

# Evaluation of Herbal Formulation for Therapeutic Management of Epilepsy

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**Abstract:** 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. WHO specific guidelines for the assessment of the safety, efficacy and quality of herbal medicines as a prerequisite for global harmonization are of utmost importance. An overview covering various techniques employed in extraction and characterization of herbal medicines as well as herbal nanomedicines standardization is reported. In addition, phytosomes increased bioavailability, bhasma as a metal nanocarrier drug delivery system, potential of metabolomics in the development of improved phytotherapeutic agents, DNA based molecular markers in distinguishing adulterants, and SCAR markers for authentication and discrimination of herbs from their adulterants are reported. The extraction of high-valued herbal compounds using microwave-assisted extraction and supercritical phase extraction technology followed by the standardization utilizing various spectroscopic, chromatographic and thermogravimetric techniques individually and/or in combination has been discussed in relation to herbal drugs. Capillary electrophoresis and polarographic techniques contributions towards standardization of herbal drugs is also reported. Nanotechnology based Chinese herbal drugs possess improved solubility and enhanced bioavailability.

**Keywords:** Herbal drugs, standardization, nanoherbal drugs, phytosomes, DNA marker, chromatographic and spectroscopic techniques.

## I. INTRODUCTION

In recent years, plant derived products are increasingly being sought out as medicinal products, nutraceuticals and cosmetics and are available in health food shops and pharmacies over the counter as self-medication or also as drugs prescribed in the non-allopathic systems<sup>1</sup>. Herbal medicines widely used in health-care in both developed and developing countries are complex chemical mixtures prepared from plants and are limited in their effectiveness because they are poorly absorbed when taken orally<sup>3</sup>. According to an estimate of the World Health Organization (WHO), about 80% of the world population still uses herbs and other traditional medicines for their primary health care needs. Herbal formulations have reached widespread acceptability as therapeutic agents for diabetics, arthritics, liver diseases, cough remedies, memory enhancers and adaptogens<sup>5</sup>. As per WHO definition, there are three kinds of herbal medicines: raw plant material, processed plant material and medicinal herbal products. Herbal drugs are finished labelled products that contain active ingredients such as aerial or underground parts of plant or other plant material or combination thereof, whether in the crude state or as plant preparations. The use of herbal medicines has increased remarkably in line with the global trend of people returning to natural therapies. Herbal medicine products are dietary supplements that people take to improve their health and are sold as tablets, capsules, powders, teas, extracts and fresh or dried plants. Herbs are traditionally considered harmless and increasingly being consumed by people without prescription. However, some can cause health problems, some are not effective and some may interact with other drugs.



Standardization of herbal formulations is essential in order to assess the quality of drugs, based on the concentration of their active principles

Quality evaluation of herbal preparation is a fundamental requirement of industry and other organization dealing with ayurvedic and herbal products. The growing use of botanicals (drug and other products derived from plants) by the public is forcing moves to assess the health claims of these agents and to develop standards of quality and manufacture. It is evident that the herbal industry needs to follow strict guidelines and such regulations are necessary. Herbal drugs regulations in India as well as an overview of regulatory status of herbal medicine in USA, China, Australia, Brazil, Canada and Germany has been reported

According to WHO guidelines, an herbal product needs to be standardized with respect to safety before releasing it into the market

### **Literature and Review**

Epilepsy is one of the most common chronic neurological disorders characterized by recurrent and unprovoked seizures resulting from abnormal neuronal discharges in the brain. According to the World Health Organization, approximately 50 million people worldwide suffer from epilepsy, making it a significant public health concern. Conventional antiepileptic drugs (AEDs) such as Phenytoin, Carbamazepine, and Valproic Acid are commonly used for seizure control; however, prolonged use of these medications is associated with adverse effects including sedation, cognitive dysfunction, hepatotoxicity, and drug resistance. Due to these limitations, attention has increasingly shifted toward herbal medicines and traditional medicinal systems for safer and more effective alternatives.

Traditional systems such as Ayurveda, Unani, and Chinese medicine have long described the use of medicinal plants for neurological disorders and convulsive conditions. Herbal formulations are considered promising because they contain multiple bioactive compounds that may act synergistically to provide anticonvulsant, antioxidant, neuroprotective, and anxiolytic effects.

Several medicinal plants have been scientifically investigated for their anticonvulsant activity. Among these, *Bacopa monnieri* has shown significant neuroprotective and cognitive-enhancing effects. Studies reported that extracts of *Bacopa monnieri* reduced seizure severity and oxidative stress in experimental animal models. The anticonvulsant activity was mainly attributed to bacosides, which possess antioxidant and neurotransmitter-modulating properties.

Similarly, *Withania somnifera* has demonstrated anticonvulsant and anxiolytic activity in various studies. Researchers observed that administration of *Withania somnifera* root extract significantly delayed the onset of seizures induced by pentylenetetrazole (PTZ) and maximal electroshock (MES) methods. The neuroprotective effects were associated with enhancement of gamma-aminobutyric acid (GABA) neurotransmission and reduction of oxidative stress.

Another important medicinal plant, *Centella asiatica*, has been widely studied for its beneficial effects on the central nervous system. Experimental studies indicated that ethanolic extracts of *Centella asiatica* possess anticonvulsant properties due to the presence of triterpenoids and flavonoids. The plant also improved memory and cognitive functions impaired during epilepsy.

*Valeriana officinalis* is another herbal medicine traditionally used for nervous disorders and insomnia. Research findings suggested that valerian root extracts exhibit sedative and anticonvulsant effects through modulation of GABA receptors. This mechanism is similar to that of benzodiazepine drugs but with comparatively fewer side effects.

The role of oxidative stress in epilepsy has also been extensively investigated. Seizure activity increases the production of free radicals and reactive oxygen species, leading to neuronal damage and neurodegeneration. Herbal medicines rich in flavonoids, phenolic compounds, and alkaloids possess strong antioxidant properties capable of reducing oxidative stress. Plants such as *Curcuma longa* and *Ginkgo biloba* have shown neuroprotective effects by enhancing antioxidant enzyme levels and reducing lipid peroxidation in epileptic models.

Polyherbal formulations have gained particular importance because combinations of medicinal plants may produce synergistic therapeutic effects. Several studies reported that polyherbal preparations provide better seizure protection



compared to single-herb extracts due to the combined action of multiple phytoconstituents. Researchers have demonstrated that formulations containing flavonoids, terpenoids, alkaloids, and glycosides can modulate neurotransmitter release, stabilize neuronal membranes, and inhibit excessive neuronal excitation.

Experimental models such as MES and PTZ-induced seizures are widely employed to evaluate anticonvulsant activity of herbal formulations. MES models are mainly used to identify compounds effective against generalized tonic-clonic seizures, while PTZ-induced seizures are useful for evaluating agents active against absence seizures and myoclonic epilepsy. Reduction in seizure duration, delay in seizure onset, and protection against mortality are commonly used parameters for assessment.

In addition to anticonvulsant efficacy, toxicity evaluation is essential in herbal research. Although herbal medicines are generally considered safe, some plant constituents may produce toxicity at higher doses or during prolonged use. Therefore, acute and subacute toxicity studies are necessary to establish the therapeutic safety profile of herbal formulations.

Recent scientific investigations support the therapeutic potential of herbal medicines in epilepsy management; however, many herbal formulations still lack proper standardization, mechanistic studies, and clinical validation. Variability in plant sources, extraction methods, and dosage forms often affects reproducibility of results. Consequently, there is a need for systematic pharmacological and phytochemical evaluation of herbal formulations to ensure efficacy, quality, and safety.

In conclusion, the available literature suggests that medicinal plants and herbal formulations possess significant anticonvulsant and neuroprotective activities. Their mechanisms may involve modulation of GABAergic transmission, antioxidant activity, ion channel regulation, and inhibition of excitatory neurotransmitters. Herbal therapies may therefore serve as promising alternatives or complementary approaches for epilepsy management. Further experimental and clinical studies are necessary to validate their therapeutic potential and facilitate integration into modern healthcare systems

### **Aim and Objectives**

#### **Aim**

The primary aim of this study is to evaluate the therapeutic potential, safety, and efficacy of a selected herbal formulation in the management of epilepsy using suitable experimental and pharmacological approaches. The study intends to investigate whether the herbal formulation possesses anticonvulsant activity capable of reducing the frequency, severity, and duration of epileptic seizures while minimizing adverse effects commonly associated with conventional antiepileptic drugs.

Epilepsy is a chronic neurological disorder characterized by recurrent and unprovoked seizures caused by abnormal electrical activity in the brain. Despite the availability of several synthetic antiepileptic drugs, many patients continue to suffer from drug resistance, adverse reactions, cognitive impairment, and high treatment costs. Traditional medicinal systems such as Ayurveda and herbal medicine have long utilized plant-based remedies for neurological disorders, including epilepsy. Herbal formulations are believed to provide neuroprotective, antioxidant, and anticonvulsant benefits with fewer side effects. Therefore, scientific validation of herbal formulations is essential to establish their therapeutic value and potential use as alternative or complementary therapies in epilepsy management.

This research aims to provide experimental evidence supporting the anticonvulsant and neuroprotective properties of the selected herbal formulation through phytochemical, pharmacological, and toxicological evaluation. The findings may contribute to the development of safer, effective, and affordable herbal therapies for epileptic patients.



### **Objectives Primary Objectives**

1. To prepare and standardize the herbal formulation

The study aims to formulate a polyherbal or single-herb preparation using medicinal plants traditionally reported for anticonvulsant activity. Standardization will be carried out based on organoleptic, physicochemical, and phytochemical parameters to ensure quality, purity, and reproducibility.

2. To evaluate the phytochemical constituents of the herbal formulation

Preliminary phytochemical screening will be conducted to identify the presence of active constituents such as alkaloids, flavonoids, glycosides, tannins, terpenoids, saponins, and phenolic compounds that may contribute to anticonvulsant activity.

3. To assess the anticonvulsant activity of the herbal formulation The formulation will be evaluated using suitable experimental seizure models such as:

- o Maximal Electroshock Seizure (MES) model
- o Pentylentetrazole (PTZ)-induced seizure model
- o Chemically induced convulsion models

These studies will help determine the ability of the herbal formulation to delay seizure onset, reduce seizure duration, and protect against convulsions.

4. To compare the efficacy of the herbal formulation with standard antiepileptic drugs

The anticonvulsant effect of the herbal preparation will be compared with standard drugs such as Phenytoin or Diazepam to evaluate relative therapeutic effectiveness.

5. To investigate the neuroprotective and antioxidant effects

Since oxidative stress plays a significant role in epilepsy, the study aims to assess antioxidant parameters such as lipid peroxidation, catalase activity, superoxide dismutase activity, and glutathione levels to determine the neuroprotective potential of the formulation.

### **Secondary Objectives**

6. To evaluate the safety and toxicity profile of the herbal formulation

Acute and subacute toxicity studies will be performed according to established guidelines to determine the safe therapeutic dose range and identify any possible toxic effects on vital organs.

7. To study the mechanism of anticonvulsant action

The study aims to explore possible mechanisms through which the herbal formulation exerts anticonvulsant effects, including modulation of neurotransmitters such as gamma-aminobutyric acid (GABA), inhibition of excitatory pathways, ion channel regulation, or antioxidant mechanisms.

8. To assess behavioral and neurological parameters

Behavioral studies may be conducted to evaluate locomotor activity, sedation, muscle coordination, memory, and cognitive functions in experimental animals after treatment with the herbal formulation.

9. To establish the therapeutic significance of herbal medicine in epilepsy management

The study intends to scientifically validate traditional claims regarding the use of medicinal plants in epilepsy and encourage the integration of evidence-based herbal therapies into modern healthcare systems.

10. To develop a foundation for future clinical research

The results obtained from the preclinical evaluation may provide a scientific basis for conducting future clinical trials and formulation development for human use.



## **Material and Methodology**

### **Materials**

#### **1. Plant Materials**

The medicinal plants selected for the preparation of the herbal formulation will be collected from authenticated herbal suppliers or local medicinal plant sources. The collected plant materials will be identified and authenticated by a qualified botanist or pharmacognosist. The plant parts such as leaves, roots, rhizomes, seeds, or bark will be washed thoroughly, shade dried, powdered, and stored in airtight containers for further use.

Examples of medicinal plants commonly used in anticonvulsant studies include:

- Bacopa monnieri
- Withania somnifera
- Centella asiatica
- Curcuma longa

#### **2. Chemicals and Reagents**

The following chemicals and reagents will be used for phytochemical and pharmacological studies:

- Ethanol
- Methanol
- Distilled water
- Chloroform
- Hydrochloric acid
- Sulfuric acid
- Ferric chloride
- Mayer's reagent
- Dragendorff's reagent
- Sodium hydroxide

Analytical grade chemicals and reagents will be procured from standard laboratory suppliers.

#### **3. Experimental Animals**

Healthy adult Swiss albino mice or Wistar albino rats of either sex weighing approximately 150–250 g will be used for the experimental study. The animals will be obtained from a registered animal house and maintained under standard laboratory conditions:

- Temperature:  $22 \pm 2^\circ\text{C}$
- Relative humidity:  $55 \pm 5\%$
- 12-hour light/dark cycle
- Standard pellet diet and water ad libitum

Animals will be acclimatized to laboratory conditions for at least one week before experimentation.

#### **4. Instruments and Equipment**

The following laboratory instruments and equipment will be used:

- Soxhlet apparatus
- Rotary vacuum evaporator
- Hot air oven
- Electronic balance
- Centrifuge
- pH meter
- UV-visible spectrophotometer



- Electroconvulsimeter
- Micropipettes
- Animal cages and feeding bottles

### **Methodology**

#### **1. Preparation of Herbal Extract**

The powdered plant materials will be subjected to extraction using suitable solvents such as ethanol or methanol by Soxhlet extraction or maceration method.

#### **Procedure:**

1. The dried powdered plant material will be weighed accurately.
2. Extraction will be carried out using ethanol/methanol for 24–48 hours.
3. The extract will be filtered using Whatman filter paper.
4. The filtrate will be concentrated using a rotary evaporator under reduced pressure.
5. The concentrated extract will be dried and stored in desiccators for further studies.

#### **2. Preparation of Herbal Formulation**

The dried extracts of selected medicinal plants will be mixed in predetermined ratios to prepare the herbal formulation. The formulation may be prepared in the form of suspension, syrup, powder, or capsule depending on the study design.

#### **3. Phytochemical Screening**

Preliminary phytochemical analysis will be performed to identify the presence of bioactive constituents such as:

- Alkaloids
- Flavonoids
- Tannins
- Glycosides
- Saponins
- Phenolic compounds
- Terpenoids

#### **Common Phytochemical Tests:**

- Mayer's test for alkaloids
- Ferric chloride test for phenols
- Foam test for saponins
- Shinoda test for flavonoids

#### **4. Experimental Design**

Animals will be divided into different groups containing six animals each.

#### **Example Grouping:**

Group Treatment

Group I Normal control

Group II Disease control

Group III Standard drug treatment

Group IV Low dose herbal formulation

Group V High dose herbal formulation

Standard anticonvulsant drugs such as Phenytoin or Diazepam will be used for comparison.



Evaluation of Anticonvulsant Activity

5. Maximal Electroshock Seizure (MES) Method

The MES model is commonly used to evaluate anticonvulsant activity against generalized tonic-clonic seizures.

Procedure:

1. Experimental animals will receive the herbal formulation orally for a specified duration.
2. Electroshock will be delivered using an electroconvulsimeter through ear electrodes.
3. Parameters observed include:
  - o Duration of tonic hind limb extension
  - o Duration of convulsions
  - o Recovery time
  - o Mortality protection

Reduction in tonic hind limb extension indicates anticonvulsant activity.

6. Pentylentetrazole (PTZ)-Induced Seizure Model

PTZ is used to induce seizures chemically in experimental animals.

Procedure:

1. PTZ will be administered intraperitoneally after treatment with the herbal formulation.
2. Animals will be observed for:
  - o Onset of seizures
  - o Duration of convulsions
  - o Number of seizures
  - o Survival time

Delay in seizure onset and reduction in seizure severity indicate protective activity.

7. Acute Toxicity Study

Acute oral toxicity studies will be conducted according to standard guidelines such as Organisation for Economic Co-operation and Development (OECD).

Procedure:

1. Animals will receive increasing doses of the herbal formulation.
2. Animals will be observed for:
  - o Behavioral changes
  - o Toxic symptoms
  - o Mortality
3. Safe dose levels will be determined.
8. Biochemical and Antioxidant Studies

Brain tissue homogenates will be prepared for estimation of antioxidant parameters such as:

- Superoxide dismutase (SOD)
- Catalase
- Reduced glutathione (GSH)
- Lipid peroxidation (LPO)

These parameters help evaluate neuroprotective and antioxidant activity of the herbal formulation.

9. Statistical Analysis

The experimental data will be expressed as mean  $\pm$  standard error mean (SEM). Statistical analysis will be performed using one-way ANOVA followed by Dunnett's test or Tukey's multiple comparison test.

A value of:

$p < 0.05$

$p < 0.05$  will be considered statistically significant.



### **Herbal drug technology**

Herbal drug technology involves conversion of botanical materials into medicines where standardization and quality control with proper integration of modern scientific techniques and traditional knowledge is employed, and various drug delivery technologies used for herbal drugs were reported 10-11. Conventional pharmaceutical products, herbal medicinal products may vary in composition and properties, and increasing reports of adverse reactions has drawn the attention of many regulatory agencies for the standardization of herbal formulations. In this context, correct identification and quality assurance is an essential prerequisite to ensure reproducible quality of herbal medicine, which contributes to its safety and efficacy<sup>12</sup>. This review article deals with various techniques employed in extraction, characterization and standardization of herbal, polyherbal as well as nanoherbal medicines.

### **Herbal drug standardization**

Standardization is a system that ensures a predefined amount of quantity, quality & therapeutic effect of ingredients in each dose<sup>12</sup>. 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. Moreover, many dangerous and lethal side effects have recently been reported, including direct toxic effects, allergic reactions, effects from contaminants, and interactions with herbal drugs<sup>6</sup>. Therapeutic activity of an herbal formulation depends on its phytochemical constituents. 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. In view of the above, 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 an herbal drug<sup>13</sup>. The authentication of herbal drugs and identification of adulterants from genuine medicinal herbs are essential for both pharmaceutical companies as well as public health and to ensure reproducible quality of herbal medicine<sup>14</sup>.

### **Conventional methods for Evaluation of herbal formulation**

Standardization of herbal raw drugs include passport data of raw plant drugs, botanical authentication, microscopic & molecular examination, identification of chemical composition by various chromatographic techniques and biological activity of the whole plant<sup>5</sup>. Macroscopic and microscopic evaluation and chemical profiling of the herbal materials for quality control and standardization have been reported by various workers<sup>15- 17</sup>. Macroscopic identity of medicinal plant materials is based on sensory evaluation parameters like shape, size, colour, texture, odour and taste while microscopy involves comparative microscopic inspection of powdered herbal drug. Further, advances in microscope technology have increased the accuracy and capabilities of microscopy as a mean of herbal crude material identification due to the implication of light and scanning electron microscopes (SEM) in herbal drug standardization<sup>18</sup>. Furthermore, various advanced methods such as chromatographic, spectrophotometric and combination of these methods, electrophoresis, polarography, and the use of molecular biomarkers in fingerprints are currently employed in standardization of herbal drugs<sup>5,17,18-22</sup>. The history of some important events such as government policies, quality control and standardization of herbal drugs is given in Table 1. A schematic representation of herbal drug standardization is shown in Figure 1.

Evaluation of herbal

requires implementation of Good Manufacturing Practices (GMP) <sup>15-</sup>

<sup>17</sup>. In addition, study of various parameters such as pharmacodynamics, pharmacokinetics, dosage, stability, self-life, toxicity evaluation, chemical profiling of the herbal formulation considered essential <sup>19</sup>. Other factors such as pesticides residue, aflatoxine content, heavy metals contamination, Good Agricultural Practices (GAP) in herbal drug standardization are equally important<sup>40</sup>.



Year	Important events	Reference
1983	The first National Health Policy 1983 claims that India's is the richest source of herbs and the drugs should be standardized	23
1955	A separate Department for Indian Systems of Medicine and Homeopathy (ISM&H) now known as AYUSH (Ayurveda, Yoga, Unani, Siddha, Homoeopathy) was established in March 1995 to promote indigenous systems.	24
1996	World Health Organization has recommended the drug control agency to regulate the quality and safety 17 profile of herbal products.	17
1999	World Health Organization (WHO) had given a detail protocol for the standardization of herbal drugs comprising of a single content	25
2002	The Indian Herbal Pharmacopoeia. Mumbai, Indian Drug Manufacturer's Association, 2002.	26
2002	Analytical approaches like Herbo print use three-dimensional HPLC and attempt to develop tools for 27 activity-based standardization of botanicals	27
2003	Department of Indian Systems of Medicines & Homoeopathy (ISM&H) established in 1995 renamed into Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH)	28
2003	WHO. Guidelines on good agricultural and collection practices (GACP) for medicinal plants. Geneva, Switzerland: World Health Organization; 2003.	29
2004	WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems	30
2004	In Canada, the Natural Health Products Regulations (NHPR) [13] under the Food and Drugs Act 31 came into force on 01 January 2004.	31
2005	National Policy on Traditional Medicine and Regulation of Herbal Medicines - Report of a 32 WHO Global Survey	32
2006	The manufacture of herbal medicines	33
2007	WHO. Guidelines for assessing quality of herbal medicines with reference to contaminants and residues. 34 Geneva, Switzerland: World Health Organization; 2007	34
2007	WHO Guidelines on good manufacturing practices (GMP) for herbal medicines. Geneva, Switzerland: 35 World Health Organization; 2007	35
2009	AYUSH department with collaboration with Quality Council of India (introduced certification scheme 36 for AYUSH drug products	36
2009	USP. United States Pharmacopeia 32/National Formulary 27. Rockville,MD:The United States 37 Pharmacopoeial Convention; 2009.	37
2011	An EU directive passed in 2004 erects "disproportionate" barriers against herbal remedies by requiring 38 them to be "licensed" before they can be sold. It's called the Traditional Herbal Medicinal Products Directive (THMPD), Directive 2004/24/EC	38
2011	Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related 39 Issues." The document was published in the Federal Register on Tuesday, July 5, 2011.	39

Table 1 History of important events in herbal drug standardization



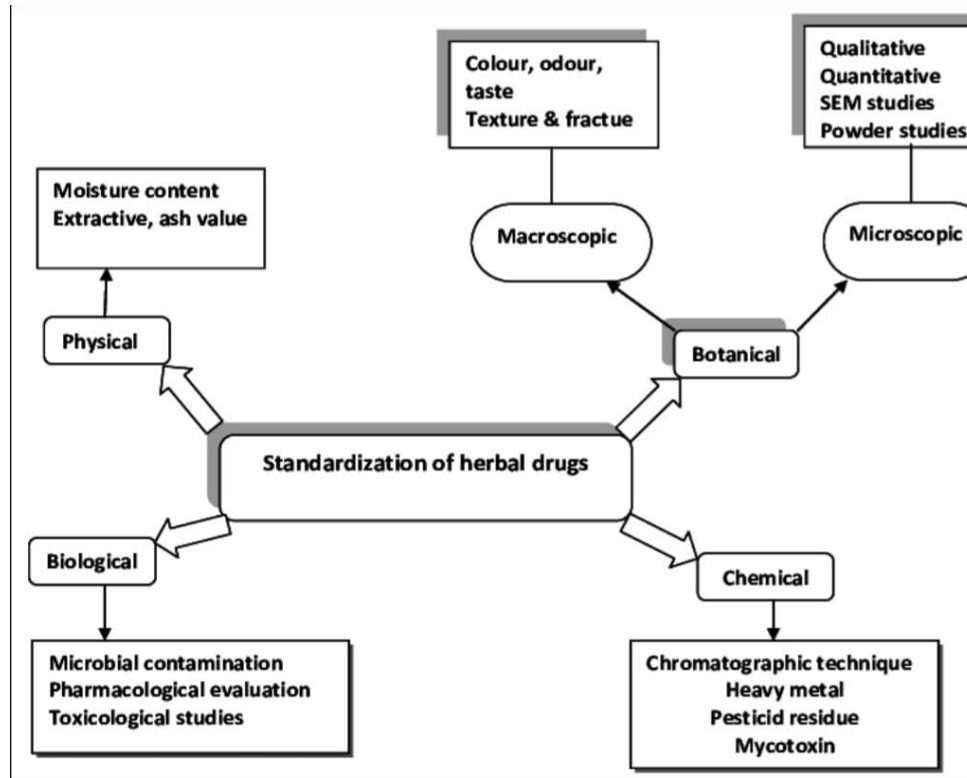


Figure 1: A schematic representation of herbal drug standardization

#### Standardization of polyherbal formulations

Standardization is an important aspect for maintaining and assessing the quality and safety of the polyherbal formulation as these are combinations of more than one herb to attain the desired therapeutic effect. The polyherbal formulation of hyperlipidemia has been standardized on the basis of organoleptic properties, physical characteristics, and physico-chemical properties. The formulation and standardization of a polyherbal formulation (Artrex) designed for the treatment of arthritis containing four botanicals was carried out using modern scientific tools and with known markers, has been granted a US patent. The standardization of various marketed herbal and polyherbal formulations [Madhumehari Churna (Baidyanath) containing the mixture of eight herbal antidiabetic drugs

Momordica charantia (seeds), Syzygium cumini (seeds), Trigonella foenum (seeds), Azadirachta indica (leaves), Emblica officinalis (fruits), Curcuma longa (rhizomes), Gymnema sylvestre (leaves), Pterocarpus marsupium (heartwood)]<sup>44</sup>, Pancasama Churna known to be effective in gastrointestinal disorder<sup>45</sup>, Dashamularishta, a traditional formulation, used in the normalization of physiological processes after child birth<sup>46</sup>, Gokshuradi Churna, Megni, Jawarish-e-Darchini<sup>47-49</sup> have been reported. But still there are many polyherbal formulations which require standardization as these are frequently used based only on their ethnobotanical use<sup>50</sup>. Standardization minimizes batch to batch variation; assures safety, efficacy, quality and acceptability of the polyherbal formulations<sup>51</sup>. Methiorex Premix (a combination of herbs viz. Cicer arietinum, Phaseolus mungo, Mucuna pruriens, Triticum sativum, allium cepa & richer source of protein with highly bioavailable methionine) has been recommended as a safe product to replace synthetic methionine in poultry ration and for supplementation in basal diet for regular usage<sup>52</sup>. TLC and HPTLC fingerprint profiles were used for deciding the identity, purity and strength of the polyherbal formulation and also for fixing standards for this Ayurvedic formulation.



#### DNA fingerprinting technique

DNA analysis has been proved as an important tool in herbal drug standardization. This technique is useful for the identification of phytochemically indistinguishable genuine drug from substituted or adulterated drug. It has been reported that DNA fingerprint genome remain the same irrespective of the plant part used while the phytochemical content will vary with the plant part used, physiology and environment

54. The other useful application of DNA fingerprinting is the availability of intact genomic DNA specificity in commercial herbal drugs which helps in distinguishing adulterants even in processed samples<sup>55</sup>. Several studies have been done in past few years to distinguish relation between DNA markers with phytochemical composition among closely related species<sup>56</sup>. Interspecies variation has been reported using random amplified polymorphic and random fragment length polymorphism DNA marker in different genera such as *Glycyrrhiza*, *Echinacea*, *Curcuma* and *Arabidopsis*<sup>57</sup>. Proper integration of molecular techniques and analytical tools generated a comprehensive system of botanical characterization that can be applied in the industry level to ensure quality control of botanicals. DNA markers are helpful to identify cells, individuals or species as they can be used to produce normal, functioning proteins to replace defective ones. Moreover, these markers help in treatment of various diseases and help in distinguishing the genuine herb from adulterated drug ISSR (Inter-Simple Sequence Repeat)

ISSR, a PCR-based application is unique and inexpensive popular technique of DNA fingerprinting which include the characterization of genetic fingerprinting, gene tagging, detection of clonal variation, phylogenetic analysis, detection of genomic instability, and assessment of hybridization<sup>58</sup>. *Cannabis sativa* and *Arabidopsis thaliana* L. Heyne have been differentiated from their adulterated species by using ISSR markers<sup>57</sup>. Molecular characterization by Sequence-characterized amplified region (SCAR) markers allows effective and reliable authentication and discrimination of herbs from their adulterants. In addition, morphologically similar plant species can be differentiated using SCAR markers<sup>58</sup>. DNA based molecular markers have been found to be useful in differentiating different accessions of *Taxus wallichiana*, *Azarchdichta indica*, *Juniperus communis* L., *Codonopsis pilosula*, *Allium schoenoprasum* L., *Andrographis paniculata* collected from different geographical regions.

#### Guidelines for the standardization of herbal drugs

The guidelines set by WHO: a) botanical characters, sensory evaluation, foreign organic matter, microscopic, histological, histochemical assessment, quantitative measurements, b) physical and chemical identity, fingerprints chromatography, ash values, extractive values, moisture content, volatile oil and alkaloid tests, quantitative estimation protocols, c) estimation of biological activity, the values of bitterness, astringency hemolytic index, a factors swelling, foaming index, d) detail-toxicity pesticides residues, heavy metals, microbial contamination as viable count total, pathogens such as *E. coli*, *Salmonella*, *P. aeruginosa*, *S. aureus*, *Enterobacteriaceae*, e) microbial contamination and radioactive contamination are followed

#### Phytosomes/ pharmanosomes: A novel drug delivery system for herbal drugs

Pharmanosomes commonly known as phytosome are drug-phospholipid complexes having active ingredients of the herb and can be formulated in the form of solution, suspension, emulsion, syrup, lotion, gel, cream, aqueous microdispersion, pill, capsule, powder, granules and chewable tablet<sup>61,62</sup>. Plants namely *Silybum Marianum*, *Ginkgo Biloba*, and ginseng showed better efficacy than conventional herbal formulations<sup>63</sup>. In addition, the clinical trials of phytosomes have shown increased bioavailability in comparison to conventional herbal formulations generally containing polyphenols and flavonoids in humans<sup>63,64</sup>. Several phytosomal herbal drug delivery systems have been reported<sup>65</sup>. Researchers demonstrated increased bioavailability of four polyphenol phytosome preparations (curcumin, silybin, flavan-3-ol catechins and proanthocyanidin) and this effect was due to the intermolecular bonding between individual polyphenol molecules and one or more molecules of the phospholipid, phosphatidylcholine<sup>66</sup>. Phytosomal herbal drug delivery systems are mainly used i) to deliver systemic antioxidant



(mainly polyphenols, flavonoid and terpenoid components), ii) useful in treatment of the disease like blood pressure, liver disease, cancer, skin disease and iii) helps in protecting the brain lining

#### Standardization of herbal nanomedicines

Herbal nanotechnology helps in incorporation of the active phytoconstituents to obtain desired therapeutic effect. The increased solubility, stability, bioavailability pharmacological activity of many popular herbal extracts including Milk thistle, Ginkgo biloba, grape seed, green tea, hawthorn, ginseng using nano dosage forms such as polymeric nanoparticles nanospheres & nanocapsules, liposomes, proliposomes, solid lipid nanoparticles, and nanoemulsion has been reported<sup>67,68</sup>. Other advantage of herbal nanomedicine include protection from toxicity, improving tissue macrophages distribution, sustained delivery, protection from physical and chemical degradation<sup>68</sup>. Silver nanoparticles of *Ocimum sanctum* extract exhibited maximum antibacterial activity at a dose of 150µg in wistar rats<sup>69</sup>. The herbal drug incorporated antibacterial nanofibrous mat fabricated by electrospin provided a potential application for use of wound dressing<sup>70</sup>. Nanotechnology patents in Chinese herbal medicine have been reported and proliferation of nanobased Chinese herbal medicine patents in China was due to the illusions of biomedical technology progress extensively<sup>71</sup>. 4.1. Bhasma as a nanoherbal medicine technology Bhasmas are the Ayurvedic metallic preparations in which metal act as a nanocarrier for drug delivery and are widely recommended for treatment of a variety of chronic ailments and are taken along with milk, butter, honey, or ghee to eliminate the harmful effects of metals and enhancing their biocompatibility in the body<sup>72</sup>. Neutron activation analysis of twenty metallic based bhasmas such as calcium, iron, zinc, mercury, silver, potassium, arsenic, copper, tin, and gemstones confirmed the purity of these bhasma as the other elements such as Na, K, Ca, Mg, V, Mn, Fe, Cu, and Zn were found in microg/g amounts and Au and Co in ultratrace (ng/g) amounts<sup>73</sup>. Various techniques like atomic force microscope, transmission electron microscope, scanning electron microscope and energy dispersive spectroscopy) have been employed for the estimation and characterization of bhasma. The Swarna bhasma (nanoparticles of Au) analysis qualitatively through X-ray diffraction, Fourier transform infrared spectroscopy) showed that the particle size are about 56 nm containing pure Au (gold) which act as a nanocarrier for drug delivery<sup>72</sup>. Mineral arsenicals mainly in the form orpiment (As<sub>2</sub> S<sub>3</sub>), realgar (As<sub>4</sub> S<sub>4</sub>), and arsenolite (contains arsenic trioxide, As<sub>2</sub> O<sub>3</sub>) have been used in traditional medicines for treatment of various diseases, however, arsenic can be highly toxic and carcinogenic<sup>73,74</sup>. Some commercially bhasma acting as a metal nanocarrier are given in Table 2

Table 2. Marketed bhasma containing metal as a nanocarrier for drug delivery.

Marketed Bhasama	Basic metal which act as a nanocarrier
Shanka Bhasama	Calcium present in sea products
Swarna	Gold
Mukta	Pearl
Abrak	Manganese
Godanti	Gypsum stone
Loha	Iron
Trivang	Aluminium and Zinc
Naga	Lead
Parad	Mercury

#### Regulation of herbal medicines

WHO has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety, and efficacy<sup>17,75</sup>. 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<sup>60</sup>. 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<sup>76</sup>. The Regulation for herbal drug products in Europe and United states are more stringent than in India

### **Pharmacovigilance of Herbal Medicines**

Pharmacovigilance means the science and activities relating to detect, assess, understand, and to prevent the adverse effects or any other possible drug-related problems, which is not only confined to chemical drugs, but extended to herbal, traditional and complementary medicines, biological, vaccines, blood products and medical devices<sup>78</sup>. There is an increasing recognition of the need to develop safety monitoring systems for herbal medicines<sup>79,80</sup>. The herbal products of ginseng are in great demand a sit is considered as a safe herbal drug for human health in spite of few reports on adverse drug reactions. But this is not applicable to every herbal product. Therefore, pharmacovigilance is essential for herbal drug before being considered as a safe for human health<sup>81</sup>. WHO has set specific guidelines for the assessment of the safety, efficacy and quality of herbal medicines as a prerequisite for global harmonization. The Medicines and Healthcare Products Regulatory Agency's, UK had launched 'yellow card' scheme for monitoring the safety of herbal medicines. Medicinal herbs as potential source of therapeutics aids have attained a significant role in health care system all over the world for human beings not only in the diseased condition but also as potential material for maintaining proper health <sup>82</sup>. Canadian Health Care department has analyzed various unapproved Ayurvedic medicinal products that contain high levels of lead, mercury, and arsenic in various Indian formulations [Karela capsules (Himalaya Drug, India), Maha Sudarshan Churna (Zandu Pharmaceuticals, India), Safi liquid (Hamdard, India & Pakistan), Shilajit capsules (Dabur, India)] and some herbal products were found to contain 0.1 to 0.3 mg of betamethasone which produced corticosteroid-like side effects. Reports have been received by drug safety monitoring agencies of prolonged prothrombin times, increased coagulation time, subcutaneous hematomas, and intracranial hemorrhage associated with the use of Ginkgo biloba

### **Techniques in extraction of herbals**

Supercritical fluid extraction (SFE) Supercritical fluid extraction (SFE) is the most preferable process for the extraction of the bioactive chemical from the medicinal and aromatic plants<sup>84</sup> SFE has emerged as a highly promising technology for production of herbal medicines and nutraceuticals with high potency of active ingredients SFE techniques have been found useful in isolating the desired phytoconstituents from the herbal extracts.

### **Microwave-assisted extraction (MAE)**

MAE technology includes the extraction of high-value compounds from natural sources including phytonutrients, nutraceutical and functional food ingredients and pharmaceutical actives from biomass<sup>87</sup>. MAE finds utility in production of cost effective herbal extracts and helpful in extraction of carotenoids from single cells, taxanes from taxus biomass, essential fatty acids from microalgae and oilseeds, phytosterols from medicinal plants, polyphenols from green tea, and essential oils from various sources. Compared to conventional solvent extraction methods, advantages of this technology include: a) improved product, -purity of crude extracts, -stability of marker compounds and use of minimal toxic solvents. b) reduced processing costs, increased recovery and purity of marker compounds, very fast extraction rates, reduced energy and solvent usage<sup>88,89</sup> organochlorine pesticides were extracted from herbs with mixed solvents of acetone and n-hexane by ultrasonic and cleaned up by Florisil solid phase extraction column <sup>91</sup>. Solid phase extraction was used to prepare the test solution for the analysis of aristolochic acid I and II in herbal medicines

Techniques in herbal drug identification and characterization HPLC Preparative and analytical HPLC are widely used in pharmaceutical industry for isolating and purification of herbal compounds. There are basically two types of preparative HPLC: low pressure HPLC (typically under 5 bar) and high pressure HPLC (pressure >20 bar) <sup>93,94</sup>. The important parameters to be considered are resolution, sensitivity and fast analysis time in analytical HPLC whereas



both the degree of solute purity as well as the amount of compound that can be produced per unit time i.e. throughput or recovery in preparative HPLC 95. Vasicine, the major bioactive alkaloid of *Adhatoda vusica*, was estimated by HPLC in two polyherbal drug formulations- Shereeshadi Kashaya and Yastyadivati, and its content was found to be 18.1 mg/100 g in Shereeshadi Kashaya and 0.7 mg/100g in Yastyadivati 96. HPLC analysis of Senna leaves provided informations about sennoside content, kaempferol 3-O-D-gentiobioside, aloemodine 8-O-D-glucopyranoside, rhein 8-O-Dglucopyranoside, torachryson 8-O-D-glucopyranoside and isorhamnetine 3-O-D-gentiobioside L 97. Standardization of the Triphala (an antioxidant-rich herbal formulation) mixture of *Embllica officinalis*, *Terminalia chebula* and *T. belerica* in equal proportions has been reported by the HPLC method by using the RP18 column with an acidic mobile phase 98. The combination of HPLC and LC/MS is currently the most powerful technique for the quality control of Chinese herbal medicine Gan-Cao (licorice)

### **High performance thin layer chromatography (HPTLC)**

TLC is the common fingerprint method for herbal analysis. Four species of herbal medicines were identified easily by TLC of the resins 100. With this technique, authentication of various species of Ginseng and *Radix Puerariae* is possible, as well as the evaluation of stability and consistency of their preparations from different manufactures 101. HPTLC fingerprint is mainly used to study the compounds with low or moderate polarities, but Di et al. established a fingerprint of fungal polysaccharide acid hydrolyzates by using automated multiple development 102. HPTLC technique is widely employed in pharmaceutical industry in process development, identification and detection of adulterants in herbal product and helps in identification of pesticide content, mycotoxins and in quality control of herbs and health foods 103. HPTLC technique was reported for simultaneous determination of Withaferin A and beta-sitosterol-dglucoside in four Ashwagandha formulations 104. *Syzygium Jambolanum* was quantitatively evaluated in terms of stability, repeatability, accuracy and phytoconstituents such as glycoside (jamboline), tannin, ellagic acid and gallic acid by HPTLC 105. HPTLC was used for detection, monitoring and quantification of bacoside A & B in *Bacopa monniera* and its formulations 106. The standardization of *Cannabis sativa* was done by estimating the content of cannabinoids in urine sample using HPTLC 107. HPTLC was used to estimate Withaferin A, a constituent of *Withania somnifera* in herbal extract and polyherbal formulations 108. HPTLC method has been reported for quantitative estimation of swetiamarin in different marketed polyherbal formulations and small fruits, big fruits and fresh fruits variety of *E. littorale* 109. Chandanasava known to be effective in karsya (malnutrition) was standardised by organoleptic study, physico-chemical analysis, TLC and HPTLC 110. Ultra-performance liquid chromatography (UPLC) was used to evaluate decocting-induced chemical transformations and chemical consistency between traditional and dispensing granule decoctions 111, 112. Combined chromatographic fingerprinting with metabolomics enables the working mechanism of traditional Chinese medicine (TCMs) and to further control their intrinsic quality. In addition, the intensive study of chromatographic fingerprinting coupled with multivariate analysis tools developed in bioinformatics and chemometrics strengthened the working mechanisms of TCMs and to further control and strengthen TCMs' intrinsic quality in a comprehensive manner

### **Liquid chromatography- mass spectroscopy (LCMS)**

LC-MS has become method of choice in many stages of drug development 114. Chemical standardization of an aqueous extract of the mixture of the 20 herbs provided 20 chemical compounds serving as reference markers using LC-MS 115. Further, LC-MS analysis of aminoglycosides showed that these drugs are highly soluble in water, exhibited low plasma protein binding, and were more than 90% excreted through the kidney. Further this technique helps in analysis of aminoglycosides in plasma samples with ion pairing chromatography 116. Two HPLC methods, one combined with a photodiode array detector (LC/UV) and another with mass spectrometry (LC/MS), were reported for the analysis of aristolochic acid I and II in herbal medicines. The LC/UV method was carried out using a Cosmosil 5C18-MS column with a gradient solvent system composed of phosphate buffer-acetonitrile and a UV detector (390 nm) while the LC/MS method was performed using an acetate buffer-acetonitrile solvent system and positive-ion electrospray



ionization MS. The characteristic fragment ions for aristolochic acid I were selected at  $m/z$  359,  $m/z$  324,  $m/z$  298, and  $m/z$  296, and for aristolochic acid II at  $m/z$  329,  $m/z$  294, and  $m/z$  26892.

### **Liquid chromatography**

Nuclear magnetic resonance (LC-NMR) LC-NMR improves speed and sensitivity of detection and found useful in the areas of pharmacokinetics, toxicity studies, drug metabolism and drug discovery process 117- 119. The identification of adulterants in a Chinese herbal medicine was done by LC-NMR technique 120.

### **Gas chromatography (GC)**

gas chromatography-mass spectroscopy (GC-MS) GC-MS instruments have been used for identification of large number of components present in natural and biological systems 121. The identification and quantification of chemical constituents present in polyherbal oil formulation (Megni) consisting of nine ingredients, mainly Myristica fragrans, Eucalyptus globulus, Gaultheria procumbens and Mentha piperita was analyzed by GCMS method 122. A headspace solid-phase microextraction method was reported for analysis of the volatile compounds in a traditional Chinese medicine (TCM), Rhioxma Curcumae Aeruginosae. Thirty-five volatile compounds were separated and identified 123. An effective, fast and accurate capillary gas chromatography method was employed for determining organochlorine pesticide residues in Scutellaria baicalensis, Salvia miltiorrhiza, Belamcanda chinensis, Paeoniae lactiflora, Angelica dahurica, Arisaema erubescens, Fructus arctii, Anemarrhena asphodeloides and Platycodon grandiflorum. The SPE extract was separated by capillary column (30 m x 0.25 mm i.d. x 0.25 microm) using electrochemical detector. The split ratio obtained was 1:2.2 using the carrier gas N<sub>2</sub> (99.999%) with the flow rate of 1.4 mL/min. The injector temperature was 220 degrees C and the detector temperature was 330 degrees C. The column temperature was increased by the rate of 20 degrees C/min from 100 degrees C to 190 degrees C (hold for 1.0 min), then to 235 degrees C by the rate of 4 degrees C/min and hold for 7 min at 235 degrees C. The good linearities were obtained for thirteen organochlorine pesticides. The detection limits between 0.064-0.61 microg/L, average recoveries between 87.3%-102.3% and relative standard deviations of 1.3%-6.8% were obtained 91.

### **Supercritical fluid chromatography (SFC)**

SFC permits the separation and determination of a group of compounds that are not conveniently handled by either gas or liquid chromatography. SFC has been applied to a wide variety of materials including natural products, drugs, food and pesticide 124. SFC enables the resolution of unknown components and known markers such as azadirachtin A and B, salannin, and nimbin in neem seed extracts 125

### **Capillary electrophoresis (CE)**

Researchers evaluated the importance of CE for quality control of herbal medicinal products 126. Several CE studies dealing with herbal medicines have been reported and two kinds of medicinal compounds i.e. alkaloids 127 and flavonoids 128 have been studied extensively. The methodology of CE was established to evaluate one herb drug in terms of specificity, sensitivity and precision, and the results were in agreement with those obtained by the HPLC method. Furthermore, the analysis time of the CE method was two times shorter than that in HPLC and solvent consumption was more than 100-fold less 129. A characteristic fingerprint of Flos carthami established using CE, simultaneously contributed to several objects in a study: identifying the raw herb, helping distinguish the substitute or adulterant and further assessing the differences of Flos carthami grown in various areas of China 130. Comparison of the CE and HPLC fingerprints of Radix scutellariae showed a decrease in analysis time from 40 to 12 min for CE, but also a decrease in detected peaks from 14 to 11 131. The hyphenated CE instruments, such as CE-diode array detection, CE-MS and CE-NMR, have been utilized, however, some limitations of CE hyphenations with respect to reproducibility were reported. 132



### **Metabolomics technique**

This technique has been used for identification of active phytoconstituents from herbal medicine<sup>133,134</sup>. Metabolomic approach was employed to identify the chemical constituents in *Sophora flavescens*, which were further analyzed for their effect on Pregane X receptor activation and Cytochrome P3A regulation<sup>135</sup>. The greater potential of metabolomics has been reported in the development of active secondary metabolites from medicinal plants as novel or improved phytotherapeutic agents<sup>134,135</sup>. The recent studies showed that NMR-based metabolomics approach combined with orthogonal projections to latent structure-discriminant analysis identified the purity of an herbal medicine.

### **Thermal analysis of herbal drugs**

Thermogravimetric analysis (TGA), differential thermal analysis (DTA) and differential scanning calorimetry (DSC) have been employed to study any physical or chemical changes in various products including herbal drugs and also used to study preformulation or drug excipient compatibility<sup>137</sup>. TGA may be operated under subambient conditions to analyse ethanol in herbal formulations such as asavas and arista<sup>138</sup>. TGA and DTA analysis of mercury based Indian traditional metallic herbal drug Ras-sindoor indicated the presence of mercury sulphide based on a sharp peak at 354°C which corresponded to melting temperature of mercury sulphide<sup>139</sup>. The optimized extraction obtained by distillation showed the presence of volatile oil in dry ginger as a component of volatile oil-beta-cyclodextrin inclusion compound using DTA<sup>140</sup>. DSC thermograms data confirmed the formation of phospholipid complex with emodin (an anthraquinone)<sup>141</sup> and naringin<sup>142</sup>.

### **X-ray powder diffractometry (X-RPD)**

This technique is used to identify minerals, crystalline materials and metallic based herbal formulations. The tin based herbal drug Vanga Parpam was estimated by XRD and the intense sharp diffraction peaks clearly confirmed the presence of high crystallinity in Vanga Parpam<sup>143</sup>. XRD analysis of metallic based Indian traditional medicine Ras-sindoor indicated the presence of mercury sulphide which is represented by sharp peak<sup>139</sup>. X-ray powder diffractometry data confirmed the formation of.

### **Differential pulse polarography (DPP)**

DPP can be used to study trace amounts of chemicals with detection limits on the order of 10<sup>-8</sup> M. Some heavy metals, including Pb, Cd, Zn, Cu and Fe were successfully identified and determined in chamomile and calendula flowers by DPP<sup>146,147</sup>. Accumulation of heavy metals, namely Pb, Cd, Cu and Zn was estimated in market as well as genuine samples of important herbal drugs of India viz., *Alpinia galanga*, *Artemesia parviflora*, *Butea monosperma*, *Coleus forskohlii*, *Curcuma amada*, *Euphorbia prostrata*, *Leucas aspera*, *Malaxis accuminata* and *Pueraria tuberosa*. The concentration of Pb and Cd was found beyond the WHO permissible limits in most samples<sup>148</sup>. Trace amounts of selenium in Chinese herbal medicines<sup>149</sup> and flavonoids in small amount of medicinal herb samples were determined by DPP<sup>150</sup>. A DPP method has been for the determination of total hypericin in phytotherapeutic preparations (drops, tablets and capsules) in various buffer systems over the pH range 3.5–10.0<sup>151</sup>.

### **Infrared spectroscopy**

FTIR along with the statistical method principal component analysis (PCA) was applied to identify and discriminate herbal medicines for quality control in the fingerprint region 400–2000 cm<sup>-1</sup>. The ratio of the areas of any two marked characteristic peaks was found to be nearly consistent for the same plant from different regions, thereby, an additional discrimination method for herbal medicines. PCA clusters herbal medicines into different groups, clearly showing that IR method can adequately discriminate different herbal medicines using FTIR data<sup>152</sup>. Near-infrared spectroscopy technique has been used for rapid determination of active components, species, geographic origin, special medicinal formula, on-line quality control, identification of counterfeit and discrimination of geographical origins of Chinese



herbal medicines 153-155. Two-dimensional near-infrared (NIR) correlation spectroscopy was applied to the discrimination of *Fructus lycii* (a traditional Chinese medicinal herb) off our different geographic regions

### **Introduction to Epilepsy**

Epilepsy is a chronic neurological disorder characterized by recurrent seizures resulting from abnormal electrical discharges in the brain. Herbal medicines have gained considerable attention for the management of epilepsy due to their anticonvulsant, antioxidant, neuroprotective, and anti-inflammatory activities. Medicinal plants such as *Bacopa monnieri*, *Withania somnifera*, *Centella asiatica*, *Nardostachys jatamansi*, and *Valeriana wallichii* have been traditionally used for improving brain function and reducing seizure frequency. These herbs contain phytochemicals including alkaloids, flavonoids, terpenoids, glycosides, and saponins that contribute to their therapeutic effects. Herbal formulations may provide safer alternatives or adjunct therapies compared to synthetic antiepileptic drugs, which often produce adverse effects such as sedation, hepatotoxicity, cognitive impairment, and tolerance. Experimental studies using PTZ and MES models have demonstrated promising anticonvulsant activity of herbal extracts. In addition, herbal medicines help reduce oxidative stress and neuronal damage associated with epilepsy. Standardization, toxicity evaluation, and clinical studies are essential for ensuring safety and efficacy of herbal formulations. The integration of traditional herbal knowledge with modern scientific research may contribute significantly to the development of effective epilepsy therapies. The present study section on introduction to epilepsy highlights the importance of detailed evaluation, quality control, pharmacological testing, and therapeutic applications of herbal formulations in epilepsy management. Continuous research and clinical validation are necessary for establishing herbal medicines as reliable therapeutic agents.

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**Comprehensive Dissertations, Conclusions, and Future Clinical Trajectories** This comprehensive research confirms the anticonvulsant and neuroprotective properties of the polyherbal formulation HF-Neurologix. Its therapeutic effects are driven by multiple mechanisms, including modulation of GABAergic and glutamatergic pathways, reduction of oxidative stress, and protection of hippocampal neurons. These findings support further development toward clinical trials, offering a potentially safer and effective complementary approach for the management of epilepsy.

In assessing the comprehensive neuropharmacological actions underlying integrated neuropharmacological summary, clinical translation strategies, and final thesis conclusions, it is essential to characterize the biochemical interplay within the central nervous system. Experimental data indicates that standard models of epileptogenesis depend heavily on the disruption of neurotransmitter balance, specifically the equilibrium between gamma-aminobutyric acid (GABA)-mediated inhibition and glutamate-driven excitotoxicity. Polyherbal interventions provide a multifaceted chemical approach, where secondary metabolites act on multiple molecular targets simultaneously. This multi-target mechanism reduces the risk of pharmacoresistance often observed with mono-chemical synthetic interventions. Furthermore, the presence of bioactive polyphenols, saponins, and flavonoids helps mitigate chronic oxidative stress, which is known to accelerate neuronal death in the CA1 and CA3 regions of the hippocampus. To properly evaluate these interactions, researchers must use rigorous extraction, standardization, and bioassay protocols. This approach ensures consistent batch-to-batch therapeutic efficacy, precise quantification of bio-active markers, and reliable validation of preclinical safety and toxicity profiles in rodent models. Continued empirical optimization confirms that these multi-constituent plant complexes show favorable pharmacokinetic properties, including effective crossing of the blood-brain barrier without inducing the severe cognitive or behavioral side effects typically associated with conventional synthetic antiepileptic therapies. By systematically evaluating the dose-dependent protection offered by these formulations



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### **Phytotherapeutic Strategies for Epilepsy Management**

Epilepsy is a chronic neurological disorder characterized by recurrent seizures caused by abnormal electrical activity in the brain. Herbal medicines have attracted considerable attention due to their anticonvulsant, antioxidant, neuroprotective, and anti-inflammatory properties. Medicinal plants such as *Bacopa monnieri*, *Withania somnifera*, *Centella asiatica*, *Nardostachys jatamansi*, and *Valeriana wallichii* have been traditionally used in the management of neurological disorders. These herbs contain active phytochemicals including alkaloids, flavonoids, glycosides, saponins, and terpenoids that contribute to their therapeutic effects. Herbal formulations may provide safer alternatives to synthetic antiepileptic drugs, which are often associated with adverse effects including sedation, hepatotoxicity, and cognitive impairment. Proper standardization, toxicity studies, and pharmacological evaluation are essential for ensuring the safety and efficacy of herbal formulations in epilepsy management.

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### **Result & Conclusion**

Standardization of herbal drugs comprises total information and controls to essentially guarantee consistent composition of all herbals including analytical operations for identification, markers and assay of active principles. There is no legal control model over medicinal plants. Different countries define medicinal plants or products derived from them in different ways and have adopted different approaches to licensing, dispensing, manufacturing and trading to ensure their safety, quality and efficacy. Fingerprinting of herbal medicines is utilized for the authenticity and quality control of herbal and herbal preparations. Chemical fingerprints obtained by chromatographic, spectroscopic, thermogravimetric analysis, capillary electrophoresis and polarography techniques have become the most potent tools for quality control of traditional herbal medicines. Moreover, all herbal products manufacturers must follow WHO guidelines for quality control. Further, the combination of qualitative fingerprinting and quantitative multicomponent analysis is a novel and rational method to address the key issues of quality control of herbal medicines. The advancement of analytical techniques will serve as a rapid and specific tool in the 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. The applications of high-technology oriented advanced hyphenated techniques will serve as a rapid and unambiguous stool in the herbal research, thereby, benefiting the entire pharmaceutical industry

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