Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2023: 85.86
Volume 14, Issue 5; 2025, 01-14

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Review Article

Role of Chemical Marker in Quality Control of Herbal Drugs

Golu Kumar[1], Rameshwar Kumar[2], Ankit Kumar[3], Aditya Kumar[4], Gopal Bharti[5]

[1]Student of Krishna Institute of Nursing & Paramedical Science, Samastipur, Bihar
[2,3,4,5]Faculty of Krishna Institute of Nursing & Paramedical Science, Samastipur, Bihar

Article Info: Received: 15-07-2025 / Revised: 27-08-2025 / Accepted: 18-09-2025
Corresponding Author: Golu Kumar
DOI: https://doi.org/10.32553/jbpr.v14i5.1355
Conflict of interest statement: No conflict of interest

Abstract:

The growing global interest in herbal medicine has heightened the demand for scientifically validated, standardized, and high-quality plant-based therapeutics. However, the intrinsic complexity of herbal drugs—characterized by multiple bioactive components, environmental variability, and traditional preparation methods—presents significant challenges in ensuring product consistency, efficacy, and safety. In this context, the application of chemical markers has emerged as a critical and scientifically sound approach for the quality control and standardization of herbal drugs**.**

Chemical markers are defined as phytochemical constituents that serve as qualitative and/or quantitative indicators of the identity, purity, and potency of herbal materials. They may be pharmacologically active, characteristic of the plant species, or simply analytically convenient. Their selection is based on well-defined criteria, including their presence in significant quantities, ease of detection, stability, and relevance to therapeutic action. These markers are categorized broadly into three types: active markers (directly responsible for therapeutic effects), analytical markers (easily quantifiable and indicative of quality), and synergistic markers (compounds that contribute to efficacy through interaction with other constituents).

With advancements in analytical techniques such as High-Performance Liquid Chromatography (HPLC), Liquid Chromatography-Mass Spectrometry (LC-MS), Nuclear Magnetic Resonance (NMR), and Capillary Electrophoresis (CE), the identification, isolation, and quantification of chemical markers have become more accurate and reproducible. These tools enable the creation of phytochemical fingerprints and quantification protocols that are essential for batch-to-batch consistency, contamination detection, and shelf-life determination.

Keywords: Herbal drugs, Quality control, Standardization, Pharmacognosy, Marker compounds, Phytochemistry, Chromatography, HPTLC, HPLC, LC-MS, DNA barcoding, Pharmacopoeia.

1. Introduction

Herbal medicines, also known as botanical medicines or phytomedicines, refer to the medicinal products of plant roots, leaves, barks, seeds, berries or flowers that can be used for the treatment as well as wellbeing of mankind and to promote better health. Medicinal use of plants has a long history worldwide. Quality control of herbal medicines aims to ensure their consistency, safety and efficacy.

It is very much essential that even the quality of the herbal medicines is being controlled as that of the chemically synthesized medicines. According to the World Health Organization

(WHO), traditional herbal preparations account for 30–50% of the total medicinal consumption in China. But unfortunately, the regulation norms for the herbals are not as strict when compared to the synthetic drugs. This is leading to a decrease in the quality standards of the herbal products by intentional and sometimes unintentional adulteration, spurious drugs, substitution of drugs, and many other ways which are prone to decreasing the quality of the herbal materials which are marketed and consumed for the healthy survival. But instead of this, it is leading to hazardous effects on the health of the consumers. So, it is very much required to control the quality standards of the herbal drugs and products for the betterment of the mankind.

Standardization and the phytochemicals investigation are carried out; apart from these, there are various quality control tools which are used to assure the quality aspects of the herbals. Both qualitative and quantitative measures are required for the quality assurance of them. Different techniques like layer chromatography, HPLC (high pressure/performance liquid chromatography), SFC (supercritical fluid chromatography), thermal analysis, ICPMS (inductively coupled plasma-mass spectroscopy), LCMS (liquid chromatography-mass spectroscopy), and GCMS (gas chromatography-mass spectroscopy) are used for the quantitative estimation of the herbal products for quality control assessment. As there is a growing demand for herbal pharmaceuticals, there is a need to assure their quality. [1]

So, the different tools and techniques must be implied to verify and ensure the required quality to be incorporated into the herbal material and products. There must be guidelines and/or norms framed for carrying out the quality control testing of the herbs which are almost or equally strict as that of the synthetic pharmaceuticals. This will help to maintain the quality standards of the herbal. [2]

2. Aim and Objectives:

Aim and objectives of quality control of herbal drugs-

1. Improvement of quality.
2. Reduction of scrap and rework.
3. Efficient use of men and machines.
4. Economy in use of materials.
5. Removing production bottle-necks.
6. Decreased inspection costs.
7. Reduction in cost per unit.
8. Scientific evaluation of quality and production.
9. Quality caution at all levels.
10. Reduction in customer complaints.
11. To decide about the standard of quality of a product.

3. Quality Control of Herbal Drugs:

Herbal Drugs:

The term “herbal drugs" denotes plants or plant parts that have been converted into phytopharmaceuticals by means of simple processes involving harvesting, drying, and storage.

Quality:

Quality can be defined as the status of a drug that is determined by identity, purity, content, and other chemical, physical, or biological properties, or by the manufacturing processes.

Quality control of herbal drugs is mainly based on the following Parameter:

a) Identity
b) Purity
c) Assay/ content

Identity:

It can be achieved by macro and microscopic examination. Outbreak of diseases among plants may result in changes to the physical appearance of the plant and lead to incorrect identification. At times an incorrect botanical quality with respect to the labelling can be a problem.

Purity:

It is closely linked with the safe use of drugs and deals with factors such ash values, contaminants (e.g., foreign matter in the form of other herbs) and heavy metals. Due to the application of improved analytical methods, modern purity evaluation also includes microbial contamination, aflatoxins, radioactivity and pesticide residues.

Analytical methods such as photometric analysis, thin layer chromatography (TLC), high performance liquid chromatography (HPLC), and gas chromatography (GC) can be employed in order to establish the constant composition of herbal preparations. [3]

Assay:

It is the most difficult area of quality control to perform, since in most herbal drugs the active constituents are not known. Sometimes markers can be used. In all other cases, where no active constituent or marker can be defined for the herbal drug, the percentage extractable matter with a solvent may be used as a form of assay.

4. **Methods for Quality Control of Herbal Drugs:**

Various methods have been given by WORLD HEALTH ORGANIZATION for the quality control of herbal drugs. Some of the following methods are given as below.

- Powder fineness and sieve size
- Determination of foreign matter
- Macroscopic and microscopic examination
- Thin layer chromatography
- Determination of ash value
- Determination of extractable matter
- Determination of water and volatile oil
- Determination of bitterness value
- Determination of haemolytic activity
- Determination of tannins
- Determination of swelling index
- Determination of foaming index
- Determination of pesticide residue
- Determination of heavy metals
- Determination of microorganism
- Radioactive contamination determination

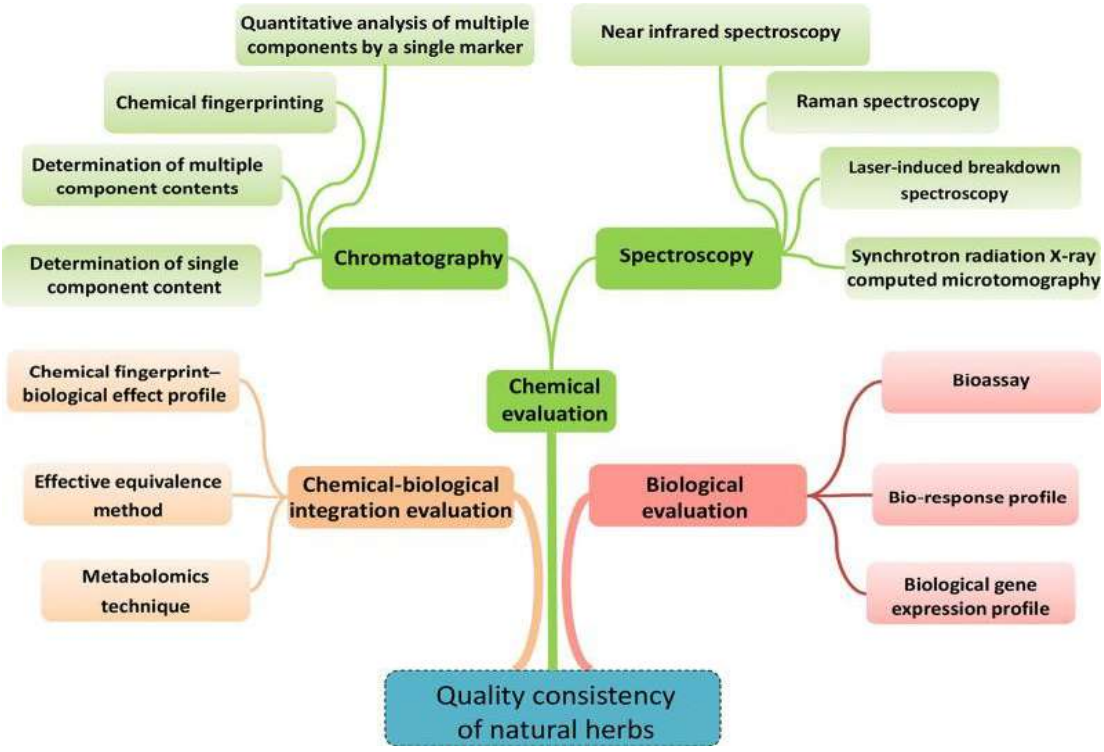

Figure 1: Modern Methods For Quality Control

5. **Markers in the Quality Control of Herbal Medicines:**

Markers/ Marker compound:

Marker compound is a chemically defined constituents of herbal drugs which are used for quality control purposes and they are independent of therapeutic activity. Markers may serve to calculate the amount of active component of herbal drug or preparation in finished product. They help to establish internationally recognized guidelines for assessing the quality of the herbal drugs.

Types of markers:

There are mainly two types of markers.

A. Molecular or DNA markers.
B. Chemical markers.

Molecular markers:

Molecular marker is identified as genetic marker. Molecular marker is a DNA or gene sequence within a recognized location on a chromosome which is used as identification tool. In the pool of unknown DNA or in a whole chromosome, these molecular markers help in identification of specific sequence of DNA at particular location.

Types of molecular markers:

- Restriction Fragment Length Polymorphisms (RFLPs)
- Amplified Fragment Length Polymorphisms (AFLPs)
- Randomly Amplified Polymorphic DNA (RAPD)
- Simple Sequence Repeats (SSRs)
- Inter Simple Sequence Repeats (ISSR)
- Sequence Characterized Amplified Regions (SCAR)
- Loop Mediated Isothermal Amplification (LAMP)
- Single Nucleotide Polymorphisms (SNPs)

Application of molecular markers:

1. **In herbal drug technology:**

DNA based markers have been proved their importance in fields like taxonomy, physiology, embryology, and genetics.

2. **Genetic variation/genotyping:**

Random Amplified Polymorphic DNA(RAPD) based molecular markers have been found to Be useful in differentiating different accessions of Taxus wallichiana, Neem, Allium sphenogram, Andrographis paniculate collected from different geographical regions. Interspecies variation has been studied using RFLP (Random Fragment Length Polymorphism) and RAPD in different generation such as Glycyrrhiza, Echinacea, Curcuma. RAPD has served as a tool for the detection of variability in Vitis vinifera L. and tea (Camellia sinesis).

3. **Authentication of medicinal plants:**

Sequence Characterized Amplified Region (SCAR), RAPD and have been successfully applied for differentiation of plant and to detect substitution by other closely related species. Certain rare and expensive medicinal plant species are often adulterated or substituted by morphologically similar, easily available or less expensive species. For example, Swertia chirata is frequently adulterated or substituted by the cheaper Andrographis paniculata.

4. **Marker assisted selection of desirable chemo types:**

Amplified Fragment Length Polymorphism (AFLP) analysis has been found to be useful in predicting phytochemical markers in cultivated Echinacea purpurea germplasm and some related wild species.

5. **Medicinal plant breeding:**

Molecular markers have been used as a tool to verify sexual and apomictic offspring of intraspecific crosses in Hypericum perforatum, a well-known anthelminthic and diuretic.

6. **Foods and nutraceuticals:**

Soybeans, maize and capsicum have been successfully discriminated from non-GM products using primers specific for inserted genes and crop endogenous genes.

7. **As New Pharmacogenetic tool:**

These markers have shown remarkable utility in quality control of important like Ginseng, Echinaea, Atractylodes. Although DNA analysis is currently considered to be cutting-edge technology, it has certain limitations due to which its use has been limited to academia another important issue is that DNA fingerprint will remain the same irrespective of the plant part used, while the phytochemical content will vary with the plant part used, physiology and environment.

6. **Chemical Markers:**

The European Medicines Agency (EMEA) defines chemical markers as chemically defined constituents or groups of constituents of a herbal medicinal product which are of interest for quality control purposes regardless whether they possess any therapeutic activity. [5]

- Chemical makers refer to as biochemical constituents in which primary and secondary metabolites and other macromolecules of interest for quality control purpose are used whether they possess any therapeutic activity or not.
- The quantity of chemical marker is the indicator of the quality of the herbal medicine.
- The use of chemical markers is applicable to various fields of research such as authentation of genuine species, search of new resources or substitutes of raw material, optimization of extraction and purification methods, structure and purity determination.
- For example, in the case of say, Boswellia serrata also known as Shallaki or Salai Guggul. It is extensively used in Ayurveda for joint support and provides an overall sense of well-being. It offers broad health and immunomodulating benefits, anti-inflammatory, antiatherosclerosis and antiarthritic activities. It also improves circulation of blood and it is also used in cosmetic products. The gum resin of Boswellia serrata is known to contain 4 major Pentacyclic Triterpenic acids which are as Beta- Boswellic acid, acetyl beta-boswellic acid, 11-keto-beta-boswellic acid and acetyl-11-ketobeta-boswellic acid.

Types of chemical markers:

1. **Active principles:** Well defined chemicals with known clinical activity e.g Ephedrine in Ephedrasinensis, Silymarin in Silybum marianum.
2. **Active markers:** They are the constituents or groups of constituents with known pharmacological activity that contribute to efficacy. May or may not have proven clinical efficacy. e.g Allin in Allium sativum, Hypericin in Hypericum perforatum.
3. **Analytical markers:** They are the constituents or groups of constituents that serve solely for analytical purposes & have no clinical or pharmacological activities. Aid in the positive identification of raw material and extracts or used to achieve standardization. e.g., Different alkylamides found in roots of Echinacea angustifolia and Echinacea purpurea but totally absent in Echinacea pallid. [9]
4. **Negative markers:** Demonstrate allergenic or toxic properties or those which interfere with bioavailability. Example- Gingolic acids in ginkgo preparations (allergenic agent).

Pharmacological Activities of Herbal Markers

1. **Curcumin** (from Turmeric)
   -**Activity**: Anti-inflammatory, antioxidant, anticancer
   -**Effect**: Inhibits inflammatory pathways; scavenges free radicals.
2. **Allicin** (from Garlic)
   -**Activity**: Antibacterial, cardioprotective, antifungal
   -**Effect**: Kills pathogens, reduces cholesterol and blood pressure.
3. **Gingerol** (from Ginger)
   -**Activity**: Antiemetic, anti-inflammatory, analgesic

-**Effect**: Reduces nausea, inflammation, and pain.

4. **Ginsenosides** (from Ginseng)

-**Activity**: Apoptogenic, neuroprotective, immunomodulatory

-**Effect**: Enhances mental performance and resistance to stress.

5. **Withanolides** (from Ashwagandha)

-**Activity**: Anti-stress, anti-inflammatory, anticancer

-**Effect**: Balances cortisol levels; may inhibit tumor growth.

6. **Eugenol** (from Tulsi & Clove)

-**Activity**: Analgesic, antiseptic, anti-stress

-**Effect**: Used in dental care; reduces oxidative stress.

7. **Glycyrrhizin** (from Licorice)

-**Activity**: Anti-ulcer, anti-viral, anti-inflammatory

-**Effect**: Protects gastric mucosa; modulates immune response.

Table no. 1 Pharmacological Activities of Herbal Markers

Sl. No.	Herb	Marker	Pharmacological Activity
1.	Turmeric	Curcumin	Antioxidant, Anti-inflammatory
2.	Garlic	Allicin	Antibacterial, Cardioprotective
3.	Ginseng	Ginsenosides	Neuroprotective, Antifatigue
4.	Tulsi	Eugenol	Antiviral, Anti-stress
5.	Cinnamon	Cinnamaldehyde	Antidiabetic, Antifungal

7. **The New Classification of Chemical Markers:**

A. Therapeutic components,
B. Bioactive components
C. Synergistic components
D. Characteristic components
E. Main components
F. Correlative components
G. Toxic components
H. General components used with fingerprint spectrum.

A) **Therapeutic component:**

Therapeutic components possess direct therapeutic effects of the herbal medicine. They may be used as chemical markers for both qualitative and quantitative assessments.

Examples:

- Isosteroidal alkaloids of Bulbus Fritillariae, was identified as the major therapeutic component which comprises of antitussive effect. Therefore, isosteroidal alkaloids were selected as the chemical markers for the quality assessment of Bulbus Fritillariae.
- Artemisinin from Herba Artemisia Annuae. It is well known for its potent anti-malarial activity. Artemisinin inhibits Plasmodium falciparum and Plasmodium vivax, two pathogens that cause malaria. Artemisinin is now used as a chemical marker in HPLC-ELSD, GCFID and GCMS for assessing the quality of the plant (parts and whole) at various stages, including the green and dead leaves of the plant.

B) **Bioactive components:**

Bioactive components are structurally different chemicals present in the herbal medicine. Alone they do not have any therapeutic effect but in combination they show therapeutic effect. Bioactive components may be used as chemical markers for qualitative and quantitative assessment.

Example:

According to Chinese medicine theories, Radix Astragali (Huangqi), derived from the roots of Astragalus membranous shows pharmacological actions in immune and circulatory systems. These bioactive components, including isoflavonoids and saponins, were used simultaneously in the evaluation of the quality of Radix Astragali.

C) **Synergistic components:**

Synergistic components do not contribute to the therapeutic effects or related bioactivities directly. However, they act synergistically to reinforce the bioactivities of other components, thereby modulating the therapeutic effects of the herbal medicine. Synergistic components may be used as chemical markers for qualitative and quantitative assessment.

D) **Characteristic components:**

These components present in the herbal medicine may contribute to the therapeutic effect so these are unique ingredients which help in assessment of the quality of herbal drug.

Example:

Terpene lactones in the leaves of Ginkgo biloba L. exemplify characteristic components. EGb 761, a standardized leave extract of Ginkgo biloba is a well-defined product for the treatment of cardiovascular diseases, memory loss and cognitive disorders associated with age-related dementia. Flavonoids and terpene lactones are responsible for the medicinal effects of EGb 761. Flavonoids, terpene lactones including ginkgolides A, B and C, and bilobalide are

- Valerenic acids, the characteristic components of valerian derived from the roots of Valeriana officinalis L., have sedative effects and improve sleep quality. Valerenic acids are used as chemical markers to evaluate the quality of valerian preparations although their sedative effects have not been fully elucidated.

E) **Main components:**

Main components are the most abundant in a herbal medicine (or significantly more abundant than other components). They are not characteristic components and their bioactivities may not be known. Main components may be used for both qualitative and quantitative analysis of herbal medicines especially for differentiation and stability evaluation.

Example:

- Four well-known Chinese herbal medicines derived from the genus Panax, namely (1) Radix et Rhizoma Ginseng (Renshen), (2) Radix et Rhizoma Ginseng Rubra (Hongshen), (3) Radix Panacis Quinquefolii (Xiyangshen) and (4) Radix et Rhizoma Notoginseng (Sanqi), contain triterpenoid saponins including ginsenoside Rg1, Re, Rb1 and notoginsenoside R1 as their main components. Through qualitative and quantitative comparison of the saponin profiles, these four herbs can be differentiated from one another.

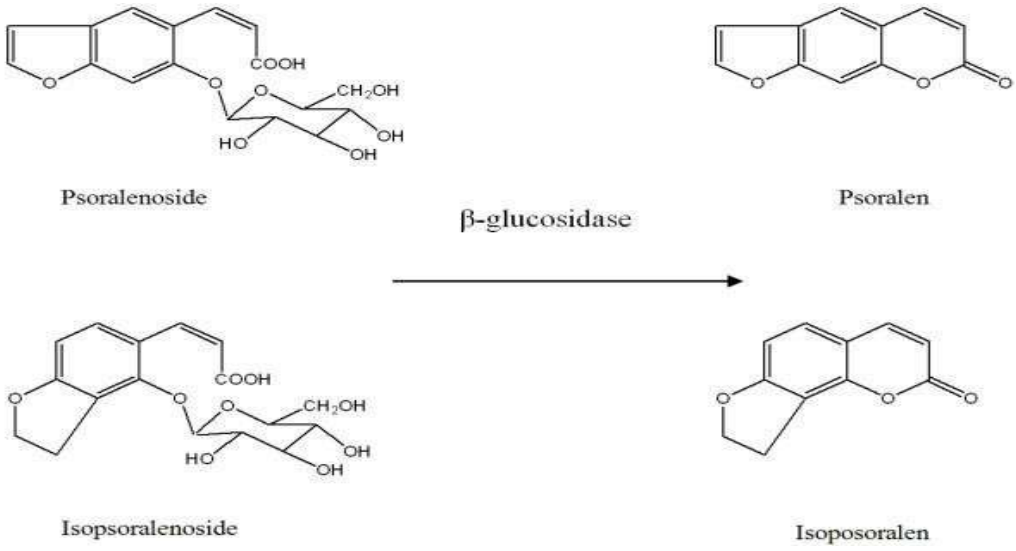

Figure 2: Chemical Marker For Fructus Psoraleae

1. **Toxic components:**

Traditional Chinese medicine literature and modern toxicological studies documented some toxic components of medicinal herbs. For instance, aristolochic acids and pyrrolizidine alkaloids may cause nephrotoxicity and hepatotoxicity respectively.

Example:

These components present in the herbal medicine may contribute to the therapeutic effect so these are unique ingredients which help in assessment of the quality of herbal drug.

- The use of three herbal medicines that contain aristolochic acids, namely Radix Aristolochiae Fangchi (Guangfangji), (Guanmutong) and (Qingmuxiang). Aristolochic acids are now used as mark ers to control nephrotoxic herbs and proprietary herbal products.

2. **General components coupled with 'fingerprints':**

General components are common and specific components present in a particular species, genus or family. These components may be used with 'fingerprints' for quality control purposes.

Example:

Lobetyolin, a polyacetylene compound, is used as a marker for Radix Codonopsis (Dangshen) TLC. Radix Codonopsis is derived from the roots of three Codonopsis species, namely Codonopsis pilos ula (Franch.) Nannf., C. pilosula Nannf. var. modesta (Nannf.) L. T. Shen or C. tangshen Oliv.

Table no. 2 Various Herbs and Their Chemical Markers

Herb	Scientific Name	Key Chemical Marker(s)	Major Uses
Turmeric	Curcuma longa	Curcumin	Anti-inflammatory, antioxidant
Neem	Azadirachta indica	Azadirachtin	Antibacterial, insect repellent
Tulsi (Holy Basil)	Ocimum sanctum	Eugenol, Ursolic acid	Adaptogen, antimicrobial
Ashwagandha	Withania somnifera	Withanolides	Stress relief, immunity booster
Ginger	Zingiber officinale	Gingerol	Digestive aid, anti-nausea
Ginseng	Panax ginseng	Ginsenosides	Energy booster, cognitive support

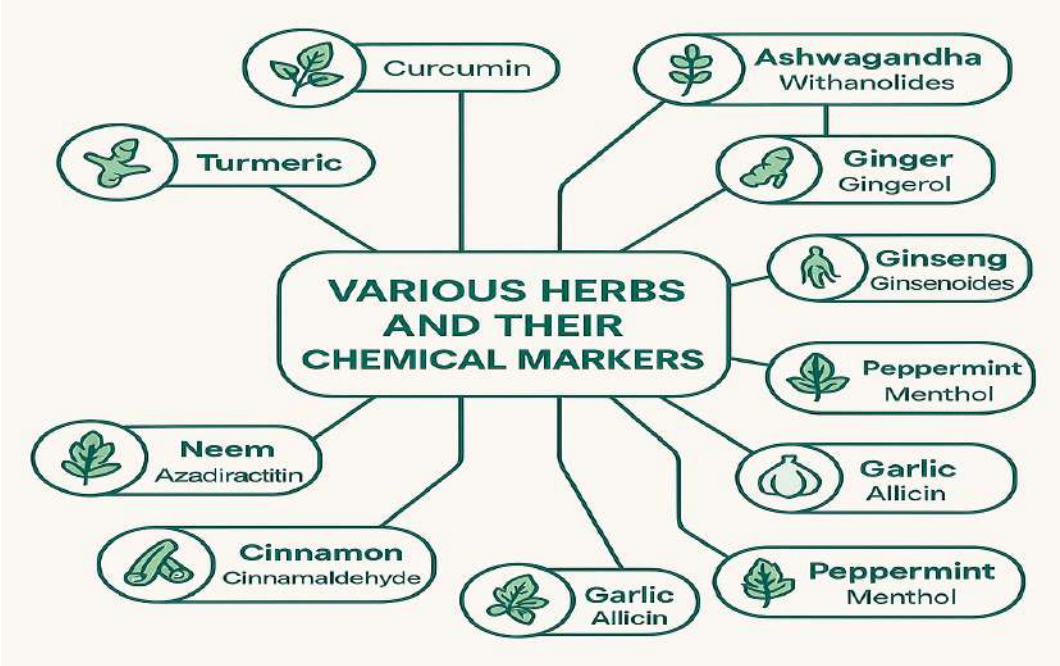

Fig No. 3 Various Herbs and Their Chemical Markers

8. **Common Extraction Methods for Herbal Markers**
    1. **Solvent Extraction**
        - **Used for**: Turmeric, Ashwagandha
        - **Targets**: Curcumin, Withanolides
        - **Note**: Uses solvents like ethanol or water to extract polar compounds.
    2. **Steam Distillation**
        - **Used for**: Peppermint, Tulsi
        - **Targets**: Menthol, Eugenol (essential oils)
        - **Note**: Ideal for volatile oils; involves steam passing through plant material.
    3. **Cold Pressing**
        - **Used for**: Neem seeds, Citrus peels
        - **Targets**: Fatty oils, Azadirachtin
        - **Note**: Mechanical pressing without heat; retains delicate compounds.
    4. **Maceration**
        - **Used for**: Garlic, Liquorice
        - **Targets**: Allicin, Glycyrrhizin
    5. **Supercritical CO_2 Extraction**
        - **Used for**: Ginger, Ginseng
        - **Targets**: Gingerol, Ginsenosides
        - **Note**: Uses CO_2 under high pressure and temperature; high purity, solvent-free.
    6. **Ultrasound-Assisted Extraction (UAE)**
        - **Used for**: Aloe vera, Fenugreek
        - **Targets**: Polysaccharides, Flavonoids
        - **Note**: Uses ultrasonic waves to break cell walls and release contents.
    7. **Microwave-Assisted Extraction (MAE)**
        - **Used for**: Cinnamon, Clove
        - **Targets**: Cinnamaldehyde, Eugenol
        - **Note**: Fast method using microwave energy; suitable for heat-stable compounds.
    8. **Percolation**
        - **Used for**: Chamomile, Valerian root
        - **Targets**: Apigenin, Valepotriates
        - **Note**: Continuous flow of solvent through herb; common in tincture prep.
9. **Application of Markers:**

- Discovery of a lead compound for new drug development:
- One of the xanthones of gamboges, is used as a chemical marker for quality control and safety evaluation of gamboges. As its cytotoxicity is attributed to cell apoptosis induction, gambogic acid is a potential lead compound for new anti-cancer drugs.
- Identification of adulterants
- Various herbs when collected for processing then there are the chances of adulteration of the other herbs with the specific herb. Sometimes the marketed formulations may also consist of various herbs.
- **Differentiation of herbal medicine from different sources:**

  It includes identification of a specific chemical constituent which present in many species of the herbs but the pharmacologically active constituent is present in only one of the species.
- **Determination of best harvesting time:**

  As the plant grows certain chemical constituents starts to develop. The marker is determined which helps us to know the specific stime of harvesting the plant. For example, markers suggested that the best harvesting time for Rhizoma Chuanxiong is from mid-April to late May.
- **Assessment of processing method:**

  Most herbs must be processed to reduce toxicity. For example, Radix Aconiti derived from the root of Aconitum carmichaeli Debx, is a well-known for toxic and potent herbal medicine. The herb is processed by

boiling in water for 4–6 hours or steaming for 6–8 hours. The toxic components of this herb are aconitine, mesaconitine and hypaconitine. When processed, these alkaloids hydrolyse into their respective analogues collectively known as monoester alkaloids. Monoester alkaloids are much less toxic than diester alkaloids. These Aconitum alkaloids may be used to evaluate Radix Aconiti.

- **Conformation of collection site:**

  Radix Stemonae, four chemical profiles of S. tuberosa of different geographic sources were characterised using croomine, stemoninine, neotuberostemonine or tuberostemonine as markers. Croomine, stemoninine, neotuberostemonine, and tuberostemonine may be used as markers to confirm the collection sites for S. tuberosa which contains higher levels of stemoninine, neotuberos temonine or tuberostemonine, and a low level of croomine.

- **Quality evaluation of herbal parts:**

  Traditionally, Radix Astragali is graded according to its diameter, length and physical appearance. Isoflavonoids and saponins were recognised as the major bioactive components attributed to the therapeutic effects of Radix Astragali. These two types of components were used to evaluate the quality of Radix Astragali. According to the traditional notion, thin roots contained more astragalosides than thick ones. Moreover, the content of astragalosides in the bark were over 74-fold higher than that in the xylem. There was no difference in isoflavonoid content between the thin and thick roots, or the bark and the xylem. These results suggest that the thin root Radix Astragali is of better quality.

- Identification and quantitative determination of proprietary medicines:

- Qingfu Guanjie Shu (QGS, also known as JCICM-6) capsule is a proprietary product to treat rheumatoid arthritis. QGS has significant suppressive effects on arthritic and acute inflammation in animal models. The formula of QGS is composed of five anti-inflammatory and anti-arthritic herbs, namely Caulis Sinomenii, Radix Paeoniae Alba, Cortex Moutan, Rhizoma Curcumae Longae and Radix Aconiti Lateralis Preparata. Sinomenine, paeoniflorin, paeonol, cucurmin and hypaconitine are the major constituents of the five herbs respectively, all of which have significant in vivo and in vitro effects including anti-inflammation, analgesia, anti-arthritis and immunosuppression.

- **Stability test for proprietary medicines:**

  Stability test is used to evaluate product quality over time and determine recommended shelf life. The five markers mentioned above were used as indicators to evaluate the product stability of QGS. For example, the accelerated conditional stability test was carried out with four time points in a period of three months in chambers at 40 ± 2°C and 75 ± 5% of humidity. The five markers were quite stable during the period; only paeonol showed a slight decrease of 5% immediately after production.

10. **Problems Related to the use of Markers: -**

There are some of the problems which may arise in use of chemical markers in quality control of herbal drugs.

1. **Shortage of chemical markers:**

At present, some herbs do not have markers for quality control. According to the Chinese Pharmacopoeia (2005 edition), only few herbs have chemical markers for quality control. A total of 282 chemical makers has been listed for qualitative or quantitative analysis of herbs. Moreover, many herbal medicines share the same chemical markers for quality control.

2. **Unqualified purity:**

Inconsistency in quality is a common problem among the commercially available chemical markers. The overall quality of chemical

markers may be influenced by various physical and chemical factors.

3. **Solvent selection for separation of chemical markers:**

Gambogic acid is one of the major characteristics of xanthones in gamboges and is therefore an ideal chemical marker for quality control. However, during the isolation and purification processes, gambogic acid can be transformed by the nucleophilic addition of methanol to the olefinic bond at C-10 when stored in methanol solution at room temperature.

4. **Temperature:**

Isoflavonoid glycoside malonates present in radix astragali, used as chemical marker were converted into their respective glycosides or flavonoid glycon during the prolonged conventional extraction procedures with Soxhlet and reflux at higher temperature.

5. **Light:**

Cinnamaldehyde is the chemical marker for the quantitative evaluation of Cortex Cinnamomi. This compound is light-sensitive. When exposed to light at room temperature for six hours, 10% of the content of cinnamaldehyde was lost; and 36 hours later, only 25% was left. Later studies indicated that this compound gradually transformed to crystallized cinnamic acid when exposed to light.

6. **Lack of Standardization**

Inconsistent levels of markers in different batches of herbs due to growing conditions, harvesting, or processing variations.

7. **Marker ≠ Total Activity**

A single marker may not represent the herb's full therapeutic effect, which often relies on multiple synergistic compounds.

8. **Degradation of Markers**

Markers may degrade due to improper storage, light, temperature, or humidity, leading to reduced potency.

9. **Extraction Limitations**

Some markers require specific and sometimes expensive extraction methods (e.g., supercritical CO_2), making standardization costly.

10. **Marker Identification Errors**

Misidentification of active markers can lead to poor quality control and ineffective herbal products.

11. **Adulteration & Substitution**

Presence of markers is sometimes used to justify adulterated or substituted herbs that may still contain the marker but not the intended therapeutic profile.

12. **Toxicity at High Concentrations**

Over-standardizing based on a marker may lead to excessive concentrations, potentially causing adverse effects (e.g., high glycyrrhizin in liquorice).

13. **Lack of Regulatory Uniformity**

Different countries follow different marker-based standards, causing confusion in international trade and quality assurance.

14. **Complexity in Multi-Herb Formulations**

Identifying and quantifying markers in polyherbal formulations is challenging due to interaction and overlap between constituents.

15. **Insufficient Research on Some Markers**

For many herbs, the choice of marker is based on tradition or limited evidence, not comprehensive pharmacological studies.

11. **Conclusion:**

Quality control of herbal medicines aims to ensure its quality, safety and efficacy. Chemical makers are pivotal in the current practice of quality control. Chemical makers should be used at various stages of the development and manufacturing of an herbal medicine, such as authentication and differentiation of species, collecting and harvesting, quality evaluation, stability assessment, diagnosis of intoxication and discovery of lead compounds. Lack of chemical markers remains a major problem for

the quality control of herbal medicines. In many cases, we do not have sufficient chemical and pharmacological data of chemical markers. For example, temperature, light and solvents often cause degradation and/or transformation of purified components; isomers and conformations may also cause confusions of chemical markers.

The application of chemical markers has emerged as a pivotal strategy in the quality control of herbal drugs, addressing the longstanding challenges of variability, authenticity, and standardization in herbal formulations. Unlike synthetic drugs, herbal medicines are complex mixtures of multiple constituents, and their therapeutic efficacy often arises from synergistic interactions among various bioactive compounds.

By selecting appropriate chemical markers whether active constituents, major components, or characteristic phytochemicals researchers and industry professionals can effectively monitor the identity, purity, and potency of herbal products. Advanced analytical tools such as HPLC, LC-MS, and NMR have further enhanced the ability to detect and quantify these markers, making quality control more precise and reproducible.

However, the successful implementation of marker-based quality control also depends on thorough pharmacological validation, regulatory harmonization, and an understanding of traditional medicinal knowledge.

In summary, chemical markers are not just analytical tools but are integral to bridging traditional knowledge with modern quality assurance practices, thus ensuring that herbal drugs remain effective, safe, and trustworthy in contemporary healthcare systems.

12. **References:**

1. Kamble MA, Mane MR, Ingole AR, Dhabarde DM (2018) Standardization of some marketed herbal formulation used in diabetes. J Adv Res Pharmaceut Sci PharmacolInterven 2(1):22–26.
2. Shaheen N, Imam S, Abidi S, Sultan RA, Azhar I, Mahmood ZA (2018) Comparative pharmacognostic evaluation and standardization of Capsicum annuum L. (red chili). IJPSR 9(7):1000–1005.
3. Quality control method of herbal drug, published by world health organization 1998:56-59
4. Li S, Han Q, Qiao C, Song J, Lung Cheng C, Xu H. Chemical markers for the quality control of herbal medicines: an overview. Chin Med. 2008 Jun:12-21
5. Li, S., Han, Q., Qiao, C. et al. Chemical markers for the quality control of herbal medicines: an overview. Chin Med 2008 Jul:15-20
6. Chinese Pharmacopoeia Commission, Pharmacopoeia of the People's Republic of China. Vol. 1 Beijing: People's Medical Publishing House; 2005. p. 201.
7. Chemical marker compounds and their essential role in quality control of herbal medicines N.M.A Rasheed, K. Nagaiah, P.R. Goud and V.U.M. Sharma Organic Biomolecular Chemistry, Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500007, A.P., India Received for publication February 7, 2012; accepted March 30, 2012 Annals of Phytomedicine, an international journal p-302.
8. Wei XC, Cao B, Luo CH, Huang HZ, Tan P, Xu XR, Xu RC, Yang M, Zhang Y, Han L, Zhang DK. Recent advances of novel technologies for quality consistency assessment of natural herbal medicines and preparations. Chin Med. 2020 Jun 1;15-56.
9. Li S, Han Q, Qiao C, Song J, Lung Cheng C, Xu H. Chemical markers for the quality control of herbal medicines: an overview. Chin Med. 2008 Jun 28;3:7. doi: 10.1186/1749-8546-3-7.
10. Showkat Hussain Ganie, Priti Upadhyay, Sandip Das, Maheshwer Prasad Sharma, Authentication of medicinal plants DNA markers, Plant Gene, Volume 4, 2015, Pages 83-99.

11. Pharmacopoeia of The People's Republic of China 2010,published by republic govt.of China:p278.
12. WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues, Publications of the World Health Organization,2007:p-167-171
13. Chemical markers for the quality control of herbal medicines: An overview - Scientific Figure on ResearchGate: published on 2018:p-54-65
14. Liu, C., & Chen, S. (2010). Quality control of Chinese medicines: chemical marker as a criterion for quality assessment. Journal of Chromatography B, 812(1–2), 53–70.
15. Liang, Y. Z., Xie, P., & Chan, K. (2004). Quality control of herbal medicines. Journal of Chromatography B, 812(1–2), 53–70.
16. World Health Organization (WHO). (2007). WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues.
17. Mukherjee, P. K. (2002). Quality Control of Herbal Drugs: An Approach to Evaluation of Botanicals. Business Horizons Pharmaceutical Publishers.
18. Zhao, Z., Hu, Y., Liang, Z., & Yuen, J. P. (2006). Quality control of herbal medicines: challenges and solutions. Chin Med, 1, 7.
19. EMA (European Medicines Agency). (2017). Guideline on quality of herbal medicinal products/traditional herbal medicinal products.
20. Zhang, A., Sun, H., Wang, P., Han, Y., & Wang, X. (2013). Modern analytical techniques quality control of traditional Chinese medicines. Trends in Analytical Chemistry, 43, 63–75.
21. Xu, J., Xu, Y., & Shen, X. (2015). Strategies for chemical marker selection in quality control of traditional Chinese medicine. Frontiers of Medicine, 9(1), 1–7.
22. Zhang, W., Zhang, Y., Xu, H., & Wang, H. (2018). Role of chemical markers in standardization and quality control of herbal medicines. Phytomedicine, 50, 105–113.
23. Wagner, H. (2011). Synergy research: Approaching a new generation of phytopharmaceuticals. Fitoterapia, 82(1), 34–37.
24. Li, S., Han, Q., Qiao, C., Song, J., Cheng, C. L., & Xu, H. (2008). Chemical markers for the quality control of herbal medicines: an overview. Chin Med, 3, 7.
25. Xie, P., Chen, S., Liang, Y. Z., Wang, X., Tian, R., & Upton, R. (2006). Chromatographic fingerprint analysis—A rational approach for quality assessment of traditional Chinese herbal medicine. Journal of Chromatography A, 1112(1–2), 171–180.
26. Upton, R., Graff, A., Jolliffe, G., & Länger, R. (2003). American Herbal Pharmacopoeia: Botanical Pharmacognosy—Microscopic Characterization of Botanical Medicines. AHP.
27. Bhutani, K. K. (2003). Herbal medicines enigma and a challenge for science and guidelines for quality control. Indian Journal of Natural Products, 19(1), 3–10.
28. Fan, X. H., Cheng, Y. Y., Ye, Z. L., Lin, R. C., & Qian, Z. Z. (2006). Multiple chromatographic fingerprinting and its application to the quality control of herbal medicines. Analytica Chimica Acta, 555(2), 217–224.
29. EMEA. (2006). Guideline on the assessment of herbal medicinal products (EMEA/HMPC/32116/2005).
30. Liu, J., Wang, Y., & Lin, L. (2011). Chemical marker-based fingerprint analysis for quality control of herbal medicine. Analytical Letters, 44(11), 1934–1949.
31. WHO. (2011). Quality Control Methods for Herbal Materials. World Health Organization.
32. Aggarwal, B. B., & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases.

33. Amagase, H., & Milner, J. A. (1993). Impact of various sources of garlic and their constituents on 1,2-dimethylhydrazine-induced colon cancer in rats. Cancer Letters, 66(2), 123–129.
34. White, B. (2007). Ginger: An overview. American Family Physician, 75(11), 1689–1691.
35. Attele, A. S., Wu, J. A., & Yuan, C. S. (1999). Ginseng pharmacology: Multiple constituents and multiple actions. Biochemical Pharmacology, 58(11), 1685–1693.
36. Mishra, L. C., Singh, B. B., & Dagenais, S. (2000). Scientific basis for the therapeutic use of Withania somnifera (ashwagandha): A review. Alternative Medicine Review, 5(4), 334–346.
37. Prakash, P., & Gupta, N. (2005). Therapeutic uses of Ocimum sanctum Linn (tulsi) with a note on eugenol and its pharmacological actions: A short review. Indian Journal of Physiology and Pharmacology, 49(2), 125–131.
38. Asl, M. N., & Hosseinzadeh, H. (2008). Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 22(6), 709–724.
39. Rao, P. V., & Gan, S. H. (2014). Cinnamon: A multifaceted medicinal plant. Evidence-Based Complementary and Alternative Medicine, 2014.