

REVIEW

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# Quality control of the traditional herbs and herbal products: a review



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## Abstract

**Background:** Herbal medicinal material and product need is increasing, and with this increase in the need, it is very much an essential requirement to maintain the quality of them.

**Main body:** The quality of the herbals is altered by various physical, chemical, and geographical aspects which contribute to the quality of these materials. Apart from that, adulteration is also an increasing concern when it comes to herbal material quality. Various chemical and phytochemical test, analytical techniques, and hyphenated analytical techniques are used for determining the quality aspects of the herbal materials in the herbal pharmaceuticals.

**Conclusion:** These techniques can be used as quality control tool in assessing the quality of herbal materials and herbal pharmaceuticals.

**Keywords:** Quality, Herbals, Analytical technique

## Background

Quality is of prime concern to human beings in all aspects of life. When it comes to the quality of the pharmaceuticals which are consumed by humans, it is of utmost important as they are used for the wellbeing of the human kind. There are stringent guidelines and regulation for the quality control of the synthetically synthesized chemical pharmaceuticals. They have to undergo various series tests and quality control checks before being marketed and consumed by the patients and consumers. Due to this stringency in the regulations, the quality of the synthetically manufactured pharmaceuticals is maintained up to the mark which assures both safety and efficacy of the pharmaceutical products.

Herbal medicinal products are the ones which are obtained from the plant resources for the treatment and wellbeing of mankind. It is very much essential that even the quality of the herbal medicines is being controlled as that of the chemically synthesized medicines. 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 UV (ultraviolet) and IR (infrared) are mostly used for the qualitative aspects whereas HP-TLC (high-performance thin-layer chromatography), HP-LC (high-pressure/performance liquid chromatography), SFC (supercritical fluid chromatography), thermal analysis, ICP-MS (inductively coupled plasma-mass spectroscopy), LC-MS (liquid chromatography-mass spectroscopy), and

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GC-MS (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. Almost about 80% of the population is depending on the herbs for the treatment, cure, and prevention. So the different tools and techniques must be implied to verify and insure 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 pharmaceutical which is the challenging task and need of the hour in the pharmaceutical research and quality assurance.

## Main text

### Standardization of medicinal herbs and products

The phytochemical constituents present in herbal formulations vary with the variation in the climate, composition, and components of the soil and the region where grown; all these parameters contribute as the obstruction in the process of standardization. The gradual increase in the adulteration and also substitution of herbal drugs are due to the rise in deforestation area. This adulteration and substitution harms the safety and efficacy of the drug.

Adulteration, substitution, and lack of skilled personnel are the main reasons for unavailability of genuine herbal drugs. By use of advanced quality control technique and suitable standards, there is need to assure the quality of the medicinal herbal products. Identification, quality, and purity of herbs and herbal product confirmation are done by the means of standardization. Preliminary identification, physical properties, chemical properties, and biological properties together contribute to the purity of herbs. This purity defines the freshness as well as the quality of the herbal products.

Quality control of herbals is of greater importance for preservation of quality of the natural herbs and products. When the quality control aspect has identification of substance, adulterants, and substitutes; purity of material; and assay of active chemical constituent of greater importance of the particular herb, then they are called as pharmacopeial aspects of quality control. The process where the qualitative and quantitative values of herbs are measured against the prescribed or set standards and parameters is standardization.

Based on the different important evaluation parameters like organoleptic properties, ash values, moisture content, microbial contamination, and chromatographic and spectroscopic evaluations, the WHO for the standardization of herbal drugs with current and future trends has set guidelines for standardization methods and procedures [1–3].

Modern analytical techniques for the analysis of the herbal drugs are very much essential for global acceptance of Ayurveda and traditional herbs. Scientific basics of quality of the traditional herbs and ayurvedic products can be gained by complete and accurate pharmacognostical assessment. For the authentication and standardization the organoleptic tests, physicochemical studies and pharmacognostical scheme are at most needed [4]. For the prevention of the genuine herbal materials getting adulterated, the data reported from microscopic and macroscopic studies can serve as an added advantage for identification of adulterants and authentication of genuine herbs. Moreover for confirmation of parameters for the standardization and the identification of the secondary metabolites (alkaloids, tannins, glycosides, saponins, and flavonoids) will act as a useful tool [5–7].

In accordance with the process for formulation of standard setting of herbal drugs in the pharmacopeia and other standard texts, the microscopic investigation (qualitative and quantitative), macroscopic (shape and markings), identifications (adulterants and genuine drug), physicochemical parameters (moisture content, acid insoluble ash, water soluble ash), pharmacognostical scheme, and other parameters reported for the first time can play a role of significant tool for authentication of herbs in future studies [8–10].

### Thermal analysis for the characterization of herbs and herbal products

In verification of quality, purity and integrity of the herbals special techniques and strategies are applied due to the complex nature of the components of the herbals. Thermal stability of the samples, determination of the mass and enthalpy variation, high sensitivity, reproducibility and rapid response to the variation of results are the qualities of the thermal techniques like thermo gravimetric analysis (TGA) and differential thermal analysis (DTA) [11].

For the characterization of herbal extract and herbal drug products, thermal analysis can be used as an effective tool. Control of raw material quality, determination of purity, determination of thermal stability, compatibility of stability of substances, qualitative and quantitative drug analysis are important applications of the thermal methods. The reaction order ( $n$ ), activation energy ( $E_a$ ), frequency factor ( $A$ ), and degradation constant are the different parameters used in the characterization of the herbal extracts which can be evaluated and studied with the thermal techniques (like TGA and DTA). Further, the absolute water content, crystal water content, and thermal degradation can also be assessed by these thermal techniques [12, 13].

In thermal analysis, time and temperature functions are used as defining parameters. The temperature ranges from 25 to 1000 °C are used in the thermal analytical

procedures. Mass Signals are obtained during the heating processes of the analysis which reveal about the mass loss (mass lost in the thermal degradation process) in different defining steps (endothermic and exothermic) [14].

Determination of the variation in both iso-thermal and non-iso-thermal conditions contribute for the stability of aspects of the substances under the thermal analysis.

Interaction between the components of the drugs is studied by the interaction between the excipients and the active pharmaceutical ingredients (API) as the compatibility criteria by the means of TG, DTG (differential thermo gravimetric analysis), and differential scanning calorimetry (DSC) thermal analytical techniques. For the thermal behavior of polymers, TG and DSC are used as an evaluating tool for polymer and drug compatibility as pre-formulation study of the new formulations to be established [15].

The drugs are to be disposed after the thermal degradation is taken place, so prior to this disposal process, studies are conducted where in the behavioral patterns of the drug after and during the degradation process are studies so that the level of toxicity nature of the drugs and drug product can be analyzed which can help in accessing the process to be selected for disposing of such degraded drugs and drug product as the preventive measure to reduce the potential hazard caused by the disposed degraded substances to the environment.

Arrhenius equation is of utmost importance for calculations to be carried out from the data collected from thermal analysis,

$$\ln K = \ln A - E_a/RT \quad [\text{OR}] \quad k(T) = A.e^{-E_a/RT}$$

where  $A$  = frequency factor,

$K$  = rate constant,

$E_a$  = activation energy, and

$R$  = gas constant ( $8.314\text{Jk}^{-1}\text{mol}^{-1}$ )

When the value of the temperature component increases in the equation, the value of the exponential part reduces and in turn there is an increase in the value of  $k$ .

The minimum energy required for the thermal process is called activation energy. As the particle size of the sample plant material decreases there is increase in the surface area and instability of sample, so this increase in the surface area leads to the lowering of the activation energy for the thermal process. So as the particle size decreases the value of activation energy also decreases (Table 1) [12].

#### HP-TLC analytical technique for the herbal botanical formulation quality control

To establish the pharmacopeial standards of various herbal ayurvedic, Siddha as well as other medicinal herb formulations by the means of HPTLC fingerprinting profile as a major quality control aspect. By this, HPTLC means phytochemical components of the formulations can be disclosed and efficacy, safety, and quality can be assured [19, 20].

The efficiency and safety of the final herbal medicine is based on the quality and the profile of the components of the formulations. Difficulty or barriers in the way of quality control testing of the herbal formulations are due to the complexity and variation in the chemical components of herbal-based formulations or compositions. Modern analytical techniques like HPTLC are used to bypass the problems which are covering the way of quality control aspects of herbal formulations [21–23].

With the growing advances in science, HPTLC is becoming one of the prime options for the quality control of the herbal plants. HPTLC technique is used simultaneously in comparison with both reference and samples and can work as quality control tool apart from identification. Based on the recommendation of monographs,

**Table 1** Non iso-thermal/dynamic kinetic study and iso-thermal study in thermal analysis [16–18]

Non iso-thermal/dynamic kinetic study	Iso-thermal study
To obtain the thermo gravimetric curve, the heating rate is variable in non iso-thermal process/study.	In iso-thermal study/process, the heating rate is always kept same whereas the temperature of isotherms is varied and the estimation of decomposition time is carried out for the selected range.
When heating rate of the non iso-thermal process is increased the thermal curves as well as the fractional conversion move into the high temperature zones. The initial gasification temperature and the total gasification temperature when increasing the time taken for the gasification process reduces.	In iso-thermal process when temperature is increased, the gasification processes gets accelerated. The time which is required to reach the peak conversion is reduced as the gasification rate and gasification temperature is increased.
The Ozawa dynamic method is applied for studying the non iso-thermal process in thermal analysis. In this Ozawa dynamic model, different heating rates ( $\beta$ ) $^{\circ}\text{C min}^{-1}$ and the dynamic air atmosphere ( $50\text{ mL min}^{-1}$ ) is maintained and the sample was analyzed.	In the iso-thermal study, the sample is heated with the heating rate ( $\beta$ ) of $20^{\circ}\text{C min}^{-1}$ from room temperature till it reduces to $T_{\text{isotherm}} - 10^{\circ}\text{C}$ ; further, the sample is heated with heating rate ( $\beta$ ) of $2^{\circ}\text{C min}^{-1}$ from $T_{\text{isotherm}} - 10^{\circ}\text{C}$ to $T_{\text{isotherm}}$ , and finally the temperature is kept constant until the sample mass is reduced by at least 10% of the initial sample mass.
Activation energy is obtained by plotting $\log \beta$ vs $1/T$ further kinetic parameters frequency factor and reaction order can be obtained by implying Arrhenius equation $k(T) = A.e^{-E_a/RT}$	Activation energy is obtained by plotting $\ln T$ Vs $1/T$ at constant conversion level and calculations are carried out using Arrhenius equation $k(T) = A.e^{-E_a/RT}$ and reaction order and frequency factors are calculated.

various tests are carried out for the identification and quality control of the herbal plants and formulations. Peak profiles and their intensities are obtained from the HPTLC fingerprint images which give both qualitative and quantitative results in comparison with reference standards. Marker compound identification, percentage of purity, and minimum content information is also obtained by this technique of HPTLC [24–27].

For preliminary analysis for identification of adulteration and substitutes, pharmacognostic and phytochemical test and physicochemical properties act as the quantitative tests. For quantitative estimation of the phyto-constituents, HP-TLC technique is widely used due to the accuracy and simplicity of the technique. When samples are collected which differ in the area where they are grown and the climatic conditions, they are evaluated for different properties and phytochemical components. Apart from chromatograms and fingerprints digital images, visual detection is also possible even when the amount of samples and standards are prepared in microliter concentration. Simultaneous application of samples and standards on the same HP-TLC plate is possible and due to this property, it becomes easier during the comparative studies of herbal drugs and formulations [28–31].

#### **HP-LC analytical technique for analysis of botanical formulations for the quality control**

In the discovery domain, the identification (quantitative and qualitative) of active compounds from the herbal extract is the most difficult and challenging task. In modern discovery, the processes like isolation with preparative bio-activity do not match the pace as they are slow and tedious, whereas modern systems prefer for easy, accurate, and fast processes to be utilized. Traditional techniques, which use multiple isolations, can lead to decrease or completely vanishing of the activity of the active compound. So to overcome the drawbacks, profiling of compounds with HPLC analytical technique is done in modern discovery to identify the multiple compounds accurately due to versatility of the analytical technique [32–34].

For the quality assurance, herbs and traditional medicinal products obtained from the extract of plants can be estimated for the chemical components with HPLC technique. In the identification of chemical phyto-constituents in herbal medicine products, the standardization technique with the marker profile is of greater benefit as the quantifications of the multiple constituents from the herbal medicinal formulations have issues related to safety and efficacy of the active essentials.

Separation of the components from traditional poly-herbal medicinal formulations HPLC serves as one of the

convincing analytical technique as it has been gaining importance for qualification, quantification, and authentication aspects in the quality control of herbs.

Further harvesting season, drying techniques, plant origin, presence of heavy metals, and microbial contents are the major reasons which vary the quality of the herbs and come in the way of quality control of herbs [35–37].

In the estimation of presence of active chemical and biological markers in the complex traditional herbal products, HPLC can be used as a beneficial tool for standardization with both quantitative and qualitative estimation. For the analysis of the thermo-labile substance present in the traditional herbal formulations, one of the prime options of analysis is HPLC technique with advancement of isocratic and gradient elution. Analysis of poly-component medicinal herbal products is also possible as well as effective with RP-HPLC (reverse phase-high-performance liquid chromatography). The technique of HPLC and RP-HPLC serves high reproducibility and ease of automation in the identification of multiple constituents of botanical preparations.

The liquid-liquid partitioning, solid-extraction, preparative liquid chromatography, and thin-layer chromatographic fractionation are the sampling techniques used to reduce the complexity of the matrix effect. Due to the complexity of the matrix the co-elution of the peaks of the multi-components of the herbal marker compound takes place during the HPLC analysis process of that particular compound under analysis [38].

#### **Supercritical fluid chromatography (SFC) as a tool for quality control of herbs**

The growing hazardous effect of the synthetic chemicals and organic solvents on the environment has developed need for the focus towards the green chemistry principles with increase in number of methods and processes which comply with the same. To acquire the principle analytes from the compounds even when different matrices are being used, supercritical fluid chromatography technique is used as an alternative for conventional organic solvent methods (like HPLC) [39].

In supercritical fluid chromatography method, compressed carbon dioxide (CO<sub>2</sub>) with small part of organic solvents (like methanol) are together used as the mobile phase, where major part is of carbon dioxide and minor is organic solvent; due to this ratio, the supercritical fluid chromatography (SFC) method is named as an alternative chromatography.

SFC method is an eco-friendly method as it utilizes very less quantity of organic solvents and the low viscosity of mobile phase as the pressure drop is less when compared with liquid chromatographic techniques [40]. The organic solvents being used are to be stored properly with proper precautions as they are highly

flammable in nature and hence utmost care must be taken for prevention of dangerous accidents causing fire and explosions. The high purchase price and disposal of organic also adds up to the disadvantage of the organic solvents [41].

Lipid, flavonoid, phenolic, alkaloids, saponins, carbohydrates, and analysis of wide variety of analytes can be carried out with the SFC technique. The fat-soluble vitamin analysis is gaining more importance.

Fast analysis in comparison with HPLC and GC technique SFC analysis uses significant shorter period of time and low amount of solvents and is eco-friendly which are the most important characteristics of the SFC technique. A broad multi-residue method can be carried out with the SFC technique as it analyses both polar and non-polar compounds with very high sensitivity. In the analytical SFC method, development has rapid equilibrium of volume as well as enhanced hydrophobic component (molecule) elutions. As water is absent in the system, this serves as an advantage for the SFC technique for the residues from ionization point.

SFC is also been noted as an unconventional method of sample preparation. It also finds application in large scale industries due to selective techniques and environment-friendly method. The integrity and quality of the analytical material is maintained prior to analysis due to absence of oxygen (no oxidation process), absence of light (no photolysis), and low temperature (no temperature dependent degradation) in the working environment of the SFC technique which also adds up to the advantages [42, 43].

#### **ICP-MS (inductively coupled plasma-mass spectroscopy)**

Elemental composition present in medicinal plants play crucial role in the biological system of living organisms the medicinal herbs can serve as an essential part in providing trace elements to humans in their diet. Medicinal plants during the process of cultivation get easily contaminated and therefore there must be well-defined limits of elemental composition decided for medicinal plants. The ability of element accumulation of plant and the geochemical nature of the soil are responsible for the level of presence of the elements in the medicinal plants. These medicinal plants are the connecting link between the living beings and trace elements. Natural origin of the medicinal herbals cannot assure the quality and safety as the quality dilutions take place due to industrialization, fertilizer, agricultural pesticides, pollutants, storage, and marketing process.

Ionic and non-ionic are the two forms in which the trace elements are available in plants. And these ionic and non-ionic forms are responsible for toxicity and level of bioavailability in living organisms. Chromium (Cr), copper (Cu), cobalt (Co), ferrous (Fe), and zinc

(Zn) are the metals which when consumed in excess amounts lead to toxicity, whereas cadmium (Cd), lead (Pb), and mercury (Hg) are toxic elements even when consumed in low concentrations [44].

The elemental content associated with active chemical compound of the medicinal plant adds up both benefits and hazardous effects to the herbal product. The concentration of elemental content differs with the different geographical variation, and its most influencing factors are rainfall, type of soil and its pH, and temperature. So the environmental geographical condition in which the medicinal herbs are grown plays a crucial role and is to be taken in consideration. ICP-MS (inductively coupled plasma-mass spectroscopy) and PIXE (partial induced X-ray emission) are the methods being used for analytical and chemo-metric studies on herbs. These methods are useful to gain information about the relation between the medicinal plant elemental content and their effect on particular disease treatment [45].

For quality and safety of the herbal products, heavy metal testing is of the crucial concern. Elemental specificity, multi-isotope detection, high sensitivity, dynamic range, and possibility of extremely low detection limit are the advances provided by the ICP-MS analytical technique used for trace and ultra-trace element concentration detections [46].

Medicinal plants that undergo the elemental content analysis can be used as an alternative over the synthetically fortified drugs when we get a clear picture of the elemental composition of the medicinal herbs; hence, this medicinal herb can be used to overcome the trace metal deficiencies as well as no side effect of the chemically metal fortified synthetic products [47].

Disorders related to brain, digestive, kidney, liver, pancreas, reproductive system, and central nervous systems are caused when the elemental components go on accumulating in the living human body. Further, this can lead to various cancer cells developing if the exposure is high and repetitive. So it is very much required to analyze the limit of elemental content and composition in the medicinal herbal products [48].

#### **LC-MS for the quality control of botanical herbs**

When HPLC method is used individually without other method in combination, it has certain drawbacks in the raw material extract in complex matrix analysis where prior treatment for the API concentration and purification is needed for the process to be simplified and give better results. This drawback is overcome by using the mass spectroscopy (MS)-coupled HPLC technique that is LC-MS (liquid chromatography-mass spectroscopy), in which the technique highly improves the sensitivity of detection. For the method simplification of LC-MS-ion trap mass spectroscopy (Ion trap LC-MS), quadrupole

time of flight high-resolution mass spectroscopy (Q-TOF HRMS) and triple-quadrupole mass spectroscopy (TQ LC-MS) are the different technique which can be coupled with the HPLC analytical method [49].

Structure characterization, molecular mass, information of fragmentation, retention time, and broad range of detection and high separation of analytical compounds are the abilities of the LC-MS technique. Raw plant material extract and marketed product identification, quantification, and quality control of the herbs can be carried out with LC-MS combined technique [50].

Complete documentation of the data necessary for the online qualitative analysis of the herbal extract can be acquired by performing LC fingerprinting process. The hyphenated LC-MS technique is employed where the structure elucidation of chemical components of the herbal extract is not possible individually with the HPLC analytical method. Identification of chromatographic peaks and the comparison study online is possible by use of the LC-MS technique.

Further, the detection of the adulterants in the extracts and botanical products and phytochemical analysis of the herbs has become easier due to the advantageous LC-MS technique which is applied for the process. The separation process as well as the identification process of the various compounds which are structurally similar can be identified; this serves as one of the most superior qualitative tool among the various tools for the analysis of different herbs and the adulterants. With the advances of the LC-MS technique, the screening and characterization of the adulterants (unknown and known) which are novel analog can also be detected and identified by applying this technique in the quality control of the materials [51].

For the analysis of the complex traditional herbals with high resolution, efficiency and sensitivity which is used to gain accurate mass information are all present in the powerful tool for analysis which is UHPLC-Q-TOF/MS (ultra-high-performance liquid chromatogram coupled with electrospray ionization tandem quadrupole-time of flight/mass spectroscopy). For the potential analysis of components of the chemical markers, the multivariate statistical analysis which are basically dependent on the available chemical information which makes the identification of the components much simpler. This UHPLC is one of the advance types in the LC-MS analytical technique [52].

#### **GC-MS (gas chromatography-mass spectroscopy) in the quality control analysis of herbs**

GC-MS (gas chromatography-mass spectroscopy) is the analytical technique which is the combination of GC (gas chromatography) which separates the different components of the mixtures of the chemical

compounds whereas the MS (mass spectroscopy) which analyses the components which are being separated by the GC. In case of the herbal product analysis, the extract can be analyzed for the principle component by the GC-MS technique. GC-MS can also be used in the pharmaceutical industries, cosmetic products, food industry, and environmental and forensic application for the analysis of the components of the compound basically the active pharmaceutical ingredients.

The most important analysis which is carried out by GC-MS is the analysis of the thermo-stable volatile compounds and the volatile derivatives. Qualitative and quantitative analysis of the volatile oil determination is carried out by the GC-MS technique; it is also possible to determine the multiple components of the compound and drug metabolites. LC-MS is comparatively more sensitive than the GC-MS but LC-MS cannot analyze the thermally stable volatile components whereas it is only able to analyze the thermally unstable non-volatile compounds.

Identification of components (qualitative), separation of components, and quantification of different compounds are both volatile and non-volatile in a single analysis. It is possible to carry out the simultaneous analysis of different compounds [53–55].

In the field of the forensic science the GC-MS technique pre-treatment process is being used which is extremely simple when compared to the conventional pre-treatment process that is less complex in nature; this process is called as headspace solid-phase microextraction (HS-SPME) and together with GC-MS it is said to be HS-SPME-GC/MS. Different detection techniques are used in coupling with the GC-MS techniques that are electron capture detection (ECD) and electron ionization (EI) with single quadrupole MS and/or triple quadrupole MS (MS-MS) [56, 57].

Matrix-matched calibration standards are used in the gas chromatography to compensate for the matrix effect in this technique and this is one of the simple most and cheap technique. The GC-MS/MS technique performance is affected by the extract purity which is under analysis and is injected to the system, as the biochemical range of the herbs is wide in range and the nature of the herb is also complicated.

The GC-MS technique is not suitable for the thermo-labile compounds. In case of the non-volatile components, they must be derivatized and then the analysis must be carried out [58, 59].

#### **Comparison of HPLC, HP-TLC, and GC**

The comparison of chromatographic techniques is shown in Table 2.

**Table 2** Comparison of chromatographic techniques [60–62]

Parameters	HPLC	HP-TLC	GC
Stationary phase	Column	Paper/glass	Liquid/solid
Mobile phase	Solvent mixture	Solvent mixtures	Pure inert gas
Sample	One at one run	Many at a single run	One at one run
Pressure	High	—	Controlled pressure
System	Closed	Open	Closed
Results	System (peaks)	System peaks and visual by bands	System (peaks)
Resolution	High to very high	Moderate to high	High to very high
Time	2–60 min	1–30 min	2–60 min
Temperature	Constant	Constant	Increasing

## Conclusion

In the case of the herbal products which are part of traditional medicine system, the novel formulations developed are required to be standardized for safety, efficacy, and potency. It is required that the various techniques are used for the quality control examination of the herbs, which can be regulated to gain the required quality products by setting proper norms. And this in turn will provide the safer use and effective treatment and required potency of the products which will benefit mankind and society by providing means of wellbeing.

## Abbreviations

A: Frequency factor; API: Active pharmaceutical ingredient; DSC: Differential scanning calorimetry; DTA: Differential thermal analysis; DTG: Differential thermo gravimetric analysis; Ea: Activation energy; ECD: Electron capture detection; GC-MS: Gas chromatography-mass spectroscopy; HP-LC: High-pressure/performance liquid chromatography; HP-TLC: High-performance thin-layer chromatography; HS-SPME: Headspace solid-phase micro extraction; ICP-MS: Inductively coupled plasma-mass spectroscopy; IR: Infrared; K: Rate constant; LC-MS: Liquid chromatography-mass spectroscopy; PIXE: Partial induced X-ray emission; Q-TOF HRMS: Quadrupole-time of flight high-resolution mass spectroscopy; R: Gas constant ( $8.314 \text{ J K}^{-1} \text{ mol}^{-1}$ ); RP-HPLC: Reverse phase-high-performance liquid chromatography; SFC: Supercritical fluid chromatography; TA: Thermal analysis; TGA: Thermo gravimetric analysis; TQ LC-MS: Triple-quadrupole mass spectroscopy; UHPLC-Q-TOF/MS: Ultra-high-performance liquid chromatogram coupled with electrospray ionization tandem quadrupole-time of flight/mass spectroscopy; UV: Ultraviolet; WHO: World Health Organization

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## Authors' contributions

AB has done data collection and major contributor in review manuscript writing. VM has designed the concept, corrections, and drafting of the manuscript. All the authors have read and approved the manuscript.

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Not applicable

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## Competing interests

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