STANDARDIZATION OF HERBAL PRODUCTS

Herbal drug, the naturally of mankind since ages in combating various diseases has received a raw deal from the practitioners of the modern medicine due to many reasons. The moment one speaks on an herbal drug (be it Ayurvedic or Unani or Siddha) many questions arises:

1. The rationality of multiple combinations of herbs.
2. Advantages on using of crude extracts/powder over isolated principles.
3. Quality control and quality assurance of raw materials and final products.
4. Efficacy.

Though a number of scientific documentations are available on crude extractives of herbs and plants, nothing has really materialized to promote them as drugs due to many factors:

1. Lack of reproducible biological effects.
2. Selection of wrong plants and lack of data on the time and area of collection and the extract processing in order to retain the biological efficacy consistent from batch to batch.

The above factors made the herbal products as simple food supplements rather than viable therapeutic agents.

Standardization of herbal drugs is not an easy task as numerous factors influence the bioefficacy 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 qurification process and rationalizing the combination in case do polyherbal drugs.

Remedial measures:

Identification of herbs: Vernacular names of herbs vary from place to place and if these are collected on the basis of experience of traditional systems of medicine, it is essential to identify the herb taken for scientific analysis which should be exactly similar to the one being used in traditional system of medicine. For example, **"Pashanbheda"** is the vernacular name of herb often used in Ayurvedic system for various diseases and there are nearly twelve varieties of "Pashanbheda" available in the market, which belong to different families and have divergent

biological effects and hence, if the right plant is not identified with needed bioefficacy, the formulations made with the plant will not be effective. Hence, while selecting the herb, it is always necessary to carryout relevant pharmacological experiments and finalizes the herbs for formulations.

Area and season of collection: The bio efficacy of herbs is certainly influence by its habitat and the time of its collection as the Phytochemical constituents vary in herbs accordingly and thus not only loose their bio efficacy but can also become toxic.

Preservation and processing: Preservation of large quantities of herbs after collection is a common practice in herbal industries due to seasonal availability of particular herb or being less costly during a particular season; however, the improper preservation affects the quality of the herb and sometimes leads to development of fungal toxins.

Processing of herbal drugs significantly contribute to the bio efficacy. In traditional systems of medicine mostly the freshly collected herbs are processed for powdering and crushing or preparing water extracts or using in fermentation process. However, the modern Phytochemical analysis is done by using mostly dried herbs which are extracted with various organic solvents from non polar to polar ones and then with water.

Rationality of polyherbal formulations: Majority of herbal drugs are multiherbal combinations whose rationality has yet to be proved in all the cases. As per the traditional system of Indian medicine (Ayurveda), the combinations of herbs are based on the "Tridoshas (Kapha, vata and pitta) and Dravyaguna theory". It is imperative that one basically initiated work on the necessity of each herb in a multiple combination formula by the way of rational biological screening and eliminate the herbs whose presence is not felt to be necessary and whose absence does not alter the therapeutic efficacy of the formulation.

Crude extracts Vs isolated compounds: It is often argued by modern scientists that herbs have one or two active compounds and rest of material is of no biological importance and hence one should work only with isolated principles. However, if the literature is any evidence, out of the hundreds and thousands of compounds that have been isolated hardly a dozen could pass the stage of clinical trails due to either being ineffective in human models or due to the narrow margin of ED50 and LD50 i.e. low therapeutic index. It is interesting to note that the crude

extracts of the herbs which form the source of such isolated compounds are still used as therapeutic agents often with proven efficacy and less toxicity. The reason could be the presence of many compounds in the extracts which may not have therapeutic value in them but they either increase bioavailability or reduce the toxicity limit of active compounds present in the extracts.

Quality control and quality assurance of herbal drugs: A great majority of drugs in modern medicine have been analyzed and their authenticity confirmed by chemical and instrumental analysis. Often the quality control and quality assurance of the drug is confirmed by these tests and no biological screening is done. However, the case of herbal drugs is different as no standard Pharmacopoeial methods are available for their identity, when they are in multiherbal formulations and more so when the extracts of herbs have been used in the formulations. As no standard chemical and analytical methods could be set up for herbal formulations nor they can be relied upon, it is necessary that if biological screening methods are adopted for regular check up of efficacy of herbal drugs, it would be possible to maintain the quality of the product and its therapeutic efficacy is assured. However, regular botanical identification and Phytochemical testing shall be of immense help if carried out for both raw materials as well as the formulations.

Physico-chemical parameters of standardization: To check any adulteration or no deliberate mixing in the commercial batches, specifications must be laid down for each herb. These specifications should be strictly followed on commercial consignments. These include following:

1. **Macroscopy:** In some cases general appearance of the herb is similar to related species. Detailed study on the morphological characters can be helpful in differentiating them.
2. **Microscopy:** Similar looking hebs of different species of the same genus can be differentiated by studying the details of the cell structure and their general arrangement, calcium oxalate crystals, starch grains, stone cells, type of trichomes, etc. Similarly measurement of starch grains, fibers, vessels, tracheids are useful for identification of a particular herb.
3. **Qualitative chemical tests and chemical fingerprinting using UV/TLC/HPTLC techniques:** UV curve and HPTLC peaks are useful in indicating the quality of the herb. It gives a rough fingerprint which may serve as a reference for quick quality control approval.

4. **Fluorescence studies:** Many herbs fluoresce when cut surface or the powder is exposed to UV light.

Once the plant is identified properly it is subjected to total quality testing. Quality of the material must be uniform and should not vary in different consignments. Quality control of a herb is very important to ascertain a particular therapeutic efficacy. Following parameters alone or in combination should be studied to ensure the quality of the herb.

1. **Chemical assay:** Specific assay for active principles eg. Total alkaloids, resins, volatile oil, glycosides, saponins, tannins etc. is carried out by different chemical methods.
2. **Instrumental analysis:** Major active constituents are quantified by using HPTLC/HPLC/GC or spectrophotometric methods. These actives are marked as marker peaks.
3. **Extractive values:** Alcohol and water soluble extractive give an idea about the quality of herb.
4. **Ash values:** Total ash, acid insoluble and water soluble ash are also helpful in standardizing the herbs.
5. **Foreign matter:** Any foreign matter other than the specified part including insects, rodents or animal excreta should not be present.
6. **Microbial contamination:** Herbs should be clean and should be free from any pathogens, bacteria, moulds or fungus. If heating is not involved in the manufacturing process, herbs should be properly sterilized by ethylene oxide or gamma radiation.
7. **Quantitative microscopy:** In case of powdered herbs, it is sometimes difficult to differentiate between adulterant and genuine plant. Quantitative microscopical techniques help to differentiate allied species.
8. **Herbicide/Pesticide residues:** Proper testing procedures should be developed so that these residues are well within limits.
9. **Absence of mycotoxins or aflatoxins:** Aflatoxins are produced from Aspergillus species. Suitable test should be carried out to ensure their absence.

Based on the above studies, specifications can be drawn for a particular herb. In commercial practice, several problems are encountered when larger consignments are received from different traders. They are adulteration/ substitution, mixture of different species, wrongly

labeled materials based on local names, substantantial quantities of foreign matter, contamination with funguses.

To eliminate such problems and to have better control on raw materials it is desirable to monitor the following:

1. Herbs should be collected when their active principles are maximum.
2. Trained taxonomist/botanists should be entrusted to distinguish between related species of a given plant.
3. Unwanted and foreign material should be removed from the herb.
4. Herbs should be sorted properly into different grades according to the quality and the best grade be used.
5. Drying of the herbs should be controlled keeping in view the type of active compounds, eg. Sun drying/ vacuum drying. Moisture should be controlled below 9-10% if it exceeds, the herb becomes prone to fungal contamination.
6. Dried herbs should be stored in closed containers. Storage place should be rodent free, cool,dark and well ventilated and moisture free.
7. Storage period of any crude drug should be studied carefully.
8. Truly representative sample must be drawn for analysis according to prescribed USP/ISI method of sampling.

In order to ensure that the finished product is consistent in quality from batch to batch, we must ensure the following:

1. Extraction can be carried out by using either individual herbs or mixed herbs. Ideally each herb should be extracted separately. To avoid degradation of active compounds, extraction and drying should be done preferably at low temperatures under vacuum.
2. While processing herbs, cleaning and size reduction is necessary. Complete extraction of herbs is generally effective in coarse powder. Chemical standardization of the product for actives should be carried out both qualitatively and quantitatively using instrumental techniques like HPTLC/TLC/GC/LC/UV spectrophotometry.

Finished product should be standardized in terms of **shelf life** and other physical parameters.

Acute toxicity studies must be conducted on the product along with biological activity in isolated organs or intact laboratory animals wherever pharmacological parameters are available. This biological assay could also be useful in standardization of the product. Controlled clinical trials of the finished products should be conducted on humans at different hospitals to substantiate the efficacy claim.

Herbal medicines can be relevant today only if they are applied and tested within the frame work of modern science and subjected to the most rigorous criteria for quality, safety and efficacy. Only then herbal products can be comparable with modern medicines and bring the necessary confidence in practicing doctors.