Research Article

Current Status of Herbal Drugs in the Development of Newer Therapeutics Agents

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ABSTRACT

This study was designed to discuss some of the important issues related to the current status of herbal drugs in the development of newer therapeutics agents. The approach to new drugs through natural products has proved to be the single most successful strategy for the discovery of new drugs. In this review we consider the past, present, and future value of employing information from plants used in traditional medical practices (ethnomedicine) for the discovery of new bioactive compounds. In the western world, as the people are becoming aware of the potency and side effect of synthetic drugs, there is an increasing interest in the natural product remedies with a basic approach towards the nature. Medicinal plants play a vital role for the development of new drugs. The bioactive extract should be standardized on the basis of active compound. The bioactive extract should undergo safety studies. Almost, 70% modern medicines in India are derived from natural products. Medicinal plants play a central role not only as traditional medicines but also as trade commodities, meeting the demand of distant markets. Currently plant based drugs are researched and formulated in modern framework of medicine rather than in the form of galenical preparations or conventional dosage. Subject is witnessing transformation from galenical to genomical. Even in the era of biotechnology and bioinformatics subject holds paramount importance because of its interdisciplinary and flexible approach.

Keywords: Herbal drugs, Newer therapeutic agents, Quality control, Drug development.

INTRODUCTION

The term “herbal drugs” denotes plants or plant parts that have been converted into phytopharmaceuticals by means of simple processes involving harvesting, drying, and storage. A practical addition to the definition is also to include other crude products derived from plants, which no longer show any organic structure, such as essential oils, fatty oils, resins, and gums (Vaidya and Devasagayam, 2007).

Why Study Medicinal Plant

India is the largest producer of medicinal herbs and approximately called the botanical garden of the world. In Indian medicinal systems the most practitioners formulate and dispense their own recipes; hence, this requires proper documentation and research. In rural India, 70% of the population is dependent on the traditional system of medicine. In western world also the practitioner of herbal medicines is steadily growing and approximately 40% of the population is taking herbs to treat diseases. Public, academic and governmental interest in traditional medicines is growing exponently due to increased incidence of the adverse drug reactions and economic burden of the modern synthetic drugs (Ali *et al*, 2009). Pharmacognosy, one of the oldest scientific disciplines is now undergoing major change. Currently plant based drugs are researched and formulated in modern framework of medicine rather than in the form of galenical preparations or conventional dosage. The Principle of Phytotherapy is the medicinal effects of plants are due to metabolites especially secondary compounds produced by plant species. Plant metabolites include: primary metabolites and secondary metabolites (Joy P.et al. 1998).

The herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. Although herbs had been priced for their medicinal, flavouring and aromatic qualities for centuries, the synthetic products of the modern age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security (Verma and Singh 2008).

The drugs are derived either from the whole plant or from different organs, like leaves, stem, bark, root, flower, seed, etc. Some drugs are prepared from excretory plant product

such as gum, resins and latex. Even the Allopathic system of medicine has adopted a number of plant-derived drugs which form an important segment of the modern pharmacopoeia. Some important chemical intermediates needed for manufacturing the modern drugs are also obtained from plants (Eg. diosgenin, solasodine, β-ionone). Not only, that plant-derived drug offers a stable market world wide, but also plants continue to be an important source for new drugs (Verma and Singh 2008).

In many of the developing countries the use of plant drugs is increasing because modern life saving drugs are beyond the reach of three quarters of the third world's population although many such countries spend 40-50% of their total wealth on drugs and health care. As a part of the strategy to reduce the financial burden on developing countries, it is obvious that an increased use of plant drugs will be followed in the future. (Verma and Singh 2008).

Background and issues

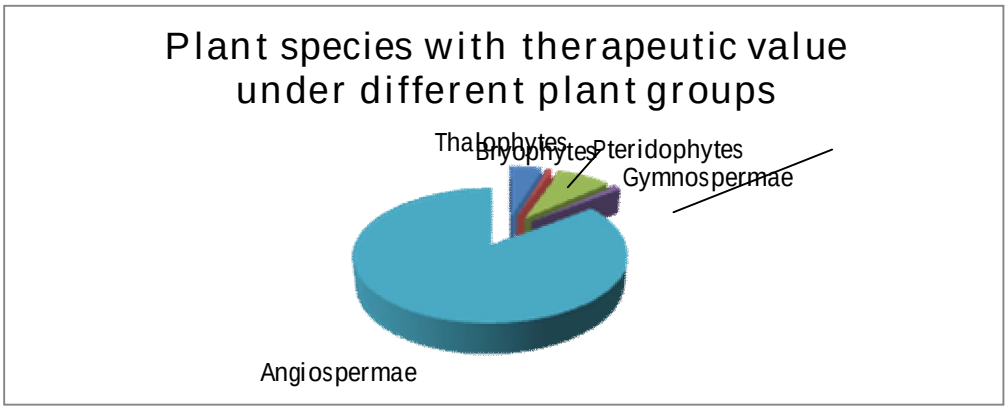
Herbs today are being increasing used to treat all kinds of disorders. From mild cases like common cold to serious diseases like cancer, there is an ever-growing need for genuine and well tested information regarding herbal cures. Many of the modern medicines are produced indirectly from medicinal plants, for example aspirin. Plants are directly used as medicines by a majority of cultures around the world, for example Chinese medicine and Indian medicine. Many food crops have medicinal effects, for example garlic. Medicinal plants are resources of new drugs. It is estimated there are more than 250, 000 flower plant species. Studying medicinal plants helps to understand plant toxicity and protect human and animals from natural poisons. Cultivation and preservation of medicinal plants protect biological diversity, for example metabolic engineering of plants (Pandey et.al 2008).

Newer therapeutic agents

Therapeutic agents found in medicinal plants are products of plant metabolism. They are produced and stored in various plant tissues including leaves, stems, flowers, roots, bark, seeds and fruits. Therapeutic agents or therapeutic components/ingredients of medicinal plants come in many forms and have varying degrees of strength. Alkaloids, for example, can be both very therapeutic as well as potentially deadly. Plants are classified according to the part used, habit, habitat, therapeutic value etc, besides the usual botanical classification. (Table-1-Classification of plants Based on therapeutic activity) Here therapeutic classification is shown (Vermani and Garg 2002). Several plant extracts and their constituents possess activity against sexually transmitted diseases indicating their huge potential as an effective measure for prevention and treatment of STDs including AIDS. This section enlists the commonly used Indian medicinal plants used for the development of a safe, new, effective and economical alternative to drugs (Vermani and Garg 2002, Pandey *et.al* 2008).

Plant resources for new medicine

Plant derived drugs came into use in the modern medicine through the uses of plant material as indigenous cure in folklore or traditional systems of medicine. *Bryophytes* (nonvascular plants, e.g. liverwort and moss), *Seedless vascular plants* (commonly called fern) and the number of higher plant species (angiosperms and gymnosperms)(fig1- Boston fern ,2-Christmas fern,3-Ginkgo biloba and 4- Angiosperm) on this planet is estimated at 250, 00028, with a lower level at 215, 00029, 30 and an upper level as high as 500, 00031 and only about 6% have been screened for biologic activity, and a reported 15% have been evaluated phytochemically (Rout et al. 2009). (Table 2. Plant species with therapeutic value under different plant groups (Joy P.et al. 1998).



The large proportion of natural products in drug discovery has stemmed from the diverse structures and the intricate carbon skeletons of natural products. Since secondary metabolites from natural sources have been elaborated within living systems, they are often perceived as showing more "drug likeness and biological friendliness than totally synthetic molecules," making them good candidates for drug development (Joy P.et al. 1998). The value of natural products can be assessed from: (i) the rate of introduction of new chemical entities of wide structural diversity, including serving as templates for semisynthetic and total synthetic modification, (ii) the number of diseases treated or prevented by these substances, and (iii) their frequency of use in the treatment of disease (Rout et al. 2009). Analysis of the sources of new and approved drugs during the period 1981 to 2002 reveals that natural products play a highly significant role in the drug discovery and development process. Review of all approved agents during the time frame of more than 25 years from 01/1981 to 06/2006 for all diseases worldwide and from 1950 (earliest so far identified) to 06/2006 for all approved antitumor drugs worldwide reveals the utility of natural products as sources of novel structures, but not necessarily the final drug entity, is still alive and well (Rout et al. 2009).

The development of high throughput screens based on molecular targets had led to a demand for the generation of large libraries of compounds. Various names have been given to this process, including "Diversity Oriented Syntheses", preferably can be termed as "more natural product-like". The antitumor compound known as sorafenib from Bayer, approved by the FDA in 2005. Proudfoot also reported that 8 out of 29 small molecule drugs launched in 2000 were derived from Natural Products or hormones (Rout et al. 2009).

Despite competition from other drug discovery methods, Natural Products are still providing their fair share of new clinical candidates and drugs and there is rapidly evolving recognition that a significant number of natural product drugs/leads are actually produced by microbes and/or microbial interactions with the "host from where it was isolated", and therefore this area of natural product research should be expanded significantly (Rout et al. 2009).

Significances of Medicinal Plants to Human Being

Most allopathic medicines have side effects that can range from mild to severe. The reason for this is that most of these chemicals have certain toxic properties. This is why there have been so many prescription drugs that got pulled from the market after enjoying several years of FDA approval. The sad thing is that very few doctors nowadays bother to inform patients about possible side effects due to close and cozy relationships with the pharmaceutical industries. Half of the truth is that pharmaceutical companies will only tell doctors as much as they want to and not reveal the complete picture. Therefore, the doctors are not completely to blame because they cannot warn patients against side effects of chemicals they are not aware of. Herbal remedies treat the cause of the disease and not the symptoms (like conventional drugs). What is says is that improving health is better than fighting disease. So no matter how much noise the pharmaceutical companies make, you should at least give some time to listen to nature and her own remedies (Vaidya and Devasagayam 2007).

Importance of plants as a source of new drugs

It is often noted that 25% of all drugs prescribed today come from plants. This estimate suggests that plant-derived drugs make up a significant segment of natural product–based pharmaceuticals. Out of many families of secondary metabolites, or compounds on which the growth of a plant is not dependent, nitrogen-containing alkaloids have contributed the largest number of drugs to the modern pharmacopoeia, ranging in effects from anticholinergics (atropine) to analgesics (opium alkaloids) and from antiparasitics (quinine) to anticholinesterases (galantamine) to antineoplastics (vinblastine/vincristine) Although not as plentiful as alkaloids in the modern pharmacopoeia, terpenoids (including steroids) have made an equally important contribution to human health. They range from Na+/K+ pump-inhibiting cardiac glycosides from *Digitalis* spp., to antineoplastic paclitaxel to antimalarial artemisinin, to anti-inflammatory triptolide (Rout et al. 2009).

The isolation and purification of another active compound from the methanolic root extract of *Hemidesmus indicus*, which was responsible for snake venom neutralization. Antagonism of both viper and cobra venom and antiserum action potentiation, antioxidant property of the active compound was studied in experimental animals. The mechanism of action of the plant derived micromolecules induced venom neutralization need further attention, for the development of plant-derived therapeutic antagonist against snakebite for the community in need. However, the toxicity of

plants has known for a long period of time, and the history of these toxic plants side by side with medicinal ones are very old and popular worldwide, they considered the major natural source of folk medication and toxication even after arising of recent chemical synthesis of the active constituents contained by these plants (Samy and Gopalakrishnakone 2007).

It is important to note that, the activity of some natural products has yet to be certified by extensive testing or clinical trials; as multicomponent botanical therapeutics (MCBTs). This over representation of natural product– derived drugs begs the question of whether plant secondary metabolites and related synthetic compounds perform better as drugs than randomly synthesized compounds. Despite the increasing use of medicinal plants and their importance in drug discovery, their future, seemingly, is being threatened by complacency concerning their conservation (Rout et al. 2009).

The goals of using plants as sources of therapeutic agents are, *a*) to isolate bioactive compounds for direct use as drugs, e.g., digoxin,digitoxin, morphine, reserpine, taxol,vinblastine, vincristine; *b*) to produce bioactive compounds of novel or known structures as lead compounds for semisynthesis to produce patentable entities of higher activity and/or lower toxicity, e.g., metformin, nabilone, oxycodon (and other narcotic analgesics), taxotere, teniposide, verapamil, and amiodarone, which are based, respectively, on galegine, morphine, taxol, podophyllotoxin, khellin, and khellin; *c*) to use agents as pharmacologic tools, e.g., lysergic acid diethylamide, mescaline, yohimbine; and *d*) to use the whole plant or part of it as a herbal remedy, e.g., cranberry, echinacea, feverfew, garlic, ginkgo biloba (Rout et al. 2009).

Papaverine, useful as a smooth muscle relaxant, provided the basic structure for verapamil, a drug used to treat hypertension. Galegine was isolated as an active antihyperglycemic agent from the plant *Galega officinalis* L. used ethnomedically for the treatment of diabetes. Galegine provided the template for the synthesis of metformin and opened up interest in the synthesis of other biguanidine-type antidiabetic drugs (Rout *et al*. 2009).

i) Plant derived ethnotherapeutics

One of the remarkable contributions of Indian scientists is exploration of medicinal properties of folklore herbal drugs. In this respects India is leading to the neighboring countries Nepal, Pakistan and Sri Lanka and even the European and African countries but lacking behind the South American and pacific countries. Among 65 international Indian research papers between 1980-2005, herbal drugs of Andhra Pradesh and Uttar Pradesh have been explored extensively. However, little efforts have been carried out in Manipur, Nagaland and Tripura. Majority of the plant drugs have not been examined for bioactivities, clinical effects and potent phytoconstituents. Ethnobotanical approaches have explored many new herbal drugs, therapeutic uses and their mode of administration. (Ali *et al* 2009, Samy and Gopalakrishnakone 2007) (Table 3: Plant derived ethnotherapeutics and traditional modern medicine, Table 4: Some of the important medicinal plants used for major modern drugs for cancer).

ii) Agrotechnological approach

It is necessary to initiate systematic cultivation of medicinal plants in order to protect endangered species and for the development of new and effective variety of medicinal plants in India. In the pharmaceutical industry, where the active medicinal principle cannot be synthesised economically, the product must be obtained from the cultivation of plants. Systematic conservation and large scale cultivation of the concerned medicinal plants are thus of great importance. (Table 5. New varieties of medicinal plants developed in India) Cultivation of this type of plants could only be promoted if there is a continuous demand for the raw materials for the development of crude drugs, plant extracts and new therapeutic bioactive molecule.

iii) Quality Control Techniques

It is therefore, necessary to develop genetically superior planting material for assured uniformity and desired quality and resort to organized cultivation to ensure the supply of raw material at grower's end. Post harvest storage and process technologies need to be developed to produce the value added finished products that may be directly utilized by the industry.

Hence research and development work has to be done to formulate Good Agricultural Practices (GAP) which should include proper cultivation techniques, harvesting methods, safe use of fertilizers and pestisides and waste disposal. (Joy P.*et al*. 1998)

Several problems not applicable to synthetic drugs influence the quality of herbal drugs

- Herbal drugs are usually mixtures of many constituents.
- The active principle(s) is (are), in most cases unknown.
- Selective analytical methods or reference compounds may not be available commercially.
- Plant materials are chemically and naturally variable.
- The source and quality of the raw material are variable.
- The methods of harvesting, drying, storage, transportation, and processing (for example, mode of extraction and polarity of the extracting solvent, instability of constituents, etc.) have an effect.
- Strict guidelines have to be followed for the successful production of a quality herbal drug. Among them are proper botanical identification, phytochemical screening, and standardization. Botanical extracts made directly from crude plant material show substantial variation in composition, quality, and therapeutic effects. Standardized extracts are high-quality extracts containing consistent levels of specified compounds, and they are subjected to rigorous quality controls during all phases of the growing, harvesting, and manufacturing processes.
- When the active principles are unknown, marker substance(s) should be established for analytical purposes and standardization.
- Marker substances are chemically defined constituents of a herbal drug that are important for the quality of the finished product. Ideally, the chemical markers chosen would also be the compounds that are responsible for the botanical's effects in the body.

Quality control requirement of new preparation of traditional medicines

1. Prescription and its basis
2. Literature and research data of physico-chemical characteristic concerned with quality
3. Preparation technology and its research references
4. The draft of the quality standard and explanation of medicinal material, and medicament.
5. Literature and test data of initial stability for clinical research
6. The reports of quality detection and hygiene standard detection of the preparation for clinical research
7. Property and specification of the packing material of the medicament, design draft of the label and applied instructions.

International scheme for quality assurance of pharmaceutics

International scheme for quality assurance of pharmaceutics involves the following standard practices.
GAP: Good Agricultural Practice
GLP: Good Laboratory Practice
GMP: Good Manufacturing Practice
GCP: Good Clinical Practice
GALP: Good Analytical/Automated Laboratory Practice (Joy P.*et al.* 1998).

iv) clinical approach

Like international trade of herbal drugs, clinical studies on the Indian medicinal plants is unorganized and about 0.75 per cent of these drugs, based on reports published in national journal, have been screened in clinical trial for a particular disease. If international status of the clinical reports is considered, then this figure will be less than 0.1 per cent. There are numerous ethical, technical and logistic hindrance involved in conducting many clinical trials. Generally drug powders are used in these studies and experiments have been conducted mainly on popular Ayurvedic drugs without involvement of biostaticians to substantiate the traditional uses of plant drugs. Some of the clinical reports are included in the monographs to encourage a subsequent proper scientific clinical study. There are nearly 40 Indian research journals in which clinical reports are published. In order to take a scientific approach towards herbal drugs, the following steps may be followed:

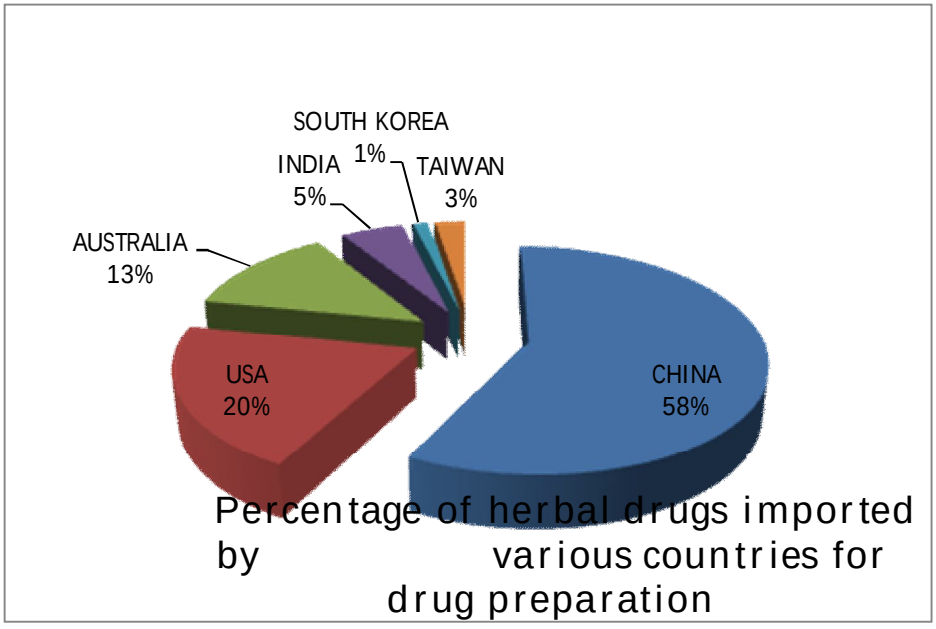
- A therapeutically and clinical approach is needed
- High throughput bioactivity screening methods should be introduced and the active fractions are to be explored phytochemically.
- Methods for biological test, e.g., anticancer, anti HIV and immuno-modulating screening should be developed.
- Work should be carried out with total recipe or particular plant fraction.
- The active potent constituent should be isolated to know mechanism of

action and to enhance its activity by chemical reactions.

- Coordination amongst various stake holders such as agencies of the central and state governments, industries, academic institutions and international network should be developed. (Ali *et al*, 2009).

Market Scenario

Plants are the main source of medicine. Two of the largest users of medicinal plants are China and India. Traditional Chinese Medicine uses over 5000 plant species; India uses about 7000. According to Export-Import Bank, the international market for medicinal plant related trade having a growth rate of 7% per annum. China's share in world herbal market is US$ 6 billion while India's share is only US$1 billion. India exports crude drugs mainly to developed countries viz. USA, Germany, France, Switzerland, UK and Japan. Aconite, Aloe, Belladonna, Acorus, Cinchona, Cassia tora, Dioscorea, Digitalis, Ephedra, Plantago and Senna are the principal Indian herbal drugs exported to foreign countries. Deficient toxicological studies and quality control affect the export of herbal drugs (Verma and Singh S.P.2008) (Table 6. Market size of phytomedicine and their sale in US Dollar, Table 7. Medicinal plant parts exported from India, importing medicinal plants and their parts).



Percentage of herbal drugs imported by various countries for drug preparation

A significant number of modern pharmaceutical drugs are derived from medicinal plants. The derivatives of medicinal plants are non-narcotic with little or no side effects. Some of the useful plant drugs include vinblastine, vincristine, taxol, podophyllotoxin, camptothecin, digitoxigenin, gitoxigenin, digoxigenin, tubocurarine, morphine, codeine, aspirin, atropine, pilocarpine, capscicine, allicin, curcumin, artemesinin and ephedrine among others. In some cases, the crude extract of medicinal plants may be used as medicaments. On the other hand, the isolation and identification of the active principles and elucidation of the mechanism of action of a drug is of paramount importance. Hence, works in both mixture of traditional medicine and single active compounds are very important. Where the active molecule cannot be synthesised economically, the product must be obtained from the cultivation of plant material. About 121 (45 tropical and 76 subtropical) major plant drugs have been identified for which no synthetic one is currently available (Verma and Singh .2008, Samy and Gopalakrishnakone. 2007) (Table 8. Major plant drugs for which no synthetic one is currently available).

Future perspectives

Despite several problems, one cannot discount the past importance of plants as sources of structurally novel drugs and it provides a great opportunity to the scientists in the field of Natural Product Chemistry, Pharmacognosy, Pharmacology, Ethnobotany and other related fields of life science to come together and work in the direction of getting new drugs from Natural Sources, especially from Plants for betterment of mankind. The importance of natural products in the future of drug discovery is clear: novel biologically

active natural products will continue to serve as lead compounds for drug development and is biochemical probes for the discovery of pharmacological and biochemical process. Combining the strengths of the knowledge base of traditional systems such as ayurveda with the dramatic power of combinatorial chemistry and it will help in the generation of structure–activity libraries. Traditional knowledge and experiential database can provide new functional leads to reduce time, money and toxicity – the three main hurdles in drug development (Rout *et al.* 2009).

These records are particularly valuable, since effectively these medicines have been tested for thousands of years on people. Bioprospecting demands a number of requirements which should be cocoordinated, such as team of scientific experts along with expertise in a wide range of human endeavours, including international laws and legal understanding, social sciences, politics and anthropology. In order to screen thousands of plant species at one go for as many bioassays as possible, we must have a collection of a large number of extracts. Globally, there is a need to build natural products extract libraries. The extract libraries offer various advantages, such as reduction in cost and time for repeat collection of plants and availability of properly encoded and preserved extracts in large numbers for biological screening in terms of high-throughput screenings and obtaining hits within a short period (Rout *et al*. 2009).

Innovation and creativity regarding the molecular scaffolds will be substantially enhanced with the discovery of relatively simple, small molecular weight bioactive natural products. Combinatorial approach with a nucleus that is already known to possess exciting biological activity will increase the likelihood of creating interesting drug candidate. Similarly, mixing of genetic information encoding for specific secondary metabolites may produce “unnatural” natural products with specific therapeutic activity (Rout *et al*. 2009).

Studies can show that the toxic effects of radiations and chemotherapy in cancer treatment could be reduced by Ayurvedic medications and similarly surgical wound healing could be accelerated by Ayurvedic medicines. Modern science and technology have an essential role to play in the process. Anintegrated approach for the cultivation, conservation and preservation of important plant species through plant molecular biology, plant tissue culture; research on the rationale and methodology of Ayurvedic medical practice; isolation of active constituents and their development into new therapeutics; standardisation and validation of known herbal medicines and other related aspects need to be focussed upon (Sharma, 1997).

CONCLUSION

A golden triangle consisting of Ayurveda, modern medicine and science will converge to form a real discovery engine that can result in newer, safer, cheaper and effective therapies. Nature is the best combinatorial chemist and till now natural products compounds discovered from medicinal plants (and their analogues thereof) have provided numerous clinically useful drugs. In spite of the various challenges encountered in the medicinal plant based drug discovery, natural products isolated from plants will still remain an essential component in the search for new medicines. Proper utilization of these resources and tools in bioprospecting will certainly help in discovering novel lead molecules from plants by employing modern drug discovery techniques and the coordinated efforts of various disciplines. Key factors to remain competitive with the modern system of medicine includes continual improvements in the speed of isolation, structure elucidation, and compound supply processes and selection of drug targets for the screening of Natural Product libraries. In this paper we have focused on the strategies, significance, guidelines and the research methods to be followed in order to develop herbal medicines which will gain international acceptance. Researches on pharmacognosy, chemistry, pharmacology and clinical therapeutics have been carried out on ayurvedic medicinal plants and many of the major pharmaceutical corporations have renewed their strategies in favour of natural products drug discovery. Numerous drugs have entered the international pharmacopoeia through the study of ethnopharmacology and traditional medicine. The R & D thrust in the pharmaceutical sector is focused on development of new innovative / indigenous plant- based drugs through investigation of leads from the traditional system of medicine. It is necessary to develop methods for rapid precise and accurate identification and estimation of active constituents in order to bring out consistency of important constituents in the formulations. Ayurveda and modern medicine techniques must be coupled in order to bring out high quality herbal products with rapid onset of action and good bioavailability. Herbal drug development is possible only through the development of standardized

herbal products with reference to their active phytoconstituents present for commercialization, correct identification and supply of raw material and to avoid adulteration. The concept of active markers needs a flexible approach in favour of the complex nature of this material. Therefore, these scientific investigations may be utilized for the development of newer therapeutic agents.

Table 1: Classification of plants Based on therapeutic activity

Antimalarial :	*Cinchona officinalis, Artemisia annua*
Anticancer :	*Catharanthus roseus, Taxus baccata*
Antiulcer :	*Azadirachta indica, Glycyrrhiza glabra*
Antidiabetic :	*Catharanthus roseus, Momordica charantia*
Anticholesterol :	*Allium sativum*
Antiinflammatory :	*Curcuma domestica, Desmodium gangeticum*
Antiviral :	*Acacia catechu*
Antibacterial :	*Plumbago indica*
Antifungal :	*Allium sativum*
Antiprotozoal :	*Ailanthus sp., Cephaelis ipecacuanha*
Antidiarrhoeal :	*Psidium gujava, Curcuma domestica*
Hypotensive :	*Coleus forskohlii, Alium sativum*
Tranquilizing :	*Rauvolfia serpentina*
Anaesthetic :	*Erythroxylum coca*
Spasmolytic :	*Atropa belladona, Hyoscyamus niger*
Diuretic :	*Phyllanthus niruri, Centella asiatica*
Astringent :	*Piper betle, Abrus precatorius*
Anthelmentic :	*Quisqualis indica, Punica granatum*
Cardiotonic :	*Digitalis sp., Thevetia sp.*
Antiallergic :	*Nandina domestica, Scutellaria baicalensis*
Hepatoprotective :	*Silybum marianum, Andrographis paniculata*

Table 2: Plant species with therapeutic value under different plant groups (Joy P.et al. 1998)

Thalophytes	230
Pteridophytes	382
Gymnospermae	55
Angiospermae:	
a) Monocotyledones	676
b) Bryophytes	39
Dicotyledones	3495
Total	4877

Table 3: Plant derived ethnotherapeutics and traditional modern medicine (Samy and Gopalakrishnakone .2007)

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

Table 4: Some of the important medicinal plants used for major modern drugs for cancer (Samy and Gopalakrishnakone .2007)

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

Table 5: New varieties of medicinal plants developed in India (Joy P.et al. 1998)

Crop	Variety	**Characters** (Institution where developed)
Sarpagandha *Rauvolfia serpentina*	RS-1	High seed germination (50%). Root yields 2.5t/ha in 18 months. Roots carry 1.45-1.80% of total alkaloids; half of it yields reserpine + serpentine combined (JNKVV, Indore)
Dioscorea floribunda	FB(C)-1 Arka-Upkar	A composite culture, produces fast growing vines relatively free from diseases and pest attack; produces 50t/ha of fresh tubers in 2 years containing 3.5% diosgenin (IIHR, Bangalore) Selection through hybridisation, producing 60t of fresh tubers containing 3.5-4.0% diosgenin (IIHR, Bangalore)
Khasi-kateri *Solanum viarum*	Glaxo IIHR 2n-11	Plants devoid of spines, produces high berry yield at high density planting containing 2.5-3.0% solasodine (Glaxo, India). Completely devoid of spines, produces high berry yield at high density planting containing 2.5-3% solasodine (IIHR, Bangalore)
Henbane *Hyocyamus niger*	IC-66, Aela	Short duration (100 days), early *rabi* crop in plains. Yields 2.5t/ha of dry herb with minimum 0.05% total alkaloids (NBPGR, Delhi) A mutant characterised by yellow flower petals, produces 7.5t/ha dry herb or 23kg total alkaloids/ha (CIMAP)

Table 6: Market size of phytomedicine and their sale in US Dollar (Samy and Gopalakrishnakone .2007)

No.	Country	Years	Drugs sales in US $ (billion)
1	Europe Germany France Italy Others	1991	6.0 3.0 1.6 0.6 0.8
2	Europe	1996	10.0
3	USA	1996	4.0
4	India	1996	1.0
5	Other countries	1996	5.0
6	All countries	1998	30.0 - 60.0

Table 7: Medicinal plant parts exported from India, importing medicinal plants and their parts (s

Exporting of herbals		Importing of herbals	
Botanical names	**Parts used**	**Botanical name**	**Parts used**
Acorus calamus	Rhizome	*Aloe vera*	Dried leaf
Argemone mexicana	Fruit	*Adhatoda vasica*	Bark and leaf
Curcuma longa	Rhizome	*Curcuma aromatica*	Rhizome
Curcuma aromatica	Wild turmeric	*Garcinia indica*	Fruit
Cassia lanceolata	Leaves	*Gloriosa superba*	Tuber and seed
Glycyrrhiza glabra	Root	*Juniperus communis*	Fruit
Withania somnifera	Vegetable rennet	*Myrica nagi*	Bark
Piper longum	Fruit	*Phyllanthus amarus*	Fruit
Swertia chirata	Whole plant	*Ocimum sanctum*	Leaf and essential oil
Zingiber officinale	Rhizome	*Vinca rosea*	Leaf, seed and stem

Table 8: Major plant drugs for which no synthetic one is currently available (Joy P.et al. 1998)

Drug	Plant	Use
Vinblastine	*Catharanthus roseus*	Anticancer
Vinblastine	*Catharanthus roseus*	Anticancer
Ajmalacine	*Catharanthus roseus*	Anticancer
Rescinnamine	*Rauvolfia serpentina*	Tranquilizer
Reserpine	*Rauvolfia serpentina*	Tranquilizer
Quinine	*Cinchona sp.*	Antimalarial
Pilocarpine	*Pilocarpus jaborandi*	Antiglucoma
Cocaine	*Erythroxylum coca*	Topical anaesthetic
Morphine	*Papaver somniferum*	Painkiller
Codeine	*Papaver somniferum*	Anticough
Atropine	*Atropa belladonna*	Spasmolytic, cold
Atropine	*Hyoscyamus niger*	Spasmolytic, cold
Artemisinin	*Artemesia annua*	Antimalarial,
Berberine	*Berberis*	For leishmaniasis
Pristimerin	*Celastrus paniculata*	Antimalarial
Quassinoids	*Ailanthus*	Antiprotozoal
Plumbagin	*Plumbago indica*	Antibacterial
Gossypol	*Gossypium sp.*	Antispermatogenic
Emetine	*Cephaelis ipecacuanha*	Amoebiasis
Glycyrrhizin	*Glycyrrhizia glabra*	Antiulcer
Nimbidin	*Azadirachta indica*	Antiulcer
Catechin	*Acacia catechu*	Antiulcer
Digitoxin, Digoxin	*Digitalis, Thevetia*	Cardio tonic
Elipticine	*Ochrosia*	Anticancer
Homoharringtonine	*Cephalotaxus*	Anticancer

Fig. 1:

Fig 2:

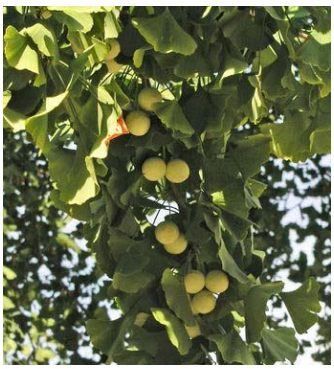


Fig. 3:

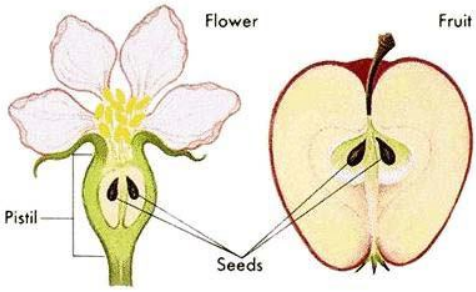


Fig. 4:

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