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A Composite Overview on Safety, Quality Control and Standardization of Herbal Medicine

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Abstract

Herbal medicines (phytotherapeuticagents) have reached extensive acceptability as therapeutic agent for several diseases like diabetics, liver diseases, cough remedies, memory enhancers. They are standardized herbal preparations consisting of complex mixtures of one or more plants in the crude or processed state.A marked growth in the worldwide phytotherapeutic market has occurred over last 25 years and has thus attracted the interest of most large pharmaceutical companies including the multinationals. But the idea that herbal drugs are safe and free from side effect is false. Plants contain hundreds of constituents and some of them are very toxic. It may be contaminated with excessive or banned pesticides,microbial contaminants, heavy metalsor adulterated. So the safety, quality control and standardization is major challenge. Standardization is an important step for the establishment of a consistent biological activity, a consistent chemical profile or simply quality assurance program for production and manufacturing of herbal drug. The paper illustrateSafety, Quality Control and various techniques employed for standardization of herbal medicine.

Keywords

Safety, quality, control, standardization, WHO

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INTRODUCTION

Herbal drugs have been used since ancient times as medicines for the treatment of a range of diseases. In CharakSamhita importance of drug had been stated as below.

भिषग्द्रव्याण्युपस्थातारोगीपादचतुष्टयम् ।
गुणवत्कारणंज्ञेयंविकारव्युपशान्तये।। [1]

Herbal medicinal preparations are normally marketed as standardized preparation in the form of liquid, solid(powdered extract)or viscous preparations. They are prepared by maceration, percolation or distillation(volatile oils). Ethanol, water or mixtures of ethanol and water are used for the production of fluid extracts. Solid or powered extracts are prepared by evaporation of the solvents used in the process of extraction of the raw material. Several regulatory models for herbal medicines currently exist, including prescription drugs, over the counter drugs, traditional medicines and dietary supplements[2].

AIMS AND OBJECTIVES

1) To study the safety, qualitycontrol, principle and various methods for standardization according to Ayurved and modern concept.

MATERIALS AND METHODS

Review of literature regarding herbal medicine - Ayurved Samhita-Charak, Sushruta, Vagbhata (AshtangaHrudayam), Bhavprakash, Phytotherapy- Journals and related Websites

Safety :-

- Usually the active principles responsible for their pharmacological action are unknown.
- Standardization, stability and quality control are feasible but not easy.
- Well-controlled double-blind clinical and toxicological studies to prove their efficacy and safety are rare [2]
- Over the counter (O.T.C.) products may be contaminated with excessive or banned pesticides, microbial contaminants, heavy metals chemical toxins and with orthodox drugs[3].
- Several manufacturing problems such as misidentification of plant lack of standardization, failure of good manufacturing practice, contamination, substitution, and adulteration of plants, incorrect preparations or dosage[4].

- There are case reports of serious adverse effect after administration of herbal products. In a lot of cases the toxicity has been traced to contaminant and adulteration. However some of the plants used in herbal medicines can also be highly toxic. As a hole herbal medicines can have a risk of adverse effect and drug- drug and drug-food interaction if not properly assessed[5].

Assessment of the safety of herbal products therefore is the first priority in herbal research.

Quality control of herbal drugs:-

Quality control for efficacy and safety of herbal product is of paramount importance. Quality can be define as the status of a drug that is determined by identity, purity, content and other chemicals, physical or biological properties or by the manufacturing processes. Quality control is term that refers to processed involved in maintaining the quality and validity of a manufactured product. In general quality control is based on three important pharmacopeia 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 define limit[6].

For covering contamination because of environment related factors can be controlled by implementing Standard operating procedures (S.O.P), Leading to good agricultural practice (G.A.P),Good supply practice (G.S.P) and Good manufacturing practice(G.M.P)[7] .

For producing these medicinal products from herbal or natural sources – fresh plants, temperature, light exposure, water availability, nutrients, period and time of collection, method of collecting, drying, packing, storage and transportation of raw material, age and part of the plant collected.

Standardization:-

In Ayurveda, the principle for standardization of herbal medicines are stated in CharakSamhita inVimansthanas[8].

i. *Prakruti*(Natural Character)
ii. *Guna* (Pharmacological property)
iii. *Prabhav*(Pharmacological property)
iv. *Desh* (Habitat and Ecology)
v. *Sangrahkal* (Time of Collection)
vi. *Samrakshan* (Storage and Preservations)
vii. *Kalpa*(Pharmacological property)
viii. *Matra* (Doses)
ix. *AamayikPrayog*(Therapeutic uses)
x. *VyadhitPrakruti*(Patient Constitution)
xi. *Karma* (Effect)

Standardization of herbal formulations is essential in order to assess of quality drugs, based on theconcentration of their active principles physical, chemical, phyto chemical, standardization and in vitro, in vivo parameters.

Standardization of raw materials includes the following step.

1. **Authentication:-**

Each and every step has to be authenticated, area of the collection, parts of the plant collection, the regional situation, as phytomorphology, botanical identity, microscopic and histological analysis[9].

2. **Pharmacognosticevaluation :-**

It includes color, odor, taste, texture, size, shape, microscopically characters and histological parameters.

3. **Physico-chemical parameters:-**

It includes foreign matter, total ash, acid-insoluble ash, swelling and foaming index, assay, successive extractive values, moisture content, viscosity, pit, disintegration time, friability, hardness, flow capacity, flocculation, sedimentation, alcohol content.

4. **Chemical parameters:-**

It includes limit tests, chemical tests etc.

5. **Microbiological parameters:-**

It includes the full content of viable, total mould count, total coli forms count. Limiters can be used as quantitative tool or semi-quantitative to determine and control the amount of impurities, such as reagents used in the extraction of various herbs, impurities ships directly from the manufacturing solvents etc[10].

- **Modern Techniques of Extraction Methods[11]**

1. Supercritical Fluid Extraction (SFE)

SFE techniques have been found useful in isolating the desired phytoconstituents from plant extracts. Supercritical fluid extraction is the most preferable process for the extraction of the active constituents from the medicinal and aromatic plants[12].

2. Solid Phase Extraction (SPE)

SPE technique is applied for isolation of analyses from liquid matrix and purified herbal extracts.

3. Spouted Bed Extraction (SBE)

SBE has been investigated for annotto production[13].

4. Counter – Current extraction

This is a liquid-liquid extraction process and the principle involved in similar to partition Chromatography[14.]

5. Microwave Assisted Extraction (MAE)

MAE technology includes the extraction of high value compounds from natural sources including phytonutrients, neutral-ceutical and functional food[15].

Modern techniques in herbal drug identification and characterization[16,17].

1 High Performance Liquid Chromatography HPLC:-

The preparative and analytical HPLC are widely applicable in pharmaceutical industry for isolating and purification of herbal compounds. This is most important in the pharmaceutical industries because newer formulations have to be introduced in the market as early as possible

2 High Performance Thin Layer Chromatography (HPTLC)

HPTLC is the common fingerprint mainly used to analyze the compounds which is having low or moderate polarities. HPTLC technique is widely used in the pharmaceutical industry for process development, identification and detection of adulterants, substituent in the herbal products and also helps in the identification of pesticide content, mycotoxins and in quality control of herb and health products.

3 Gas Chromatography-Mass Spectroscopy (GC-MS)

The identification and quantification of chemical constituents present in the polyherbal oil formulation analyzed by GC-MS method.

4 Liquid Chromatography – Mass Spectroscopy (LC-MS)

The chemical standardization of an aqueous extract of the mixture of the herbs provided chemical compounds serving as reference markers using LC-MS. It is useful to analyze the aminoglycosides showed that these drugs are highly soluble in water, showed low plasma protein binding and more than 90% extracted through the kidney.

5 Supercritical fluid chromatography:

The super critical fluid and micro bore liquid chromatography offer potential applications for the drug analysis.

6 Capillary Electrophoresis (CE)

The methodology of CE was introduced to evaluate one drug in terms of specificity, sensitivity and precision and the results were in agreement with those obtained by the HPLC method.

7 Atomic Absorption Spectroscopy (AAS)

Atomic Absorption Spectroscopy in analytical chemistry is a technique for determining the concentration of particular

metal element within a sample. Atomic Absorption Spectroscopy can be used to analyze the concentration of over 62 different metals in a solution.

8 Atomic Emission Spectroscopy (AES)

Atomic Emission Spectroscopy is a method of chemical analysis that sues the intensity of light emitted from a flame, plasma, arc or spark at a particular wave length to determine the quantity of an element in a sample. The wave length of the atomic spectral line gives the identity of the element while the intensity of the emitted light is proportional to the number of atoms of the element.

9 X-ray powder diffractometry[18].

X-ray diffraction is a basic scientific tool capable of supplying the investigator with fundamental data and information unobtainable by any other technique. This technique is used to identify minerals, crystalline materials and metallic based herbal formulations. It tells the state of chemical combination of the elements in the material

10 DNA fingerprinting Technique:

This technique is useful for the identification of phyto-chemically indistinguishable genuine drug from substituted or adulterated drug[19].

WHO Guidelines for quality standardized herbal formulations- [20]

1. Quality control of crude drugs material, plant, preparation and finished products.
2. Stability assessment and shelf life.
3. Safety assessment; documentation of safety based on experience or toxicological studies.
4. Assessment of efficacy by ethno medical information and biological activity evaluations.
5. The bioactive extract should be standardized on the basis of active principles or major compounds along with the chromoto-graphic fingertips (TLC, HPTLC. HPLC and GC).

Regulation of herbal medicines

WHO has evolved guidelines to support the member status in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety and efficacy. In India, traditional medicine is governed by the Drugs and Cosmetics Act, 1940 and the provisions of the Act are implemented by the State Governments. The first Indian National Health Policy 1983 claims that India's is the richest source of herbs and the drugs should be standardized. The department of AYUSH, Government of

India, launched a central scheme to develop standard operating procedures for the manufacturing process to develop pharmacopeial standards for Ayurvedic preparations[21,22].

Observations:

The advancement of analytical techniques will serve as a rapid and specific tool in herbal research thereby allowing the manufacturers to set quality standards and specifications, so as to seek marketing approval from regulatory authorities for therapeutic efficacy, safety and shelf life of herbal drugs.

DISCUSSION

Drugs are the most important aspect of medical care system. Hence, the manufacturer as well a search of the literature shows that over the last 25 years, a great growth and worldwide interest in herbal medicines has taken place, both in developed and developing countries. India can emerge as the major country and play the lead role in production of standardized, therapeutically effective Ayurvedic formulation. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization such as TLC, HPLC, HPTLC, GC-MS, AAS and AES and other methods. These guidelines for the assessment of herbal medicines are intended to facilitate the work of regulatory authorities, scientific bodies and industry in the development, assessment and registration of such products. Moreover, all herbal products manufacturers must follow WHO guidelines for quality control.

CONCLUSION

Drugs are the most important aspect of medical care system. Hence, the manufacturer as well as practitioner should ensure its purity, efficacy and stability. In the past, the physician himself used to prepare the medicines for his patients, following all the standards laid down in the tent. But, today, the commercialization of Ayurvedic medicines has arisen the necessity of their biological and chemical standardization to prove their efficacy and safety. Standardization of methods of manufacturing for surety of quality, method of storage and preservation so that it can last for a long time.

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