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A Note on Variation of Active Principles in Indian Medicinal Plants and TIM Formulations

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Dr. Amritpal Singh

Herbal Consultant, Ind- Swift Ltd, Chandigarh

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The active principles or constituents (phytochemicals) in medicinal plants are chemical compounds known as secondary plant products. Some secondary products discourage herbivores; others inhibit bacterial or fungal pathogens. Active principles in medicinal plants may affect health, but are not-essential nutrients as our diet does not require them to sustain life in the same way as vitamins and minerals.

Ayurvedic scholars established fundamental rules for medicinal plant identification, collection and storage of drugs. According to Ayurveda, habitat an ecological factors have influence on pharmacological activity of plant based drugs. According to Ayurveda, habitat is known as desha. Plants growing in *jangala desha*, *anoop desha*, and are known as xerophytes, hydrophytes and mesophytes, respectively

Season has impact on availability of active principles in medicinal plants. According to principles of Western Herbal Medicine, Therapeutic efficacy varies during different times or seasons of the year. The constituent and active principles vary quantitavely at different seasons of the year and the majority of plant materials are usually best collected during the dry season, when the herbs are at peak maturity and concentration. *Charaka* and *Sushruta* stress timely collection of medicinal parts of plants. It is self-explanatory that ancient physicians were aware about relation between period of collection and distribution of active principles. *Virya* signifies energy or potency of a drug or medicinal plant. *Charaka* defines *virya* as driving force behind the therapeutic activity of the drug. According to some experts, *virya* is comparable to active constituent of a drug.

Standardization of medicinal plants used in Ayurveda, is global perspective. Numerous papers addressing the all important issue of standardization have been published; still no definite conclusion has been withdrawn. Work has been done on chemical standardization of medicinal plants used inAyurveda. Standardized herbal extracts are available in the market, indicating the percentage of active principle on the label of the pack. Contrary to it, papers addressing the issue of standardization, challenges the percentage of active principles in several commercial preparations.

Standardization does have impact on quality of finished product. Mere chemical standardization of herbs is not sufficient for therapeutically active formulation. Biological standardization is crucial for establishing clinical efficacy of plant based products. As an instance foxglove, *Digitalis purpurea* (*Tilpushpi* in *Ayurveda*) provided the medical fraternity with most efficacious cardiac tonic, digoxin. As per instructions in the British Pharmacopoeia, the digoxin is standardized biologically, rather than chemically. Further, standardizing an herbal drug to one chemical marker as been challenged as synergy among various chemical constitutes, contribute towards medicinal activity.

Recent times have witnessed increased sale of herbal products in the international market. According to World Health Organization, present demand for medicinal plants annually, is about US$14 billion. Traditional Chinese Medicine (TCM) has made tremendous advances in terms of modern scientific research, and according to latest studies it contributes 80 % of the annual turnover of the total herbal drug industry.

Medicinal plant-related trade in India is estimated to be around Rs. 550 crores per year. While the value of global trade in medicinal plants has been put at over $ 60 billion per year, of which Indians total turnover of Rs. 2300 crores (US$551 million) of Ayurvedic and herbal products. Exports of Ayurvedic medicines have reached a value of 100 million dollars a year. About 60% of this is crude herbs, about 30% is finished product shipped abroad for direct sales to consumers, and the remaining 10% is partially prepared products to be finished in the foreign countries. With the standardization wave sweeping the herbal drug industry, several companies in India are selling standardized products. The commonly available standardized Ayurvedic herbs are:

1. *Adhatoda vasica* (0.5% Vasicine)
2. *Andrographis paniculata* (10% Andrographolide)
3. *Azadirachita indica* 2% (Azadiractin)
4. *Bacopa monneri* 20% (Bacoside)
5. *Boswellia seratta* (40% and 70% Boswellic Acid).
6. *Centella asiatica* (3% Asiaticoside)
7. *Commiphora mukul* (5% Guggulsterones)
8. *Curcuma longa* (95% Curcumin)
9. *Embelia ribes* (8% Embellin)
10. *Glycyrrihiza glabra* (20% Glycyrrhizin)
11. *Gymnema sylvestre* (25% Gymnemic Acid).
12. *Momordica charantia* (3% bitters).
13. *Phyllanthus niruri* (2% bitters)
14. *Picrorrhiza kurroa* (10% bitters)
15. *Tribulus terrestris* (20% and 40% Saponin)
17. *Trigonella foenum graceum* (10% Saponin)
18. *Withania somnifera* (1.5% withanolides / 1% Alkaloid).

Majority of the companies promoting herbal products have fixed standards (percentage of active principle). Since the efficacy of herbal product is based on percentage of active principle, it becomes mandatory that claimed percentage of active principle, should be present in the finished product. Consumer laboratory in America have issued several alerts addressing batch to batch variability active constituents in commercial preparations for herbal remedies like *Hypericum perforatum*, *Ginkgo biloba* and *Silybum marianum*.

Good Agricultural Practices (GAP) need to be standardized for enhancing quality of finished Ayurvedic products. With introduction of organic farming and transgenic crops, it will be possible to get standardized raw material for therapeutically active finished products. Central Council of Indian Medicine has developed agricultural techniques for prioritized Ayurvedic plants and commercialized the technology. Ayurveda recommends use of fresh herbs rather than stored herbs. Although it is not practically possible to have all herbs in on store, one has to depend on the market for buying. Shelf-life and transportation are other factors responsible for variation of active principles in herbs purchased from the market.

***Ashwagandha* (reference to withaferin-A)**

An interesting study reported variability of withaferin-A in commercial preparations of Ashwagandha (*Withania somnifera*). Commercial samples consisting of 250 mg Ashwagandha (as indicated on the label) were investigated for their phytochemical contents. The samples were quantified by High Performance Liquid Chromatography. The amount of withaferin-A estimated in commercial samples is given in table 14. There was significant variation in relative amount of withaferin A. The study reflected a 117-fold higher concentration of withaferin A in the highest holding product compared to one with the least. Further, according to the recommended intake of the product as mentioned on the label, dose of withaferin A ranged from 0.02 mg to 1.4 mg (Sangwan *et al*., 2004).

***Brahami* (reference to bacoside-A)**

Brahami is used as brain tonic in Ayurveda. The activity is due to presence of Bacosides. As already discussed, the maximum level of bacosides in Indian products corresponds to 20 percent. Bacoside-A content of herb was reported to be high from September through March and in June. Suitable harvest times for high yields of bacoside-A were June and September through November. An accession from Guwahati in Assam state of India yielded more Bacoside-A than all other accessions (Mathur *et al*, 2002).

Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, India, has developed improved varieties like Pragyashakti, Subodhak and CIM-Jagriti have been developed. Pragyashakti is a selection from Orissa. The yield of dry herb is 65 quintal/ha from which 118 kg/ha Bacoside A (1.8%) can be obtained in single harvest. Subodhak is also collected from wild collections. The yield of dry herb is 47 quintal/ha from which 77 kg/ha Bacoside A (1.6%) can be obtained in single harvest. CIM-Jagriti has the potential of producing average 85 kg/ha of bacoside A from an average dry herb yields of 40 quintal/ha. Regional Research Laboratory, Jammu, India, has worked on a variety of *B. monnieria* containing 1.8 - 2.2% Bacoside A.

Kalmegh

An experiment was conducted in Bangalore, Karnataka, India, during 2001-02 to determine the effect of aging on androghrapholide content in *A. paniculata* and to establish the best harvesting time. The growth and yield parameters were studied at 30, 60, 90, 120 and 150 days after sowing. The andrographolide content was estimated by HPLC method. The best harvesting time was observed at 120 days after sowing to get higher biomass containing maximum andrographolide content (Ashok et al ., 2002))

***Vasaka alkaloids* (reference to vasicine)**

Adhatoda zeylanica Medic (Acanthaceae) is bronchodilator drug of Ayurevda. It is rich in quinazoline alkaloids. The plant shows wide seasonal variation in vasicine content in its leaves. It exhibited higher levels of vasicine twice in a year i.e. 3.0% in March and 1.4% in September. Interestingly, it coincided with the flowering of the plant. In March, it was full bloom condition and in September, it was partial flowering. During the vegetative stage, the plant contained very low concentration of vasicine. (Bagachi et al., 2003).

The yield of the vasicine from different samples in India ranged from 0.541 to 1.105% on dry basis. Yield as high as 2.18% on dry basis has been reported from a foreign sample of which more than half was the *l* -form and the remainder the *dl*-form of the alkaloid (Arambewela, Ratnayake et al., 1988).

Conclusion:

Geographical distribution (bacoside-A and vasicine) and method of manufacturing or processing (withaferin-A) seems to be factors are responsible for variation of active principles of medicinal plants. Shelf-life has obvious impact on availability of active principle. Although, standardization of herbal products is not easy task, manufactures must ensure proper testing of raw material for better product development. Bodies like AYUSH should issue standards for presence of active principles in finished Ayurvedic products.

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