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QUALITY AUDIT OF HERBAL DRUGS - A REVIEW

Geeta Deswal[1*] and Dr. Vipin Saini[2]

[1]Guru Gobind Singh College of Pharmacy, Yamunanagar, 135001, Haryana, India.

[2]M.M. College of Pharmacy, M.M.U. Mullana, Ambala, Haryana, India.

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***Correspondence for Author**
Geeta Deswal
Guru Gobind Singh College of Pharmacy, Yamunanagar, 135001, Haryana, India.

ABSTRACT

Standardization of herbal formulations is essential in order to assess the quality of drugs, based on the concentration of their active principles, physical, chemical, phyto-chemical, and standardization, and In-vitro, In-vivo parameters. Evaluation of herbal drug is an important tool in the formulation of high quality herbal products. Quality of herb is depends upon on many factors like cultivation, collection, drying, storage, processing for market etc. Now a day's substitution and adulteration of herb is very common due to scarcity of drug and its high price prevailing in the market. Owing to medicinal properties attributed to an herb, it is necessary to maintain its quality and purity in the commercial market. A present overview covering various tool like morphological, microscopical, physical, chemical and biological employed for evaluation of herbal drugs.

KEYWORD: Herbs, Adulteration, Quality, Evaluation, Microscopy.

INTRODUCTION

Recent adverse events with Herbal Supplements in countries such as the US, clearly point towards the urgent need for Herbal Standardization and Evaluation of Safety and Efficacy.[6] Drugs from botanical sources (herbal medicines) are routinely used in India from ancient times and these botanical medicines are rapidly becoming popular in developed countries including USA. The statistics show that almost 40% of Indian population relies on these botanical medicines.[23]

Herbal medicines remain the major source of health care for the world's population. WHO has recognized herbal medicine as an essential building block for primary health care of vast countries like India and China.

Herbal drugs are probably the most common source of samples for evaluation in high-throughput screens of natural products. They have yielded many useful compounds and plant-derived ingredients, which are an important component of modern phytopharmaceuticals. Today, the global market is floated with herbal preparations. A number of companies, including some multinational are entering into the area of herbal medicines. These medicines are available for each and every disorder including diabetes, ulcer, cancer inflammation, hepatitis and asthma. Some recently introduced phytopharmaceuticals and herbal derived drugs of known structure that appear to be useful in therapeutics are briefly listed below:

- Banana powder recently launched in India as Musapep for the treatment of peptic ulcer.
- Dabur currently developed Taxol from various Taxus species for the treatment of cancer.
- Velvette has introduced Bacosides from Baccopa moniera under the brand name of 'Memory plus' as memory enchancer.
- Guggulusterols and Gugulipid from Commiphora mukul is developed by CDRI, Lunknow, as a hypolipedimic agent is being manufactured and marketed by CIPLA Ltd. in the western countries under the trade name 'Guglip'.
- Silymarin from Silybum marianum launched by Serum institute and Macro Labs under the brand name 'Limarin' and 'Silybon-70' with great success in liver diseases.
- Bioflavonoids and Gingketin from Ginkgo biloba is introduced in India by one of the world leading pharmaceutical company Ranbaxy as blood flow increasing and vascular dilating drug.
- Rutin bioflavonoids from Citrus fruit marketed by Sterling Lab and USV Ltd. under the brand name 'Kalpastic' and 'C.V.P.' respectively for increasing capillary fragility.
- Papain from Papaya fruits launched by FDC under the brand name 'Molzyme' for the treatment of indigestion and dyspepsia.
- Picroside and Kuthoside from Picrorhiza kuroos introduced by CDRI, Lucknow under the brand name 'Picroliv' for the treatment of hepatic damage.[15]

However these products, like their counterpart from synthetic sources, have never been subjected to Pharamcokinetic and bioavailability studies of the active constituents. This means that these botanical medicines are being used without the established dose and dosage

regimen. Consequently unexpected efficacy and side effects are common occurrence for these drugs.[23] So standardization is essentially a measure for ensuring the quality control of the herbal drugs.[20]

Quality of herbs has become a major concern following reports of heavy metals in Indian herbs.

For safe and effective use of herbal drugs, consistency in composition and biologic activity are essential. However, herbal drugs frequently fail to meet this standard, because there are problems of

- Difficulties in identification of plants
- Genetic variability
- Variations in growing conditions
- Diversity in harvesting procedures and processing of extracts
- The lack of information about active pharmacological principles.[4]

Evaluation of crude drugs involves the determination of authenticity, quality, purity, safety, potency, efficacy, reliability and reproducibility of the evaluation results for the varying batches of drugs.

For the evaluation of Herbal drugs in TSM (traditional systems of medicine) the parameters usually studied are:

- Authentication
- Foreign matters
- Organoleptic evaluation
- Microscopy
- Volatile matters
- Extractive values
- Ash values
- Radioactive contaminants
- Refractive index
- Marker components.[19]

In olden days these traditional medicinal formulations were prepared by vaidyas and were delivered to the patients in the fresh form where quality assurance was not needed in that way.

- For the quality assurance of churnas and Bhasmas – stomatal index, palisade ratio, fiber content, ash content. Including acid soluble and water soluble ash, particle size and numbers are measured.
- For liquid orals different analytical procedures like titrimetry, gravimetry etc.
- For lehas (the paste) extraction with solvents and their analysis by suitable techniques likes titrimetry, florimetry, nephalometry etc.

The importance of evaluation of herbal drugs is now well understood by the consumer as well as the industry. Evaluation and Standardization helps in effective quality control during commercial production of such drugs since pharmacopoeia standards are not adequate in most cases. In the past, the Ayurvedic physician would himself prepare small quantities of medicines for his patients but due to commercialization, the need for standardization has become important and necessary.[19]

During the last two decades or so emphasis has been laid on chemical ways of evaluation based on physical, chemical assays, chromatographic analysis and various spectroscopic methods. Most of these are qualitative methods though many plant materials have been evaluated quantitatively using HPLC and HPTLC and these methods are used as an effective quality control parameter. In such cases, chemical markers have been isolated and characterized.

Evaluation of herbal drugs is not an easy task as numerous factors influence the bio-efficacy and reproducible therapeutic effect. In order to obtain quality oriented herbal products care should be taken right from the proper identification of plants, season and area of collection and their extraction and purification process, and rationalizing the combination in case do polyherbal drugs Government should actively promote rational use of herbal medicines that have been scientifically validated. To do so they need a national policy for approving those that are safe and effective for specified clinical indications. The adoption of such policy will help to overcome some of the legal barriers against use of herbal medicinal plant preparations are of acceptable quality, safety and efficacy. Research on herbal medicines, which is

necessary to ensure that improved utilization by the public would benefit from strong governmental endorsement.[20]

ADULTERATION AND DETERIORATION.[16]

The term 'adulteration' or debasement of an article covers a number of conditions, which may be deliberate or accidental. Usually in crude drugs, this practice includes substitution of the original crude drugs partially or fully with other substances which is either free from or Inferior in therapeutic and chemical properties. Deterioration is an impairment of the quality or value of an article due to destruction or abstraction of valuable constituents by bad treatment or aging or to the deliberate extraction of the constituents and the sale of the residue as the original drugs Admixture is the addition of one article to another through accident, ignorance or carelessness e.g. inclusion of soil on an underground organ or the co-collection of two similar species. Sophistication is the deliberate addition of spurious or inferior material with intent to defraud; such materials are carefully produced and may appear at first sight to be genuine e.g. powder ginger may be diluted with starch with addition of little colouring material to give the correct shade of yellow colour. Substitution is the addition of an entirely different article in place of that which is required e.g. supply of cheap cottonseed oil in place of olive oil.[27]

TYPES OF ADULTERATION OR SUBSTITUTION OF HERBAL DRUGS

Generally any drugs of herbal origin are adulterated by substitution with substandard commercial varieties, inferior drugs or artificially manufactured commodities. Different methods used for adulteration may be grouped as follows:

Substitution with Inferior Commercial Varieties:

Due to morphological resemblance to the authentic drugs, different inferior commercial varieties are used as adulterant which may or may not have any chemical or therapeutic potential as that original natural drug e.g. Arabian Senna, obovate (dog Senna) and Provence Senna (C. auriculata) have been use to adulterate Senna; Cochin, African and Japanese ginger to adulterate medicinal ginger; Smyrna tragacanth and hog tragacanth as substitutes for tragacanth; Capsicum annuum fruits and Japanese chilies for fruits of Capsicum minimum etc.

Adulteration by Artificially Manufactured Substitutes

To provide the general form and appearance of various drugs, some materials are artificially manufactured and are used as substitute of the original one, e.g. compressed chicory in place of coffee; artificial invert sugar for honey; paraffin wax after yellow coloration substituted for bees wax.

Substitution by Exhausted Drugs

Here the same plant material is mixed which is having no active medicinal components as they have already been extracted out. This practice is most common in case of volatile oil containing materials like clove, fennel etc., where the dried exhausted material resembles the same like original drug (similarly with drugs like Cascara sagrada and ginger) Sometimes when colouring matters have been extracted or removed during exhaustion, the residue is re-coloured with artificial dyes as is done with saffron and red rose petals.

Substitution by Superficially Similar but Cheaper Natural Substances

Usually here the adulterated product has no relation with the genuine article, may or may not have any therapeutic or chemical component desired, e.g. leaves of species - Ailanthus are substituted for belladonna, senna, mint etc.; Leaves of Phytolacca and Scopolia for belladona; Leaves of Xanthium for stramonium and dandelion for henbane; Indian dill with European dill or caraway etc.

Adulteration by Addition of Worthless Heavy Materials

A large mass of stone mixed with Liquorice root, pieces of limestone are found in asafoetida and lead shot has occurred in pieces of opium etc.

Addition of Synthetic Principles

Sometimes to fortify inferior natural products, synthetic principles are added e.g. adding citral to oil of lemon; benzyl benzoate to balsam of Peru etc.

Usage of Vegetative Matter from the Same Plant

This is done by mixing adventitious matters or naturally occurring with the drug in excessive amount or parts of plant other than that which constitutes the drugs. For example liver warts and epiphytes growing in bark portion are mixed with Cascara or Cinchona; stem of buchu are sometimes cut into short lengths and added to the drug.[27]

Besides these some other techniques are being used for adulterating herbal medicine as by using harmful adulterants, which are mixed with the authentic drug e.g. limestone in asafetida; rodent fecal matters to cardamom seed etc. The crude drugs in powder form also are being adulterated e.g. dextrin in ipecacuanha; exhausted powder ginger in colocynth and ginger etc.

Deterioration of Herbal Drugs

Besides being adulterated by different means as discussed earlier, the crude drugs are prone to deterioration on storage. The shelf-life of crude drugs are influenced by many factors which include not only the quality of storage conditions but also the stability of the secondary (2°) metabolites present therein. Several factors are to be considered for the detrimental effects on the stored products.[19]

Primary Factors causing deterioration

Several environmental factors relating to storage e.g. light humidity, oxygen, temperature etc. can produce detrimental effects on stored products, but more deterioration usually results from a combination of these factors, which leads to the development of living organism including molds, mites, bacteria etc. The primary factors leading to the deterioration can be summarised as under:

(a) light
(b) Moisture/Humidity
(c) Temperature
(d) Airic Oxidation

Secondary Factors causing deterioration

Living organism usually develop in stored drugs where the conditions are satisfactory for them a hygienic point view. Such contaminated material should be destroyed irrespective of whether or not the active principles of drug have been affected.

(a) Bacteria and Moulds
(b) Mites and Nematode Worms
(c) Insects/Moths
(d) Coleoptera or Beetles.[19]

FACTORS AFFECTING QUALITY OF HERBAL DRUGS

The increasing demand for herbal medicines (which represent a substantial proportion of the global drug market), both in the developing and developed countries, inevitably led to maintaining the quality and purity of the herbal raw materials and finished products. The standardization problem relating to herbal drugs arises from the complex composition of drugs that are used in the form of whole plant, plant parts or extract obtained therefrom. To ensure reproducible quality of a herbal remedy, proper control of the starting material is utmost essential. To control the quality of this starting material, the following aspects need-to be considered

Authentication and Reproducibility of Herbal Ingredients

Herbal ingredients must be accurately identified by macroscopical and microscopical characteristics, comparison with authentic material or accurate description of authentic herbs. It is essential that herbal ingredients be referred to by their binomial Latin names of genus and species. Only permitted synonyms should be used. Even when correctly authenticated, it is important to realize that different batches of the same herbal ingredient may differ in quality due to a number of factors.

Inter/lntra Species Variation in Plants

There is considerable inter and intra species variations in different plants, for which the primary and secondary metabolite also varies considerably. This results in variation of the individual constituents and thereby causes difficulties in standardization. These all variations are genetically controlled which is related to the country of origin for that particular species

Environmental Factors

So many factors relating to climate, altitude, rainfall and other conditions responsible for growth of plants affect the quality of herbal ingredients present in a particular species, even if it is in the same country. This results in major variations in the herbal ingredients present in some specific species of plants.

Plant Parts Used

Usually the active constituents vary between different parts of a plant. It is not uncommon for a herbal ingredient to be adulterated with the parts of the plant not normally utilized. The same situation arises when an exhausted plant part of the same physical appearances are mixed to increase the weight of the supplied herbal ingredient causing adulteration.

Time of Harvesting

While collecting a particular herbal ingredient, the optimum time of harvesting should be specified. The constituents, like various concentrates obtained from the secondary metabolites, vary considerably during the growing cycle. That is why to get the maximum concentration of the desired constituent proper time of harvesting has a great rote to play.

Post Harvesting Factors

The treatment of the collected herbal raw materials like storage, transport etc. can greatly affect the quality of a herbal ingredient. Improper storage after collection may result in microbial contamination so also the processes such as drying etc. may result in a loss of thermolabile active constituents.

Contaminants of Herbal Ingredients

Herbal materials should be free from insect, other animal matter and excrete. As it is not possible to make the herbal materials completely free from all these contaminants, specifications have been set up to limit them. This includes the determination of ash value, which constitutes the inorganic matter after incineration of that particular herbal ingredient. Treatment of that with hydrochloric acid results in acid insoluble ash, which consists mainly of silica. This may be used to act as a measure of soil present within them. Same is the case for the presence of foreign organic matter which is usually present with almost all herbal ingredients consisting of the related parts of the plant or other plants. Standards should be set in order to fix the limit for those unwanted plant contaminates. Some times, aerobic bacteria and fungi may be present in plant material due to faulty growing, harvesting, storage or processing. It is not uncommon for herbal ingredient to have aerobic bacteria present at 10^2 to 10^8 colony-forming units per gram. Some pathogenic organisms including Enterobacter, Entrociocus, Clostridium, Pseudomonas, Shigella and Streptococcus have been shown to contaminant different herbal ingredients. Herbal drugs with high starch content are prome to increase microbial growth, so limit should be set to control all these contamination.

Pesticides, Fumigants and other Toxic Metals

Herbal materials growing as cultivated crops may be contaminated by DDT or other chlorinated hydrocarbons, organophosphates, carbamates, or polychlorinated biphenyls. Ethylene oxide, methylbromide, phosphine and other fumigants are sometime used to control pests that contaminate herbal ingredients. Lead, cadmium, mercury, thallium and

arsenic have been shown to be contaminants of some herbal ingredients. Limit tests for acceptable levels of all these pesticides, fumigants as well as the toxic metals are utmost necessary to control the quality of plant materials. To increase the quality of herbal ingredients similar fixation of limits of other contaminants as well including endotoxins, mycotoxins and radio-nuclides are essential to ensure high quality of therapeutically potent medicinal plants.

Ecological Factors

In the era of "set-aside" land, growing herbs as an organic crop offers new opportunity for the farmers who find that their usual crops are no longer economical to grow. This is one of the major implications to support the increased use of medicinal herbs. However the rise in popularity of herbal medicines directly threatens this survival of some wild species e.g. demand for Panax quinquefol/µm (American ginseng) has become so great that it now fetches around US $ 1100 per Kg. About two centuries ago it was a common plant in the woodlands of Northern and Eastern America but is now an endangered species and may become extinct in the wild. This example is by no means unique and sadly, many species are similarly threatened across the planet. This extinction of plant species as a result of over intensive collection is nothing new. The herb Silphion, member of the carrot family was used extensively as a contraceptive by the women of ancient Rome. Silphion was proved to be difficult to cultivate and was gathered from the wild in such large quantities that it become extinct during the 3rd century AD. Today, if herbal medicine is to grow at its present rate it is imperative that manufacturers should proceed with the production of herbal drugs in an ecologically sensitive manner.

Quality Assurance of Herbal Drugs

Ideally the exact geographical source of a herbal material so much so the condition under which: it has been grown, harvested, dried and stored should be known. The chemical treatment such as pesticide or fumigants used during Harvesting or storing should be known. However, in many cases since the herbal raw materials are obtained from varied geographical and commercial sources, the above conditions may not be always known. For these reasons therefore, appropriate level of testing additional to the monograph criteria of any official book should be carefully assessed, based on various factors including the nature of the material, knowledge of its batch history and test results from previous batches.

Quality assurance of herbal products may be ensured by proper control of the herbal ingredients and by means of good manufacturing practices. Some herbal products have many herbal ingredients with only small amounts of individual herbs being present. Chemical and chromatographic tests are useful for developing finished product specifications. Stability and shelf life of herbal products should be established by the manufacturers. There should be no differences in standards set for the quality of different dosage forms; such as tablets or capsules of herbal remedies as well as from those of other pharmaceutical preparations.[12, 19]

WAYS OF EVALUATION OF HERBAL DRUGS

To evaluate a drug means to identify it and to determine its quality and purity and detection of nature of adulteration. The evaluation of a crude drug is necessary because of three main.

REASONS

1. Biochemical variation in the drug.
2. Deterioration due to treatment and storage.
3. Substitution and adulteration as a result of carelessness, ignorance or fraud.[14]

- The identity of a drug can be established by its actual collection from a plant or animal that has been positively identified.
- Quality refers to the intrinsic value of the drug i.e., the amount of medicinal principles or active constituents present.
- Purity In case of crude drugs purity may be considered in terms of the presence of authentic material without any adulteration or admixture. For the evaluation of purity of drugs various methods used like :- the organoleptic, histological studies, histochemical tests, total extractives etc.[17]

The evaluation of a drug involves a number of methods that may be classified as follows:

- ORGANOLEPTIC
- MICROSCOPICAL
- BIOLOGICAL
- CHEMICAL
- PHYSICAL

ORGANOLEPTIC EVALUATION

Organoleptic (lit. impression on the organs) refers to evaluation by means of the organs of sense and includes the macroscopic appearance of the drug, its odor and taste. Occasionally

the sound or "snap" of its fracture and the "feel" of the drug to the touch. It refers to evaluation of drugs by colour, odour, taste size, touch texture etc. It is a technique of qualitative evaluation based on the study of morphological and sensory profiles of whole drugs. Organoleptic evaluation means conclusions drawn from studies resulted due to impressions on organs of senses. The study of form of a crude drug is morphology while description of the form is morphography.[17]

EG.

a) The fractured surfaces in cinchona, quillaia and cascara barks and quassia wood are imp. characteristics.
b) Aromatic odour of umbelliferous fruits and sweet taste of liquorice are the Examples of this type of evaluation.
c) The ovoid tears of gumacacia, ribbon shaped characteristic of tragacanth, disc-shaped structure of Nux-vomica, conical shaped of aconite quills of cinnamon etc. are imp. diagnostic characters.
d) Seed in colocynth, stalk in clove etc.
e) The wavy shape of rauwolfia, pungent taste of capsicum and ginger, brown colour of cinnamon, odour and taste of spice-drugs like, Asafoetida, black papper, nutmeg, caraway, cummin etc. are imp. diagnostic organoleptic characteristic.[14,28]

MICROSCOPICAL EVALUATION

Microscopically evaluations of drugs are very useful in the identification of different varieties of a drug and its adulterants. The drug is examined under a microscope. This can be performed by powdering, cutting a thin section (LS/TS) or preparing a macerate of the crude drug. After this, different reagents and stains are used to distinguish the arrangement of cellular structure.

Eg.:

- Phloroglucinol and hydrochloric acid for lignified tissues.
- Chlor-zinc iodide reagent for cellulosic tissues.

For the common microscopical studies the compound microscopes with 10x objective is generally suitable for pharmacognostic work. For higher magnification 45x or high power objectives may be used. Some histochemical tests may be performed on the microscopical sections for the study of ergastic substances like, starch, fixed oil, aleurone grains, mucilage,

calcium oxalate or even for the localization of certain secondary metabolites. Another imp. aspect of microscopical evaluation is the study of surface constants. The leaf constants like stomatal number, stomatal index, palisade ratio vein islet and vein termination number are studied by using camera Lucida.[2,17]

PHYSICAL EVALUATION

Evaluation of the drugs on the basis of important physical properties or physical characteristics of the active constituents is k/s physical evaluation. For the ease of study, these methods can be divided into various categories like foreign material, ash values, extractive values, chromatographic methods, physical constants, and spectroscopical methods.

CHEMICAL EVALUATION

Just like the physical methods of evaluation chemical nature of the constituents can be used as tool to device a method for the analysis of the active constituents. Classical titrimetric assay procedures may be used for determination of some physicochemical characteristics of the fixed oils and fats, like Acid value. Saponification value, Iodine value etc. Nonaqueous titrimetric methods can be used for the analysis of organic acids. For many crude drugs gravimetric analysis is performed in which the determination of the weight of substance in the sample or the weight of some other substance derived from the sample can be calculated. In many cases the conversion of the constituents to other derivatives which could be easily separatedout from the mixture of the other compounds and then its recovery to its original constituents can be of utility in the analysis. Many of the alkaloidal bases, organic acids or phenolic compounds are first converted to their original compounds. The chemical nature may be used to convert the molecule to a highly colored complex or chelate which facilitates its analysis by colorimetric methods.

The easier and the faster way of checking the presence of specific group of constituents in the extract of drug is proximate chemical analysis preliminary phytochemical screening. It makes use of simple chemical tests for the determination of specific organic groupings which may be present in any drug to which its therapeutic activity is attributed. Some important chemical tests used in proximate chemical analysis are given in table.[21,17,14,29]

BIOLOGICAL EVALUATION

When the estimation of potency of crude drug or its preparation is done by means of its effect on living organisms like bacteria, fungal growth or animal tissue or entire animal, it is known as bioassay. This method is generally called for, when standardization is not adequately done by chemical or physical means and also for conformity of therapeutic activity of raw material and finished product. In other words, bioassay is the measure of sample being tested capable of producing biological effect as that of the standard preparation. Such activity is represented in units known as international Unit (I.U.). The specific biological activity contained in each I.U. of the few drugs is mentioned as under:

Digitalis - 1 IU is contained in 76 mg of standard preparation

Vit. A - 1 IU is present in 0.344 micrograms of standard preparation

Vit. D - 1 IU is contained in 0.025 micrograms of standard preparation

Biological assay methods are mainly of 3 types, (i) toxic, (ii) symptomatic, (iii) tissue methods. In toxic and symptomatic techniques, the animals are used, whereas in tissue method, the effect of a drug is observed on isolated organ or tissue. Among the drugs that are subjected to bioassay are cardiac glycosides, natural pesticides and antibiotics.

NEW DEVELOPMENTS IN HERBALS

There has been a controversial discussion about herbal medicines sold outside pharmacies. One of the problems is that some of these drugs can only be sold outside pharmacies if they claim other than therapeutic indications This legislation led to fantastic indication claims as for example "blood purifier", "to fortify heart or nerves", or "heart nutrition". Other products claim prophylactic or supporting effects. Most of these products are very complex fixed combinations composed of herbal preparations and other chemically defined substances. The dosage of the active constituents is normally quite low. It is difficult to find scientific evidence of efficacy for such products. In some cases, this is even true for a traditional use within the indications claimed for the product. Consequently, the evaluation approach by the official authorities would lead to a negative vote and to the disappearance of such products from the market, even if the weakest criteria be applied. The corresponding products have to be labelled as traditionally used based on different criteria as:

- To tonify and to fortify
- For amelioration of subjective health conditions
- To support organ function
- For prophylaxis

- As mildly active drug

Because of these aspects, we would have to consider three groups of herbal medicines, which differ with respect to their indication claims:

- Herbal medicines with indication proved by new controlled clinical trails
- Those with indications proved at least by long-term traditional use which is supported by experimental data and
- Herbal medicines with documented traditional use but without further assessment of efficacy requiring a special labelling on the package of the finished drug.

BIOLOGICAL DIVERSITY-ROLE IN HERBAL DRUG DEVELOPMENT

Natural products and especially those derived from higher plants have historically-played a pivotal role in the discovery of new Pharmaceuticals. However, in the recent past" less" emphasis has been placed on higher plants as compared to other natural product-sources especially microorganisms. An important, if not predominant, consideration fostering this lack of interest in higher plant-derived leads has to do with the issue of sustainable and economic supplies of the bulk drug to meet the needs of the drug development process and ultimately the clinical use of the drug. A brief overview of alternative strategies to resolve supply issues and their relative strengths and weaknesses is presented.

Chemicals derived from higher plants have played a central role in the history of mankind. Efforts to develop new, clinically effective pharmaceutical agents have relied primarily on one of five approaches, most of which utilize existing agents in some manner as follows:

- Derivatization of existing agents
- Synthesis of additional analogues of existing agents
- Use of combination therapy of existing agents with other drugs
- Improvement of delivery of existing agents to the target site
- Discovery of new prototype pharmaceutical agents.

While approaches 1 - 4 are important and need to be continued in that they seek to utilize existing agents and information in the most effective manner, there is an urgent need for the development of totally new, prototype agents which do not share the same toxicities, cross resistance or mechanism of action as existing agents. Natural products have, in the past, provided a rich source of such prototype bioactive compounds and it is essential that the search for new drugs pursue this route. The major advantage of this approach is the likelihood of identifying new prototype drugs with quite different chemical structures and

mechanisms of action and hence, lower likelihood of similar toxicities and cross resistance.[19]

CONCLUSION

Various systems of plant based traditional medicine have been in use in India and also in many parts of the world for ages. Plants have been a source of chemical substance, which serves as drugs in their own right of as key ingredient in synthetic drugs. To ensure quality and efficacy of such drugs, there is a need to develop methods of standardization of raw materials.[11]

The subject of herbal drug standardization is massively wide and deep. There is so much to know and so much seemingly contradictory theories on the subject of herbal medicines and its relationship with human physiology and mental function. For the purpose of research work on standardization of herbal formulations and neutraceuticals a profound knowledge of the important herbs found in India and widely used in Ayurvedic formulation is of utmost importance. India can emerge as the major country and play the lead role in production of standardized, therapeutically effective Ayurvedic formulation. India needs to explore the medicinally important plants. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization such as UV-visible, TLC, HPLC, HPTLC, GC-MS, spectrofluorimetric and other methods.[10]

Herbal drug have become an indispensable part of the health care systems due to the fact that they are easily available and safe because of low toxicity and relatively low cost.[3]

The global interest in the area of natural products has risen dramatically in the past few years and this trend seems to continue in future thereby decreasing the cost of medicament considerably to a mere value.[9]

REFERENCES

1. "Ayurvedic formulary of India", Part-l, 2nd ed, Govt. of India, Ministry of Health and Family Planning, Department of Indian System of medicine and Homeopathy, Delhi.
2. Bhandari A and Singh G.K. "A Text book of Pharmacognosy" CBS Publication, 1st ed., 2004; 34.

3. Bhatnagar, S.P.., "Development of Data base for identification of crude drugs." Indian J. Pharm. Educ", 2005; 39(1): 38-41.
4. Bhatt, A. Ayurvedic Herbal Industry. QUEST for Global Acceptance "Ayurveda Heritage" 2005; 1(1): 4-6.
5. Brain, K.R. and Turnes, T.D. "The Practical evaluation of phyto-Pharmaceutical". Wright Scientechina, Bristol, 1975; 36: 81-85, 101-102.
6. Chaudhary J., Standardization and Evaluation of Traditional Medicines. "Chronicle Pharma". 2003; 12: 16.
7. Ernst E, Thompson Coon J Heavy metals in Traditional Chinese Medicines: A Systematic Review. "Clin. Pharm. Therap". 2001; 70.
8. Ernst E., Heavy Metal in traditional Indian Remedies, "Eur J Clin Pharmacol" 2002; 57: 891-6.
9. Ganapati S., Emerging Strategies in the study of natural products, "Indian J. Pharm. Educ", 2004; 38(3): .
10. Jain Sailesh, WHO Guidelines for Quality Standardization Ayurvedic Formulations, "www.ayurvedahc.com", 2005.
11. Kapadia S.N., "Quality Control & Standardization of Immunomodulator Herbal and their market Formulations" (Ph.D.) thesis. "Indian J. Pharm. Edu. Res", 2005; 39(4): 219.
12. Kapoor, V.K., and Handa, S.S., "Text book of Pharmacognosy" Vallabh Prakashan, 1st ed., 2001; 35-40.
13. Kokate, C.K., "Practical Pharmacognosy", Vallabh Prakashan, 4th ed., 1994, 122.
14. Kokate, C.K., Purohit, A.P., and Gokhale, S.B., "Pharmacognosy" Nirali Prakashan, 4th ed., 2003, 109(119): 121-123.
15. Kumar, V. and Parmar, N.S., Herbs: A Potential source for the development of new Phytomedicinals, "The Pharma Review", 2003; 1(4): 59-60.
16. Lakshmi V. Food Adulteration. International Journal of Science Inventions Today, 2012; 1(2): 106-113.
17. Marcus, D.M. and Grolman, A.P. Botanical Medicines. The Need for New Regulation. "N. Engl. J. Med.", 2002; 347: 2073-2076.

18. Ali, M., "A Text Book of Pharmacognosy", CBS Publication, 2nd ed., 2003; 52(62): 137-139.
19. Mukharjee, Pulok K., "Quality Control of Herbal Drugs", Business Horizon Publication, 1st edition, 2002; 99: 112-125.
20. Patel, P.M., Quality control of Herbal and Herbs Mineral products: An Emerging Trend., "Pharma Times", 2005; 37(11): 71-74.
21. "Pharmacopoeia of India", Ministry of Health & Family Welfare, Govt. of India, The Control of Publication, Delhi, 2nd Vol. 1996, A-A-42, A-43, A-53, A-54, A-70, A-75.
22. Rangari, Vinod., "Pharmacognosy and phytochemistry", Career Publications, New Delhi, 1st ed., 2002; 88-90.
23. Sagar Bhanu, P.S., Herbal Drug Standardization; "The Indian Pharmacist" 2005; 4(35): 19-22.
24. Samanta, M.K., Pharmaceutics of Herbal Drugs ;An Introduction, "lndian J. Pharm. Educ". 38 (1) 2004, 16-18.
25. Saper, R.B., Kales, SN.,and Pagiun, J. Heavy Metal Content of Ayurvedic Herbal Medicine Products. "JAMA", 2004; 292: 2868-2873.
26. Straus, S.E., Herbal Medicines - What's in the Bottle? "N. Engl. J. Med.". 2002; 347: 1997-1998.
27. Trease, G.E. and Evan, W.C., "Pharmacognosy", ELBS Publication, 12th ed., 1985; 131-137.
28. Tyler, V.E., Brady, L.R. and Robbers, J.E., "Pharmacognosy", 9th ,1988
29. Wallis, T.E.,"A Textbook of Pharmacognosy", CBS Publication, 5th ed., 1985; 561,562.
30. WHO, "Quality Control methods for plant materials Geneva", 1998; 1-40.
31. www.acetahort.org.
32. www.missionreach.com.
33. www.businesshorizons.com.
34. www.acetahort.org.
35. www.shriraminstitute.org.
36. www.ias.ac.incurrsci.