For this purpose, it is needed to stress on investment for R&D and upgrade manufacturing plant to the world standard.

Further, it takes long time for a new drug to come to market as a result the drug price increases to the extent of becoming unaffordable for the common people. On the other hand for quite some time, there has been a general feeling among the public that single molecule used by allopathic system of medicine are toxic. Recent investigations are proving this impression to be correct. A report published in 1998 in the *Journal of American Medical Association* (JAMA) shows that adverse reactions to prescription drugs forms 4th to 6th largest cause of death in the US. This finding is enormously alarming, on the other hand, herbal preparation are considered to be safer,

* corresponding author, email: pkbarooa@csir.res.in

¹ crore =10 million

less expensive and have been used for thousands of years in traditional system of medicine. The Food and Drug Administration (FDA) used to permit the use of herbals as food supplements earlier. However, it has now decided to permit herbals as pharmaceuticals also. It requires that these preparations have to be tested rigorously and proven to be effective and non-toxic through appropriate clinical trials.

The test procedures are however less demanding and rigorous in case of preparations, which have been in use for generations. Such preparations still have to be shown to be effective and non-toxic, but in such cases the trials are shorter and can be directly conducted on humans. One of the major requirements for herbals is that their chemical composition should fall within acceptable range. Further, if the class of compounds are available for a particular known action, then the minimum concentration of such compounds in the final preparation is to be ensured. At present a HPLC profile of the product is acceptable. This profile should fall within an accepted range for each product.

At this moment India is rich in large natural resources, particularly herbs, spices, non-traditional crops and minerals, etc. Today Indian System of Medicine (ISM), viz, Siddha, Ayurveda, and Unani seems to have come almost a full circle. For centuries Ayurveda and its Dravidian counterpart, Siddha were the repository of all medical knowledge. Even the Unani system that the Moslem conquerors brought with them did not reduce their importance. But the British Raj and the medicinal system, *i e*, introduced relegated Indian medicine to the fringes of the medical world. But now it is re-emerging as a potent system, that is seen as a panacea for diseases and problems as wide ranging as cancer, asthma, arthritis, diabetes, nervous and orthopedic disorders, impotency and more recently AIDS²⁻³. According to the WHO, 80 per cent of the world population would be relying on plant based medicines for their health care needs by the turn of the century. There is a growing resistance the worldover to chemical medicines because of their side effects. The holistic approach to the health maintained by the traditional system of medicines was making them more and more popular with people. In India more than 500 million people depend directly or indirectly on plant derived drugs for their health care needs. The socioeconomic significance of medicinal plants in the country is significant as they provide 32 million man-days of employment, particularly among tribal and local population. The demand

for medicinal plants from the multinational pharmaceutical organizations also put pressure on Indian's herb resources.

The patented drugs, available in the market, are mostly owned by the developed countries. The commercial working of patent in India is a matter of crucial importance for the technological advancement. The world picture in respect of patent holders reflects that out of 4 million of old patents stored in the world, nearly 99 per cent is owned by the industrialized countries, whereas the developing countries put together, hardly possess less than 1 per cent. In India also nearly 75 per cent of the patents are granted to the nationals or firms of industrialized countries. Therefore the reluctance of working of patents by multi-national companies is of major concern for the technological advancement in India. There is no doubt about it that the handicap situation in the field of drugs due to above reasons are reflected on the record that 650 new drugs were introduced in the global market in 1983-1998 (15 y), but only 72 new drugs out of those introduced in Indian market from 1986-1998 because multi-national companies get fear to market their product in this country due to lack of strong patent and enforcement system. The crisis of global medicines in our country is partially managed by the substitute products received from herbal drugs during this period. To ease the situation, Govt. of India has signed WTO agreement in 1994 where the trade related aspects of IPR, a part of WTO is our international obligation which is to be compiled by the year 2004⁴. Some visible advantage of herbal drugs over the synthetic drugs, are shown below in Table 1.

Herbal medicines have become a popular option in health care. Seven best selling herbal medicines⁵ in 1998 are shown below in Table 2.

Many of our present medicines are derived directly or indirectly from higher plants. While several classic plant drugs have lost much ground to synthetic competitors, others have gained a new investigational or therapeutical status in recent years. In addition, many novel plant derived substances have entered into western drug market. Clinical plant based research has made particularly rewarding progress in the important fields of anti cancer (*e.g.*, Taxoids and camptothecins) and anti-malarial (*e.g.*, artemisinin compounds) therapies. In addition to purified plant drugs, there is an enormous market for crude herbal medicines.

Table 1— Comparison of herbal drugs with synthetic ones over several parameters

Parameters	Synthetic Drugs	Herbal drugs
1 Cost	High	Low
2 Chemistry	Usually simple	Usually complex
3 Target	Usually single	Usually multiple
4 Affinity	High	Low
5 Potency	High	Low
6 Incidence of side effects	Higher, often unpredictable	Lower, usually predictable
7 Action	Drastic changes in physiological events	Restore physiological balance
8 In-vitro tests	Often adequate	Inadequate
9 Patents	Easy	Difficult

Table 2 — Some popular herbal medicine and their market

Herb name	Value, US \$, million	Per cent increase over previous year
Ginko	150	67
Ginseng	96	11
Echinacea	70	42
Garlic	84	17
Saw Palmetto	32	74
Kava	17	462
St John's wort	140	190

Natural product research can be openly guided by ethno-pharmacological knowledge, and it can make substantial contributions to drug innovation by providing novel chemical structures and/or mechanisms of actions. In the end, however, both plant-derived drug and crude herbal medicines have to take the same pharmaco-economic bundle that has become important for new synthetic pharmaceuticals⁶.

India has had a very rich and ancient heritage of traditional system of medicine-ayurveda. The system was officially recognized by Govt. of India. The practical needs of many millions of Indians are currently served by this system for curing diseases like liver disorder, and chronic asthma⁷ etc. Hence, there is ample scope for R&D for finding out important drugs and drug intermediates using traditionally used herbs available in the country.

Problems with Modern Drugs

- 1 High cost (upwards of 200 million US\$) and long time (15-20 y) taken in development of a new drug.
- 2 Toxicity—A new branch of medicine is termed iatrogenic diseases.
- 3 Non-renewable source of basic raw material. Most synthetic drugs utilize fossil resources like petro-chemicals.
- 4 Environmental pollution by the chemical industries.
- 5 Inadequacy, specially in management of certain chronic diseases.

Advantages with Plant Based Drugs

- 1 Long history of use and better patient tolerance as well as public acceptance.
- 2 Renewable source.
- 3 Cultivation and processing environmental friendly.
- 4 Local availability, specially in developing countries.
- 5 Several important recent break-through, *e g*, guggulipid, artemesinin, taxol, etc.
- 6 Plants continued to be a major source of new lead generation⁸.

Herbal Drugs for Treatment of Cancer

Taxol in India

The latest anti-cancer drug (Taxol) discovered and extracted from the pacific yew tree has also at-

tracted attention in India and the well-known manufacturer of Ayurvedic drugs and preparations, M/S Dabur India Ltd claims to have succeeded in extracting these drugs from the leaves of Indian yew trees. The drug so produced was found to be in accordance with the reported specifications of the same already extracted from barks of pacific yew and marketed in the US on trial basis⁹.

The company decided to extract taxol from Asian yew tree widely available in the Himalayan region and it is claimed that it is the first company to extract the product from the leaves of the tree¹⁰. M/s Adithya Alkaloids Ltd, Hydrabad also started manufacturing taxol to be used for chemotherapy of cancer¹¹. M/S Southern Herbals, Bangalore exported high value anti-cancer drugs prepared using herbs¹² to Western Europe during 1993-94.

Taxol, which is considered as reliable drug against breast and ovarian cancer, cost about \$13/mg (Rs 569/mg) and has a \$870 million market in the US alone. Taxol has been prepared from a rare Himalayan plant and had been extracted by scientists at CIMAP, Lucknow. The 20, 000 km belt from Kashmir to Arunachal Pradesh was surveyed for genetic variations of the plant which helped in detecting trees whose bark contained 0.05 per cent taxol and 0.5 per cent taxol analogue and leaves with 0.04 per cent taxol and 0.2 per cent DAB analogue. These elite genetic stocks could be used for new high taxol yielding plantations¹³.

Other Anti-cancer Agent

Turmeric is a commonly used Indian spice, found to have anti-cancer property according to a study conducted by Hydrabad based National Institute of Nutrition (NIN). Administration of turmeric of about 1.5 g/d for 15-30 d decreases the amount of urinary mutagens. Curcumin, the active principle in it had shown anti-tumor effects in animals treated with potent carcinogens, the study showed, adding rats fed on varying quantities of turmeric showed that it can be a potent anti-cancer agent. NIN scientists found that leaves of mustered plants help reduce the risk of cancer².

Ashwagandha, (*Withania somnifera*), a typical yellow and green flowered plant, widely used for coagulating milk and in Ayurvedic preparations, holds out great promise in the treatment of cancer. It is when administered to laboratory mice induced with flashy cancerous over growth – sarcoma 180- along

with the conventional therapies resulted in tumor regression, growth delay and higher rate of animal survival².

Herbal Drugs for Treatment of AIDS

“Herbal renaissance” is blooming across the world. This prompted researcher to share data on certain plant aids in AIDS management. Intensive chemical researches were reported in the Central Aromatic and Medicinal Plant Abstracts. A survey by Edward Robinson during 1997-99 reported that common weed *Merremia peltata* and *M. emarginata* Halier f. from India deserves investigation. Flavonoids of *Plantago asiatica* L. are effective HIV inhibitors as observed by Nishibe and his co-workers. The species is common Indian drug known as Ishabgul and needs investigation as an anti-HIV source. The Pyrenocoumarins from *Calophyllum tysmannii*, *C. lanigerum* (Clusiaceae) are specific HIV – RT inhibitors. Further, bark of *Berchemia berchemiaefolia* (Rhamnaceae), leaves of *Lindsea erythrocarpa* (Lauraceae) and whole plants of *Sigesbeckia pubescens* (Asteraceae) were found to inhibit HIV-1 pretease to the extent of 56.2, 50.8 and 46.6 per cent, respectively. Water extract from the leaves of *Ficus carica* (Moraceae), and *Hottuynia cordata* (Saurauraceae) (> 79 per cent); *Syringa dilatata* (Oleaceae) and *Hibiscus syriacus* (Malvaceae) (> 40 per cent) inhibited RT – protease activity. Various degrees of anti-HIV activities were demonstrated with compounds from *Annona glabra* (Annonaceae) and *Hopea malibato* (Dipterocarpaceae)¹⁴. Ayurveda has also recommended tubers of *Asparagus racemosus*, roots of *Withania somnifera*, stems of *Tinospora condifolia*, tubers of *Ipomoea mauritiana*, *Leptadenia reticulata*, decoction of *Azadirachta indica* and seed powders of *Glycerrhiza glabra* for curing deteriorated immunity and immuno-promoters.

Herbal Drugs for Treatment of Malaria

Artemisinin or artemisininine is a sesquiterpene lactone. The Chinese have named the compound “Qinghaosu” (QHS) meaning active principle of Qinghao (*Artemisia annua* L.). *A annua* is pervasive within China which has been used in that country for many centuries as a traditional medicine for the treatment of fever and malaria. The active principle—artemisinin, a compound having anti-malarial property was isolated from the aerial portion of the plant in 1971. *A annua* besides, artemisinin contains arteannuin-B, another anti-malarial sesquiterpene

lactone and three more anti-bacterial compounds, viz, artemisic acid, sesquiterpenoids artemisinin and artemisic acid-M ester. As artemisin is found to be highly successful for the treatment of malaria patients in China and superior to other anti-malarial drugs such as chloroquine, it received wide interest in many parts of the world. During the last two decades extensive research has been carried out in China and other countries on cultivation and isolation of artemisinin from *A annua*, estimation, structure determination, chemical reactions, testing for anti-malarial activity, metabolism and mechanism of action of artemisinin¹⁵. Research on artemisinin seems to be a very relevant area for India, because of emergence of many chloroquine resistant *Plasmodium falciparum* strain. Due to its anti-malarial activity, this plant has been introduced in India and widely studied¹⁶.

Other Important Discoveries

Studies at CDRI, Lucknow have indicated that *Picrorhiza currooa* has a preventive as well as curative effect in liver diseases. According to the researcher, the plant derived compound shows even better activity than a hepato-protective drug in Europe. Chemical extract from the roots of the plant *Withenia somnifera*, known as Ashwagandha in India and used for centuries in traditional medicine, has shown anti-tumor activity, and raised hopes of better cure rate for cancer. Root extract of the plant kills tumor cells on its own and in combination with modern cancer therapy, researchers from Kasturba Medical College, Manipal announced at a recent scientific meeting on nuclear medicine in New Delhi. It was also reported elsewhere by researchers at G B Pant Hospital, New Delhi that extract of 19 herbs was a potent hepato-protective and antifibrotic activity. Compound derived from *Curcuma longa*, a plant whose traditional use as anti-inflammatory substances has been confirmed by laboratory studies. Pharmacological studies at the CDRI, Lucknow suggest that its activity is comparable to that of phenylbutazone for rheumatoid arthritis, with the added advantage that there is less adverse effect¹⁷.

Researchers at Banaras Hindu University have found Brahmi (*Centella asiatica*) an ancient drug, to be effective in the management deficiency and to possess neurotropic properties. A joint research proposal with the US and Germany was under way to evaluate the efficacy of Ayurvedic preparation based on plants such as shankhapushpi (*Canscora decussata*), jatamansi (*Nardostachys jatamansi*), etc for

their utility as drug for curing kala-azar and other infectious diseases¹⁸.

Valerianone and valtrate are well known compounds used as sedative/tranquiliser widely used in medical practice are reported to be found in jatamansi (*Nordostachys grandiflora*). It has an additional advantage that it can be prescribed to alcoholic patients also¹³.

Rhizome extract of *Dioscorea floribunda* was also reported to be a good source of diosgenin, a steroidal chemical that serve as a precursor for the synthesis of cortisones, sex hormone and oral contraceptive¹⁷.

Tropical Botanical Garden and Research Institute, Thiruvananthapuram showed similar activity of *Trichopus zeylonicus* as that of ginseng which is found on the forest slopes of Western ghats in Kerala and used by the Kani tribes to combat fatigue. Scientists have now begun clinical trials at the Trivandrum Medical College for use of the plant as a health tonic.

Drug extracted from acacia tree (*Acacia auriculiformis*) is found to have anti-filarial activity. It was reported by a team of researchers from the Visva-Bharati University, Santiniketan and Indian Institute of Chemical Biology, Kolkata found that a drug based on two active compounds, acaciaside A and acaciaside B, isolated from *Acacia auriculiformis* could control a filarial parasite *Setaria cervi* that infects cattle. The two belongs to a class of compounds called saponins that characteristically foam when mixed with water. This has increased hopes of finding a safe and effective drugs for human consumption¹⁹.

Rauvolfia serpentina, commonly known as sarpagandha, has been widely used in India as an antidote to insect, snake bites, as a fabrifuge, as a stimulant to uterine contraction and as a sedative. It is also found to have marked action against hypertension. It was found that active principle reserpine and others were responsible for this hypotensive action. The discovery of reserpine-the unique tranquilizing drug-ajmaline and ajmaticine, the hypotensive principle triggered massive and unprecedented research on plant products through out the world including India²⁰.

Some common medicinal plants and there traditional usage is shown in Table 3 below.

Already some important drugs/drug intermediate analyzed from plants of Indian origin used by pharmaceutical industries are shown in Table 4.

Some other Indian leading medicinal plants identified are as below:

Anti-arthritis

- 1 *Boswellia serrata* (salai guggul, gum)
- 2 *Commiphora wightii* (guggul, gum)
- 3 *Curcuma longa* (Haldi, rhizome)

Bioavailability and enhancer

- 1 *Piper longum* (pippali, fruit)

Bronchial asthma

- 1 *Albizia lebbek* (shirish, bark)

Immunomodulator

- 1 *Tinospora cordifolia* (guduchi, plant)

Macrofilaricide

- 1 *Spreblus asper* (Shakotak, bark)

Pepticulcer

- 1 *Musa paradisiacal* var. *Sapientum* (Banana, green fruit)

Snake bite

- 1 *Hemidesmus indicus* (anantamul, root)
- 2 *Pluchea lanceolata* (rasna, leaf)

Conclusion

There are approximately 2,50,000 known species of higher plants on our planet, and it is estimated that a further 20,000 await discovery. About 25,000 species are at present threatened by extinction. Up till now, only about 6 per cent of all plant species have been analyzed chemically and only a small fraction analyzed pharmacologically. It is not a far-fetched hypothesis that valuable therapeutic substances may be identified in the huge of plants which are known and commonly used by traditional herbalists, but which have not yet been subjected to any phytochemical or pharmacological analysis. This hypothesis may find support in the fact that a number of substances, used in modern medicine for the treatment of serious diseases, have originated from research on medicinal plants. According to the recent reviews of national pharmacopoeia from several countries there are at least 119 distinct chemical substances derived from plants that can be considered as important drugs currently in use in one or more countries. Those 119 plants derived drugs or substances are used within a total of 62 therapeutical categories. Ninety-one species of plants have been identified as the sources of these drugs²¹.

India has a vast reservoir of nearly 400,000 practitioners of Ayurveda, Siddha, Unani medicine or homeopathy who, unfortunately, have not so far been adequately utilized in the health care delivery sys-

tems. National health policy stresses the need for preventive and promotive medicine which the systems are well placed to deliver and, at some stage, there has to be some sort of integration of all the systems if the people are to be properly served. India also earn through export of herbal items for manufacturing of drug and drug intermediates such as *Psyllium ovata* seeds and husas, *Cassia angustifolia* leaves and parts, *Vinca rosea* flowers, *Chlorophytum arundinaceum* roots, *Withania somnifera* roots, *Terminalia chebula* fruits, *Phyllanthus emblica* fruits, *Papaver somniferum*, *Opium*, and *Ocimum basilicum*. For continuous and uniform supply of crude drugs, cultivation of medicinal plants has to be given priority. However, research support is needed to provide superior genotype, agronomic practices, and linking of production with industries to ensure buy-back guarantee to the farmers³.

About 80 per cent of raw materials for drugs used in the Indian system of medicine and homeopathy are based on plant products. The credibility of these systems of medicines depends, therefore, on having available authentic raw material in sufficient quantities. With some 46,000 licensed pharmacies manufacturing the traditional remedies of these medical systems, it is necessary to plan for large-scale cultivation of medicinal plants and to ensure that they are accurately identified, properly processed, free of adulterants and of acceptable quality²². Further, there is hope that in future the process of plant drug discovery and development by way of mass screening will be greatly facilitated and made more efficient by using new automated multiple biological screening methods which are now becoming available and require only minimal amounts of test samples for evaluation²³. Following factors restricting of herbal drugs in India should be removed²⁴:

- 1 Nearly 90 per cent collection from wild, mostly involving destructive harvesting, result is unsustainable supply and threatened species,
- 2 Marketing inefficient, imperfect, secretive, and opportunistic. Little attention to patents and IPR,
- 3 Multiple stake holders with divergent interests of forest departments, cultivators, industries, policy makers, regulatory agencies,
- 4 No organization to co-ordinate various sectors and activities.

A major problem of herbals to-day has to do with the impurities in them. For example, many herb-

Table 3 — Some common medicinal plants and their traditional usage

Sl No	Botanical name	Local name	Usage
1	<i>Aegle marmelos</i>	Bel	Root is an ingredient of Dasmool. Fruit pulp treats diarrhoea, leaves treat diabetes
2	<i>Andrographis paniculata</i>	Kalmegh	A bitter tonic, and as a febrifuge and used in liver diseases
3	<i>Asparagus racemosus</i>	Shatawar	Extensively used as nutritive tonic and in various formulations
4	<i>Azadirachta indica</i>	Neem	A bio-pesticide and used in many diseases
5	<i>Bacopa monnieri</i>	Brahmi	Brain tonic in nervous disorders, e.g. insanity, epilepsy, neurastacia and nervous break-down and memory enhancing
6	<i>Berberis aristata</i>	Berberis	Roots, stem bark and Rasaut or Rasanjan are used in conjunctivities, enlargement of liver and spleen, jaundice, urino-genital disorders and ulcerative condition.
7	<i>Catharanthus roseus</i>	Periwinkle	Contents more than 100 alkaloids. Used for treatment of leukaemia.
8	<i>Cassia angustifolia</i>	Senna	Leaves and pods are purgative and laxative.
9	<i>Celastrus paniculatus</i>	Malkangni	Decoction and oil of seeds are stimulent for the neuro-muscular system and are given in rheumatism, gout and paralysis. Also used as brain tonic and to sharpen memory.
10	<i>Chlorophytum tuberosum</i>	Safed musli	Used as demulscent. Whole-sum tonic alternative nerve. Roots are highly priced drugs.
11	<i>Commiphora wightii</i>	Guggul	Used in urinary infections, piles, fistula, arthirities, rheumatism and in lowering cholesterol.
12	<i>Emblica officinalis/ Phyllanthus emblica</i>	Amla	Fruit is used as laxative, in hair oils and as general tonic.
13	<i>Ephedra gerardiana</i>	Ephedra	Used in asthma and hay fever.
14	<i>Gloriosa superba</i>	Gloriosa or Kalihari	Rhizome is extensively used to induce abortion and for pain less delivery
15	<i>Gymnema sylvestris</i>	Gurmar	Has anti-diabetic properties and used for controlling body weight.
16	<i>Hydnocarpus kurzil</i>	Chalmogra	Oil is used in treatment of leprosy.
17	<i>Mesua ferrea</i>	Nagkeshar	Used in bleeding piles, dysentery, cough, etc
18	<i>Nardostachys grandiflora</i>	Jatamansi	Used in hystaria, palpitation of hearts, menopause and various nervous diseases
19	<i>Ocimum basilicum</i>	Tukmaria	In Unani used as anti-dysentery, anti-diarrhoeal and aphrodisiac drug
20	<i>Plantago ovata</i>	Isab or Psyllum	Seeds and hush are used in chronic constipation, coltroll of diarrhoea and dysentery
21	<i>Picrorhiza kurroa</i>	Kutki	Used in the treatment of dispepsia, respiratory disorders, jaundice and anaemia
22	<i>Rauwolfia serpentina</i>	Sarpagandha	Used as sedative in insanity; it is hypotensive and tranquillizer
23	<i>Swertia chirayata</i>	Chirata	It is a tonic febrifugal, laxative, stomachic antihelmintic and antidiarrhoeal
24	<i>Santanum album</i>	Chandan	Oil used in various formulations
25	<i>Withania somnifera</i>	Ashwagandha	It is sedative, anti-inflammatory tonic and rejuvenative

als have been found to be contaminated with heavy metals, pesticidal residues or fungus. Such herbals are not accepted in the international markets where the tests for these contaminants are routinely conducted.

When herbals were initially used the notion of a molecule as we understand to-day did not exists. Hence, each herbs or extract from it was trusted as a single entity. Further, experiments were done on human. To-day, we have possibility of fractions as well

as *in vitro* and *in vivo* tests available with us. Hence, instead of full extracts, in future, fractions will be tested and those fractions, which are effective and non-toxic, will be used as drugs. These drugs will still contain several molecules, but most of these molecules will be known. Hence, most of the herbals in future will be made from mixtures of fraction, have limited number of molecules, will be molecularly defined and will use plants from other countries also.

Table 4 — Important drugs/drug intermediate analyzed from plants of Indian origin

Name of plant, part used	Major chemical constituents
1 <i>Adhoda vasica</i> (leaf)	Vasicine
2 <i>Ammi majus</i> (seed)	Xanthotoxine
3 <i>Atropa acuminata</i> (leaf, root)	Atropine, hyoscyamine
4 <i>Berberis asiatica</i> (root)	Berberine
5 <i>Carica papaya</i> (fruit, latex)	Papain
6 <i>Cassia angustifolia</i> (leaf)	Sennosoidas
7 <i>Catharanthus roseus</i> (leaf, stem, root)	Vinblastine, vincristin, ajmaline
8 <i>Cephaelis ipecacuanah</i> (root)	Emetine, cephaeline
9 <i>Cinchona</i> Sps. (stem and bark)	Quinine, quinidine
10 <i>Datura mete</i> (leaf and seed)	Hyoscyamine
11 <i>Datura stramonium</i> (leaf)	Hyoscyamine
12 <i>Dioscorea deltoidea</i> (rhizome)	Diosgenin
13 <i>Ephedra geradiana</i> (stem)	Ephedrin/pseudoephedrin
14 <i>Gloriosa superba</i> (seeds)	Colchicine
15 <i>Heracleum candicans</i> (root)	Xanthoxine
16 <i>Papaver somniferum</i> (latex)	Morphine and other opium alkaloids
17 <i>Podophyllum emodi</i> (root)	Podophyllo toxin
18 <i>Rauwolfia serpentina</i>	Reserpine and other alkaloids
19 <i>Silybum marianum</i>	Silymazines
20 <i>Strychnos nux-vomica</i>	Strychnine, brucine
21 <i>Taxus wallichiana</i>	Taxol
22 <i>Valeriana jatamansi</i>	Valpotriates

Most of these preparations will have multiple modes of actions and have synergism as their backbone. Evidently the future herbal preparation will be based on the knowledge of modern chemistry and biology and will be safer, more specific, more effective, more convenient to use and hence more universally acceptable than their present counterparts.

There are a large number of CSIR laboratories, a number of University departments and hospitals, other scientific institutions as well as their traditional systems of medicines, participating effectively in the network program. Each of these institutions has special expertise or special facilities or both. All these

have been pooled to optimally reach the goal of developing new drugs, herbal preparations, pest management agents, bio-enhancer and drug delivery systems. This network system must work effectively to get the pharmaceutical policy adopted by Government of India recently, which stressed on abundant availability of quality drugs at reasonable price within the country, implemented through all round development of herbal drugs²⁵⁻²⁶.

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A Goswami, P K Baruah* and J S Sandhu

Regional Research Laboratory, Jorhat, Assam

There are 2.5 million known species of higher plants on the Earth and and some more may be discovered. Of these, only six per cent have been analyzed chemically and only a small fraction pharmacologically. According to pharmacologists of the world, at least 119 natural chemical substances derived from plants are important drugs currently—used within 43 categories in cosmetics, and 91 species are the source of 2000 drugs. India has vast reserves of 47, 000 Ayurvedic, Siddha, Unani or Homeopathic medicines, which reach extensively in the health care delivery system. Nearly 80 per cent of drugs used in Indian system of medicine and homoeopathy are derived from plants. With 46, 000 indigenous plant species, including rare and vanishing the scope of medicinal remedies, large scale cultivation of medicinal plants need to be pursued. A network of LRR, herb gardens, University departments and hospitals, other scientific institutions are participating in the natural evaluation and harvesting of new drugs through use of modern methods and tools. With pooled resources, efforts are being made to reach the goal of development of new drugs, herbal preparations, pest management agents, bio-pesticides, and drug delivery systems. A few examples have been presented in the face of globalization and WTO.

Introduction

Since independence, the Indian pharmaceutical companies have concentrated significantly towards the growth and development of health sector. They have launched several generic drugs in the segment of antibiotics, anti-hypertensive, anti-diabetic, immunological, analgesic and anti-cancerous. However, due to the fast changing world in the world scenario in Intellectual Property Right (IPR), about \$30 billion worth of drug will go off-patent globally by 2005 and will reach 100 billion worth of drug by the year 2010. Although, this might be a rewarding situation to many Indian Multi National Companies (MNC's), however, the small and medium drug manufacturers will encounter a stiff competition. Consequently, the Indian pharmaceutical companies, which have been contributing to India's drug market, are facing great threats for their co-existence in the global market. The situation has become more alarming due to India's participation in GATT agreement, which allows 100 per cent direct investment of foreign MNCs in pharmaceutical sector of India from 2002.

Pharmaceutical R&D for new drugs has been carried out for almost five decades in India, in the government, semi-govt and industrial sectors. Indian medicinal scientists, pharmacologists, analysts, microbiologists and clinical research are of world class.

*Corresponding author: baruahpk@rediffmail.com
 baruahpk@yahoo.com

The Government of India has allocated Rs 150 crore for R&D in the pharmaceutical sector. But the cost of development of a single drug in the US is reported to be \$110 million, which will be Rs 52.8 crore at the present dollar to rupee parity*. Due to this, the drug price is going higher and unaffordable for the common people. In spite of these problems, some of the pharmaceutical R&D units of MNCs in India like CIBA-GEIGY, Hoechst, Beck's Laboratory and CSIR Laboratories have done commendable work and have developed and marketed some very important drugs. So, it is of utmost importance for our pharmaceutical industry's healthy growth and progress in the future to cover the unmet needs/availability of essential drugs. For this purpose, it is needed to stress on investment for R&D and upgrade manufacturing plant to the world standard.

Further, it takes long time for a new drug to come to market as a result the drug price increases to the extent of becoming unaffordable for the common people. On the other hand for quite some time, there has been a general feeling among the public that single molecules used by allopathic system of medicine are toxic. Recent investigations are proving this perception to be correct. A report published in 1999 in the *Journal of American Medical Association* (JAMA) shows that adverse reactions to prescription drugs forms 4th to 6th largest cause of death in the US. This finding is extremely alarming. On the other hand, herbal preparation are considered to be safer.