



Standardization of Herbal Drugs – An Overview

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ABSTRACT

The medicinal plants are important source for pharmaceutical manufacturing. Medicinal plants & herbal medicines account for a significant percentage of the pharmaceutical market. As the side effects of Synthetic medicine have started getting more apparent, majority of formulation are prepared from herbs. The herbal medicines however, suffer from lack of standardization parameters. The main limitation is the lack of standardization of raw materials, of processing methods and of the final products, dosage formulation, and the non existence of criteria for quality control. Herbal formulations have reached extensive acceptability as therapeutic agents for several diseases. The development of authentic analytical methods which can reliably profile the phytochemical composition, including quantitative analyses of marker/bioactive compounds and other major constituents, is a major challenge to scientists. Standardization is an important step for the establishment of a consistent biological activity, a consistent chemical profile, or simply a quality assurance program for production and manufacturing of herbal drugs.

Keywords: Standardization, Quality control, Medicinal plants, herbal drugs.

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INTRODUCTION

The use of herbs as medicine is the oldest form of healthcare known to humanity and has been used in all cultures throughout history. Early humans recognized their dependence on nature for a healthy life and since that time humanity has depended on the diversity of plant resources for food, clothing, shelter, and medicine to cure myriads of ailments. The knowledge of plant based drugs developed gradually and was passed on, thus, laying the foundation for many systems of traditional medicine all over the world. In some communities' herbal medicine is still a central part of their medical system. Medicinal plants are widely distributed throughout the world but most abundantly in tropical countries.¹

It is estimated that about 25% of all modern medicines are directly or indirectly derived from higher plants.

The term "herbal drugs" denotes plants or plant parts that have been converted into phyto pharmaceuticals by means of simple processes involving harvesting, drying and storage (1) Herbs include crude plant material, such as leaves, flowers, fruit, seeds, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered. Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential

oils, resins and dry powders of herbs. In some countries, these materials may be processed by various local procedures, such as steaming, roasting or stir-baking with honey, alcoholic beverages or other materials.²

Quality Control and Standardization of Herbal Medicines – Concept and Scope According to WHO (1996a and b, 1992), standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects, such as selection and handling of crude material, safety, efficacy and stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer and product promotion.³

Herbal product cannot be considered scientifically valid if the drug tested has not been authenticated and characterized in order to ensure reproducibility in the manufacturing of the product. The quality assurance is also required during cultivation, harvesting, primary processing, handling, storage, packaging, and distribution. Therefore, there has been introduced a set of criteria and guidelines by WHO to be followed at each step as an integral part of quality control standards:

- ✓ Good Agricultural and cultivation Practices
- ✓ Good storage practices
- ✓ Good laboratory Practices

CLASSIFICATION OF HERBAL DRUGS

Ayurvedic herbalism: It is derived from the from the Sanskrit word—*Ayurveda*” means “The science of life”. Which is originated in India more than 4000 years ago.



Chinese herbalism: Which is an element of traditional related medicine.

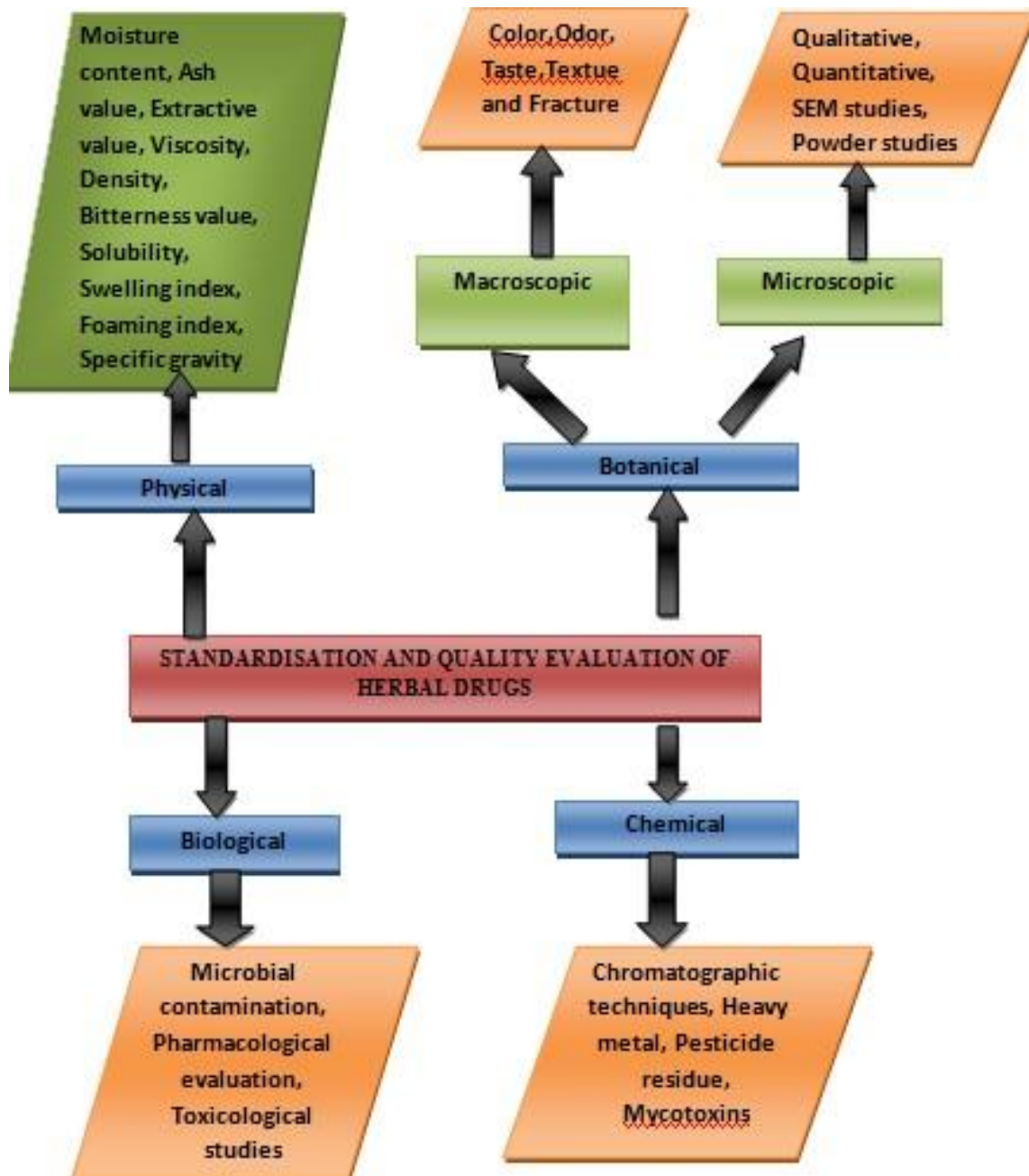
Western herbalism: which is originated from Rome, Greece and then multiply to North, Europe and South America.

NEED FOR STANDARDIZATION

In the global perspective, there is a shift towards the use of medicine of herbal origin, as the dangers and the

shortcoming of modern medicine are getting more apparent. It is the cardinal responsibility of the regulatory authorities to ensure that consumers get the medication, which guarantees purity, safety, potency and efficacy. Aim & Objectives: To describe the importance, concept, processes and the parameters required for the Standardization of herbal drugs ⁴

Methods of herbal standardization:



Starch and hemicelluloses is identified by blue color with iodine solution, All lignified tissues give pink stain with phloroglucinol and HCl etc. mucilage is stained pink with ruthenium red can be used to distinguish cellular structure.

Microscopic evaluation also includes study of constituents in the powdered drug by the use of chemical reagents.

Quantitative aspects of microscopy includes study of stomata number and index, palisade ratio, veinlet

number, size of starch grains, length of fibers etc which plays a very important role in the identification of drug.

MATERIALS

WHO Guidelines for Quality Standardized

Herbal Formulations

- ✓ Quality control of crude drugs material, plant preparations and finished products.
- ✓ Stability assessment and shelf life.
- ✓ Safety assessment; documentation of safety based on experience or toxicological studies.
- ✓ Assessment of efficacy by ethno medical information and biological activity evaluations.

Clearly described the Parameters to be assessed for rug to be standardized in Vimana 8th chapter where the concept of quality, safety and efficacy was explained elaborately Idamevamprakriti IICa Vi Prakriti Namarupavijnana Pharmacognosy Rasa, Guna, Veerya, Vipaka.⁵

Drug properties- physical & chemical & Pharmacological properties

Prabhava- Pharmacotherapeutic effect- Pharmacodynamics & Pharmacokinetics Desha - Geographical area – Distribution, cultivation, Place of collection etc. Grihita– collection practices Nihitam–storage practices Upaskrita– manufacturing process Matra – Dose Ritu– collection & cultivation time Yukta – Method of collection- Area, Time & Soil Nihitha– Storage & Preservation- Bheshjagara Upaskrita – Pharmaceutical processing of formulations Matra - Selection & fixation of specific dose Yukta – Logical interpretation and application Vyadhi– Indication in specific disease vidhisypurushasya – Similar to clinical trials Doshapakarsha & Upashamana- Act on particular dosha can be known by pathological test how much reduced or increased Generally, all medicines whether they are synthetic or of plant origin, should be pure, safe and effective⁶. In general, quality control is based on three important pharmacopeial definitions:

- ✓ Identity- it should have one herb
- ✓ Purity – it should not have any contaminant other than herb
- ✓ Content or assay-the active constituents should be within the defined limits.

SCIENTIFIC INVESTIGATIONS

✓ Physical Evaluation

Each monograph contains detailed botanical, macroscopic and microscopic descriptions with detailed illustrations and photographic images which provide visual documentation of accurately identified material. A microscopic analysis assures the identity of the material and as an initial screenin test for impurities.

✓ Chemical Evaluation

Chemical analysis of the drug is done to assess the potency of vegetable material in terms of its active principles. It covers screening, isolation, identification, and purification of the chemical components. It help to determine the identity of the drug substance and possible adulteration.

✓ Biological Evaluation

Pharmacological activity of certain drugs has been applied to evaluate and standardize them. The assays on living animals and on their intact or isolated organs can indicate the strength of the drug or their preparations.

PARAMETERS TO BE ASSESSED FOR STANDARDIZATION

➤ Macro and microscopic examination:

For Identification of right variety and search of adulterants.

➤ Foreign organic matter:

This involves removal of matter other than source plant to get the drug in pure form

➤ Ash value:

Helpful in determining the quality and purity of crude drugs, especially in powder form. The objective of ashing vegetable drugs is to remove all traces of organic matter, which may otherwise interfere in an analytical determination.⁷

➤ Moisture content:

Checking moisture content helps reduce errors in the estimation of the actual weight of drug material. Low moisture suggests better stability against degradation of product.

➤ Extractive values:

These are indicative weights of the extractable chemical constituents of crude drug under different solvents environment.

➤ Crude fibre:

This helps to determine the woody material component, and it is a criterion for judging purity.

➤ Qualitative chemical evaluation:

This covers identification and characterization of crude drug with respect to phytochemical constituent. It employs different analytical technique to detect and isolate the active constituents. Phytochemical screening techniques involve botanical identification, extraction with suitable solvents, purification, and characterization of the active constituents of pharmaceutical importance.⁸

➤ **Chromatographic examination:**

Include identification of crude drug based on the use of major chemical constituents as markers.

➤ **Quantitative chemical evaluation:**

To estimate the amount of the major classes of constituents.

➤ **Toxicological studies:**

This helps to determine the pesticide residues, potentially toxic elements, safety studies in animals like LD50 and Microbial assay to establish the absence or presence of potentially harmful microorganisms.

WHO GUIDELINES FOR QUALITY STANDARDIZED HERBAL FORMULATIONS

The bioactive extract should be standardized on the basis of active principles or major compounds along with the chromatographic fingerprints (TLC, HPTLC, HPLC and GC).⁹

The standardization of crude drug materials includes the following steps:

- ✓ Authentication (Stage of collection, parts of the plant collected, regional status, botanical identity like phytomorphology, microscopical and histological analysis, taxonomical identity etc.)
- ✓ Foreign matter (herbs collected should be free from soil, insect parts or animal excreta etc.)
- ✓ Organoleptic evaluation (sensory characters – colour, taste, appearance, odour, feel of the drug etc.)
- ✓ Tissues of diagnostic importance present in the drug powder. e. Ash values and extractive values.
- ✓ Moisture content
- ✓ Volatile matter
- ✓ Determination of heavy metals
e.g. cadmium, lead, arsenic, etc.
- ✓ Chromatographic and spectroscopic evaluation:

TLC, HPTLC, HPLC methods will provide qualitative and semi quantitative information about the main active constituents present in the crude drug. The quality of the drug can also be assessed on the basis of the spectroscopic fingerprint.

- ✓ Pesticide residue:

WHO and FAO (Food and Agricultural Organization) set limits of pesticides, which are usually present in the herbs. These pesticides are mixed with the herbs during the time of cultivation. Mainly pesticides like DDT, BHC,

toxaphene, aldrin cause serious side-effects in human beings if the crude drugs are mixed with these agents.¹⁰

Microbial contamination:

Usually medicinal plants containing bacteria and moulds are coming from soil and atmosphere. Analysis of the limits of *E. coli* and moulds clearly throws light towards the harvesting and production practices. The substance known as aflatoxins will produce serious side-effects if consumed along with the crude drugs. Aflatoxins should be completely removed or should not be present.¹¹

- ✓ Radioactive contamination:

Microbial growth in herbals is usually avoided by irradiation. This process may sterilize the plant material but the radioactivity hazard should be taken into account. The radioactivity of the plant samples should be checked accordingly to the guidelines of International Atomic Energy (IAE) in Vienna and that of WHO. Validation:

By definition, validation is the process of proving that an analytical method is acceptable for its intended purpose for pharmaceutical methods. Guidelines from the United States Pharmacopeia (USPC, 1994 to 2001), the International¹²

Conference on Harmonization (ICH), and the US Food and Drug Administration (FDA) provide a framework for performing such validations. Generally, validation investigations must include studies on specificity, linearity, accuracy, precision, range, detection, and quantitative limits, depending on whether the analytical method used is qualitative or quantitative). Also, of utmost importance is the availability of standards. For macroscopic and microscopic procedures- reliable reference samples of the plant must be available.¹³

A defined botanical source (e.g. voucher specimens) will normally solve this problem. Standards for chromatographic procedures are less easy to obtain.

Characteristic plant constituents, either active or markers, are seldom available commercially. Sometimes an LC-MS approach can be referred to as a mode of characterization.

Going one step further, after isolation of such a compound, elucidations to prove its definite structure will not be easy. The method often employed is to use readily available compounds that behave similarly in the chosen chromatographic systems, and to calculate retention values and/or times towards these compounds as a standard. Qualitative chemical examination is designed to detect and isolate the active ingredients.¹⁴ TLC and HPLC are the main analytical techniques commonly used. In cases when active ingredients are not known or too complex, the quality of plant extracts can be assessed by a "fingerprint" chromatogram

Assessment of Quality:

All procedures should be in accordance with good manufacturing practices. Crude plant material Plant preparations Finished product

Assessment of Stability:

The physical and chemical stability of the product in the container in which it is to be marketed should be tested under defined storage conditions and the shelf-life should be established

Assessment of Safety:

The toxic effects of herbal preparation may be attributed mainly to the following: Inherent toxicity of plant constituents and ingredients and Manufacturing malpractice and contamination. Evaluation of the toxic effects of plant constituents of herbal formulation requires detailed phyto-chemical and pharmacological studies.¹⁵

Assessment of Toxicity:

Toxicity investigation will also be required because the analysis alone is unlikely to reveal the contributions to toxicity itself. In assessing toxicity of an herbal medicine, the dose chosen is very important.¹⁶ Toxicity assessment involves one or more of the following techniques- In vivo techniques, in vitro techniques, cell line techniques, microarray and other modern technique Standardization techniques to adequately model toxicity.

Assessment of Efficacy:

Herbal medicines are inherently different from conventional pharmacological treatments, but presently there is no way to assess their efficacy other than by currently used conventional clinical trial methodologies, in which efficacy is conventionally assessed by clinical, the laboratory, or diagnostic outcomes.¹⁶

Analytical Specifications of Herbal Formulations Followed as per Requirement and Form of the Medicine:

Description, Colour, Odour, Total – ash, Acid – insoluble ash, Water & Alcohol-soluble extractive, Viscosity, Refractive index, Specific gravity at 250 C.¹⁷, Alcohol content Test for methanol, Total acidity, Non reducing and reducing sugar, PH, Total sugar content, Loss on drying at 105 °C, Particle size (80-100 mesh for Churna; 40- 60 mesh for Kvathachurna), Weight variation, Disintegration time -Not more than 15 min, Identification TLC/HPTLC/GLC, Assay, Test for heavy/Toxic metals: Lead, Cadmium, Mercury, Arsenic, Microbial contamination: Total bacterial count, Total fungal count, Test for specific Pathogen: E. coli, Salmonella spp. S.aureus, *Pseudomonas aeruginosa*, Pesticide residue: Organochlorine pesticides, Organophosphorus pesticides, Pyrethroids, Test for Aflatoxins,¹⁸

Organoleptic or macroscopic evaluation:

Organic evaluation of drugs by means of organs of sense (skin, eye, tongue, nose, and ear) or microscopic evaluation which include evaluation of drugs by colour, odour, taste, size, shape, and special feature, like touch , texture, etc. it is the technique of qualitative evaluation based on the study of morphological and sensory profile of whole drugs.¹⁹

The fractured surfaces in cinchona, quillia, and cascara barks and quassia wood are important characteristics. Aromatic odour of umbelliferous fruits and sweet taste of liquorices are the examples of this type of evaluation where odour of drugs depends upon the type and quality of odorous principles (volatile oils) present.²⁰

Microscopic evaluation:

It involves detailed examination of the drugs and it can be used to identify the organized drugs by their known histological characters. It is mostly used for qualitative evaluation of organized crude drugs in entire and power forms with help of microscopic. Using microscope detecting various cellular tissues, trichomes, stomata, starch granules, calcium oxalate crystals and aleuronic grains are some of important parameters which play important role in identification of certain crude drugs.²⁰

Final Product:

Prepared drug should possess standard nature of characteristics. The manufacturing procedure and formula, including the amount of recipients, should be described in detail.²¹ A finished product specification should be defined to ensure consistent quality of the product. The finished product should comply with general requirements for particular dosage forms. The processes involves wide array of scientific investigations, which include physical, chemical and biological evaluation employing various analytical methods and tools. The specific aims of such investigation in assuring herbal quality are as varied as the processes employed.²²

Labelling:

The quality of consumer information about the product is as important as the finished herbal product. Information or warning on the label helps to reduces the risk of inappropriate uses and adverse reactions. The primary source of information on herbal products is the product label. Contents of label and its Rules are prescribed and to be followed as per the Drug & Cosmetic Act Rules 1945(7). The information such as “name of the drug, manufacturer, batch number, any special category of scheduled drugs if used, date of expiry if any and assurance that the product has been manufactured according to Pharmacopoeia standards,” listing of active ingredients and amounts, directions such as serving quantity (dosage) and frequency of intake of the drug, must be on the label.²³



Currently, there is no organization or government body that certifies herb or a supplement as being labelled correctly. Studies of herbal products have shown that consumers have less than a 50% chance of actually getting what is listed on the label, and published analyses of herbal supplements have found significant differences between what is listed on the label and what is in the bottle.²⁴ The word “standardized” on a product label is no guarantee of higher product quality, since there is no legal definition of the word “standardized.” Consumers are often left on their own to decide what is safe and effective

Advantages

1. Low cost of production.
2. They may have fewer side effects.
3. Effective with chronic condition.
4. Wide spread availability.

Disadvantages of Herbal Drugs

1. Lack of dosage instruction.
2. Poison risk associated with wild herbs.
3. Can interact with other drugs.
4. In appropriate for many condition.
5. Some are not safe.

CONCLUSION

In spite of the great advances observed in modern medicine in recent decades, plants still make an important contribution to health care. Lack of availability of medicinal plant species, adulteration, dependence on the mediators for the manufactured products, preparation of medicine in the name of traditional medicine together cope up to emphasize the need for standardization right from the identification of the plant, collection the raw material to the manufacturing of the herbal compound in suitable form and marketing i.e Total quality Management. The need for standardization of herbals is now very essential considering the global acceptance of herbal products as remedies for various diseases and evidence is emerging on the dangers of indiscriminate use of certain herbs. The assurance of the quality, safety and efficacy of an herbal drug requires monitoring of the quality of the product from collection through processing to the finished packaged product. It is recommended that various government agencies should follow a more universal approach to herbal quality by adopting the WHO guidelines and also developing monographs using the various quality parameters outlined above. This will strengthen the regulatory process and minimize quality breach.

REFERENCES

1. De Smet PAGM, Keller K, Hansel R, Chandler RF. Adverse Effects of Herbal Drugs: Springer-Verlag. Heidelberg 1997;129(3): 137-145.
2. Botstein B, White RL, Skolnick M and Davis RW. Construction of a genetic linkage map in man using restriction fragment length polymorphisms: 1980;32(2):314-331.
3. Welsh J and McClelland M. Genomic fingerprints produced by PCR with consensus tRNA gene primers: 9 Nucleic Acids Res, 1991; 19:861-866.
4. Joshi K, Chavan P, Warude D and Patwardhan B. Molecular markers in herbal drug technology: *Current Science*, 2004; 87(2): 159-165.
5. Chauhan BL, Mitra SK, Mohan AR, Gopumadhavan S, Anturlikar SD. Development of high performance thin layer chromatography fingerprint technique & bioassay to establish the self life of a proprietary herbal formulation (PHF):an Ayurvedic formulation containing multiple ingredients of herbal origin. *Indian Drugs*, 1994;31 (7): 333–338.
6. Savaiano J. The Top Issues & Opportunities in Dietary Supplements: *Nutraceutical World*. 2006;9(4):34-43.
7. Lang F. Biopharmaceutical characterization of Herbal Medicinal Products: *Drugs* 2001;44(4):102-108.
8. ChuangW-C,Wu HK, Sheu SJ, Chiou SH, Chang HC, Chen YP. A comparative study on commercial samples of Ginseng radix: *Planta Med*.1995;61:459–465.
9. Kamboj VP. Herbal Medicine; *Current Science* 2000;78(1):35-39.
10. Joshi SP, Ranjekar PK and Gupta VS. Molecular markers in plant genome analysis: *Current Science* 1999;77:230-240.
11. Jeffrey AJ, Wilson V and Thein SL. Hypervariable minisatellite regions in human DNA: *Nature* 1985;314:67-73.
12. Ansari SH, Essentials of pharmacognosy: birla publications pvt ltd 2001;10-16.
13. Ahirwal B, Ahirwal D and Ram A. Evaluation of standards and quality control parameters of herbal drugs: recent trends in herbal therapy.2006;8(5):25-29.
14. De Smet PAGM. Drug Therapy: Herbal Remedies.N. Engl. J. Med 2002; 347:2046-2056.
15. Lin G, Kwan YW, Min ZD. Simultaneous quantification of five major biologically active ingredients of saffron by high performance liquid chromatography: *J. Chromatography* 1999; 849(2):349-355.
16. Li X N, Cui H, Song Y Q, Liang Y Z, Chau F T. Analysis of volatile fractions of Schisandra chinensis (Turcz) Using GC-MS and chemo metric resolution: *Phyto chemical Analysis* 2003;16(2):23 – 33.



17. Liu YM, Sheu SJ, Chiou H, Chang SH and Chen YP. A comparative study on commercial samples of ephedrae herbae: *Planta Medica* 1993;59(3):376–378.
18. Liu YM, Sheu SJ. Determination of quaternary alkaloids from *Coptidis Rhizoma* by capillary electrophoresis: *Chromatography*. 1992;623(1):196-199.
19. Stuppner H, Sturm S, Konwalinka G. Capillary electrophoresis analysis of oxindole alkaloids from *uncaria tomentosa*; *Chromatography*. 1992;60(9):375-380.
20. Liu YM, Sheu SJ. Determination of coptisine, berberine and palmatine in traditional Chinese Medicinal preparations by capillary electrophoresis: *J.Chromatography*. 1993; 639(2):322-328.
21. Zhang H. Identification and determination of the major constituents in traditional Chinese medicine; Si-Wu-Tang by HPLC coupled with DAD and ESI-MS M. *Pharm. Biomedical Analysis*. 2004;34:705-713.
22. Nyireddy S. Progress in forced flow planar chromatography: *J.Chromatography*. 2003;1000(1-2):985-999.
23. Willams JGK, Kubelik AR and Livak KL. DNA polymorphisms amplified by arbitrary primers are useful as genetic markers. *Nucleic Acids Res* 1990; 18(1):6531-6535.
24. Straus SE. Herbal Medicines- What's in the Bottle: *N. Engl. J.* 2002;347:1997-1998.

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