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NEAR INFRA-RED SPECTROSCOPY FOR QUALITY ASSESSMENT OF INDIAN TRADITIONAL HERBAL MEDICINES: A REVIEW

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ABSTRACT: Herbal Medicines (HM) and their preparations have been widely used for hundreds of years all over the world. However, they have not been officially recognized due to lack of adequate or accepted research methodology for their evaluation. Traditional systems of Indian Herbal medicine include Ayurveda, Yoga, Naturopathy, Unani and Siddha. Among them Ayurveda, Siddha and Unani systems (ASU) use plants, minerals and animal products as main drugs to cure various ailments. The quality and safety of these herbal products has now become a serious issue due to increasing pollution in air, water, soil, etc. Pharmacognostical analysis of medicinal herbs remains challenging issues for analytical chemists, as herbs are a complicated system of mixtures. This review emphasizes the significance of NIR methods in the discrimination of much herbal medicine from closely related species and from adulterants. The quality of samples from different localities and growing conditions based on their geographical origin may vary. Thus, the identification of crude herbs based on geographical origins is crucial in order to ensure authenticity, quality, safety and efficacy of the raw material before it is converted to the final product. Herbal product manufacturer always seeking for a faster and cost effective verification method since the traditional wet chemistry analysis are too laborious and time consuming. Discrimination according to geographical origin and localities, processing methods, DNA profiling and metabolomics were efficiently investigated. This paper will discuss about the various common and sophisticated techniques used for quality assessment of Indian traditional herbal medicine.

INTRODUCTION: The traditional systems of medicine have become significantly more popular all over the globe because of the curative property, less toxic and minimal side effects. It is more widely used for the human ailments from time immemorial. It has been estimated that 70-80% of world's population relies on traditional healthcare. The mode of preparation and plant used in traditional medicine varies from place to place. Among the characteristics of herbal medicine preparations, is that they are all presented either as single herbs or as a combination of several herbs in composite formulae, and extracted with boiling water during the decoction process. As pointed out in the 'General Guidelines for Methodologies on Research and Evaluation of Traditional Medicines', that despite the existence and continued use of Traditional herbal medicine over many centuries,

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and its popularity and extensive use during the past decade, traditional medicine has not been officially recognized in most countries. The quantity and quality of the safety and efficacy data on traditional medicine are far from sufficient to meet the criteria needed to support its use world-wide. The reasons for the lack of research data are due to not only to health care policies, but also to a lack of adequate or accepted research methodology for evaluating traditional medicine.

In general, one or two markers or pharmacologically active components in herbs and/or herbal mixtures have been used for evaluating the quality and authenticity of herbal medicines, both in the identification and quantization of single herbs and in multi component preparations. This kind of assessment, however, does not provide a complete picture of the herbal preparations, because multiple constituents may be responsible for its therapeutic effects. These multiple constituents may work 'synergistically' and are difficult if not impossible to separate into active parts. Moreover, the chemical constituents in component herbs may vary depending on harvest season, habitat, drying processes and many other factors.

Thus, it seems necessary to determine a profile of the phytochemical constituents of herbal products in order to ensure the reliability and repeatability of pharmacological and clinical research, to understand their bioactivities and possible side effects and to enhance product quality control. Several chromatographic techniques [1, 2, 3] (High Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), Capillary Electrophoresis (CE) and thin layer chromatography (TLC)) can be applied for this kind of herbal profiling.

Although it is possible to visually differentiate the different extract chromatograms, the process is still usually subjective and non-quantitative. In addition, minor differences between very closely related species might be missed [4]. These drawbacks are taken into account by multivariate analysis. The use of NIR was recently investigated for controlling *e.g.* the origin of the drug and quantifying its active or marker substances. It proved to be a very reliable tool compared to traditional methods of analysis.

NIR could be more widely used to monitor the complete manufacturing process of the herbal product, *i.e.* from authentication of the plants to the quantification of active compounds in the final dosage form. The chemical pattern recognition methods, such as Principal Component Analysis (PCA) and Soft Independent Modeling of Class Analogy (SIMCA), etc., are now greatly appreciated for providing reasonable characterization of traditional herbal medicines. The objective of this review is to present a concise overview of the recent applications of NIRS in quality evaluation of traditional herbal medicine.

Fundamental Principle of Near Infrared Spectroscopy: The NIR region is situated between the visible and the IR region of the electromagnetic spectrum [5] and ranges from approximately780 nm to 2500 nm, corresponding to a frequency range of 4000 cm^{-1} to12 800 cm^{-1}. The most common group frequencies seen in the NIR region are OH, CH, NH, and SH overtones. Overtone and combination transitions are much less likely than the fundamental transitions. This explains why the intensities of the generally broadly overlapping NIR bands are weaker than the intensities of the fundamental IR bands, by a factor of 10 to 1000.

Among the merits of NIR spectroscopy, the following are most important:

- Measurements are rapid and simple, and they can be conducted without special, or minimal, sample preparation.
- Spectra carry information regarding not only chemical, but also physical phenomena, making NIR spectroscopy very informative.
- Depending on the samples and problem under consideration, acquisition of spectra may be conducted in transmittance, reflectance or diffuse reflectance mode.
- NIR spectra can often be obtained through blisters or ampoules without opening them; acceptable materials are glass and plastics, but metal foil is unacceptable.

- Measurements can be performed using an integrating sphere as well as a fiber-optic probe, so testing can be performed not only in a laboratory but also on site.

NIRS coupled with spectra pretreatment methods (derivates, smoothing, normalization etc.) multivariate methods [6, 7], Principal Component Analysis (PCA), Partial Least Squares, Multiple Linear Regression (MLR), Partial Component Regression (PCR) has been successfully used for the simultaneous analysis of chemical and physical parameters in agriculture, pharmaceutical and material analysis. The commonly applied methods in quality evaluation of medicinal herb, such as Similar Analysis (SA), Principle Component Analysis (PCA), Cluster Analysis (CA), Discriminate Analysis (DA) and pattern recognition. These methods play a vital role in the discrimination and classification of medicinal herb [8]. Measurement is robust and cheap. Analysis can be carried out off-line, on-line or in-line. NIRS is highly suitable for automation and high throughput screening is guaranteed and measurements do not require special trained staff.

NIR Spectrophotometers: The essential features of NIR spectrophotometers are: a source of radiation, an operating contrivance and a detector. The NIR source produces radiation spanning a large or a narrow range of frequencies in the NIR region. They can be thermal or non-thermal sources. Thermal sources consist of an incandescent filament producing thermal radiation. Non - thermal sources usually consist of Light Emitting diodes (LED), laser diodes, or lasers that emit much narrower bands of radiation than thermal sources.

NIR spectrophotometer can be divided into three groups, those with one source and one detector, those with several sources and one detector, and those with several detectors. One of the main parts of the operating contrivance is the wavelength selection device. However, single detector instruments are normally used. Concerning detector technology, silicon.based photodetectors are recommended for the short wavelength infrared range (700-1000 nm or 14286-10000 cm^{-1}). For lower energies and longer wavelengths (1100-2500 nm or 9090-4000 cm^{-1}), semiconductors such as lead sulphide (PbS), indium gallium arsenide (InGaAs) or indium arsenide (InAs) can be used as detectors.

Use of Chemometrics: Chemometrics is a chemical discipline that utilizes mathematics and statistics to design optimal measurement procedures and experiments and to provide maximum relevant chemical information by analyzing chemical data. Traditional applications of chemometrics often involve data preprocessing for enhancing analytical measurements to obtain chemically or physically relevant information from the sample and to reduce the irrelevant variability that arises from the effect of instrument changes over time or physical phenomena, such as temperature, or scattering. Chemometrics are basically classified into two main categories; pattern recognition methods (unsupervised and supervised) when a qualitative evaluation is considered and multivariate calibration for quantitative purposes. Practical steps[9] in chemometrics analysis include design of experiment, data preprocessing, classification and calibration.

Experimental design initially involves the screening of factors important for the success of a process. This is followed by the selection and implementation of the optimized conditions under which the process will be carried out, hence saving time, and this is the main motivation for the experimental design. Data preprocessing techniques are applied in order to eliminate or reduce unwanted sources of variations due to instrumental responses from modern analytical techniques and to obtain more efficient data from which meaningful information can be extracted.

Commonly applied preprocessing techniques include centering and normalization. Other methods of mathematical pretreatments include standard normal variate (SNV) transformation, multiplicative scatter correction (MSC), and first and second derivatives [10].

Chromatographic fingerprint, associated with chemometrics, is typically used to evaluate the quality of medicinal herb by extracting useful information and supplying various methods of data processing.

Before analyzing the fingerprint, the pretreatment is essential for overlapped peaks and shifted baseline caused by the unknown components and unclear interferences. Chemometric methods are used to compare data among herbs with hundreds or even thousands of chemical components. This information can be further used to identify the origins of herbs, or to authenticate herbs. For example, research has made significant progress since the introduction of the similarity index and pattern recognition analysis. Information fusion and determination of relative entropy critical value were proposed for the similarity analysis of fingerprints of herbal medicines [11].

Chemometrics is a breakthrough for the software subjectivities development of analysis apparatus in the twenty-first century. It promotes equipment intellectualization and offers new ideas and methods for the construction of new and high-dimensional equipment. Furthermore, with the rapid development of the microcomputer (that is, establishment and retrieval of chemical spectrum library), the analysis of high-dimensional data, artificial neural networks, research of artificial intelligence of chemistry, and expert systems has made great progress. With the development of analytical chemistry, chemometrics is also being developed vigorously [12, 13].

Chromatography and Chemical Fingerprints of Herbal Medicines: In general, the methods for quality control of herbal medicines involve sensory inspection (macroscopic and microscopic examinations) and analytical inspection using instrumental techniques such as thin layer chromatography, HPLC, GC–MS, LC–MS, near infrared (NIR), and spectrophotometer, etc. [14]. On the other hand, the methods of extraction and sample preparation are also of great importance in preparing good fingerprints of herbal medicines.

As a single herbal medicine may contain a great many natural constituents, and a combination of several herbs might give rise to interactions with hundreds of natural constituents during the preparation of extracts, the fingerprints produced by the chromatographic instruments, which may present a relatively good integral representation of various chemical components of herbal medicines.

Chromatographic fingerprint / NIR signatures associated with chemometrics, is typically used to evaluate the quality of medicinal plants by extracting useful information and supplying various methods of data processing. Its analysis has made great progress Computer-based software, SPSS, supports pretreatment methods such as background and retention time correction, peak alignment, identification and matching, translating processed data into information accessible for objective analysis, and can also simultaneously evaluate many different samples.

Classification and Discrimination methods: In order to test the robustness of this study for classification and discrimination of geographical origin and varieties from herbal samples [15, 16], following classification method was used to assign unknown samples to its existing classes. There are five steps involved to obtain the classification model:

(1) Construction of separate PCA models for each class

(2) Determine the optimal number of pcs by validation

(3) Fitting the unknown samples to each predefined model, provided that the class are distinct enough

(4) Deciding whether the samples belong to the corresponding class by referring to the object-to-model distance and leverage (distance of the sample to the model center) and finally

(5) Validate the classification results with statistical test called significance test.

Principal Component Analysis (PCA) and Cluster Analysis (CA): PCA is the most commonly used method applied in the analysis of the spectra and other data sets for exploratory data analysis. It reflects the original measurement by discovering the dominant factors while excluding the relevant interference factors, thereby allowing a more accurate estimate. PCA algorithms were used in this study for reducing the high-dimensional spectroscopic data by constructing a linear

combination of the original variable into a few orthogonal principle components which contain most of the variability of the data set. This projection method allows

(a) Visualization of the natural clustering in the data,

(b) Primary evaluation of the between-class similarity and finally

(c) Finding the reasons behind the observed pattern by making correlation with the chemical or physico-chemical properties of the studied samples.

CA classifies objects based on quantitative characteristics. Generally, the different clustering techniques are divided into two subtypes: hierarchical and nonhierarchical (example, fuzzy clustering). In the quality evaluation of medicinal plants/ herbal medicine, the most popular clustering technique is hierarchical clustering analysis (HCA). The main advantage of hierarchical cluster analysis is the flexibility to alter the similarity measurement criterion and the applied linkage method to suit different applications. Fingerprint based PCA can directly reflect the difference between samples, whereas CA can classify objects based on their quantitative characteristics [17]. A combination of CA and PCA has been widely used in current quality assessment of medicinal plants.

Pattern Recognition: Pattern recognition unlike SA, PCA and HA uses discrete information on the samples in the calibration set. It can establish identification model by analyzing data, find out regular law, obtain accurate analysis of components in the spectra of herbal medicine/ medicinal plants and provide a comprehensive evaluation of their quality .Over the years, pattern recognition methods have been intensively used for the classification of samples. The pretreated data acquired from both HPLC fingerprints and HPTLC fluorescent images [18] were processed by chemometrics for similarity and pattern recognition, including Artificial Neural Networks (ANNs), k-nearest neighbor (k-NN) and an expert's panel. Among these, k- NN classifier was apparent that exhibited good performance with sufficient flexibility for processing HPTLC fingerprint images which were otherwise not easily dealt with by other algorithms due to the shift of Rf values and varying hue/saturation of the band colors between different TLC plates. The results indicated that these two chromatographic fingerprint methods can be considered complementary measure of quality control of herbal medicine [19].

Exploratory Data Analysis: In exploratory data analysis (EDA), the user aims to find patterns in the data that could not be derived from a priori available knowledge of the data. Several tools for exploring the data are available. Principal component analysis (PCA), factor analysis (FA) and projection pursuit (PP) are variable reduction techniques defining a number of latent variables by making linear combinations of the original variables following a given criterion. For all methods, the projections of the 'n' objects from the original data space on a latent variable are called the scores on this latent variable. They provide information on the (dis)similarity of the objects. The contribution of each original variable to the score is reflected by its loading, which detects the variables responsible for clustering in the data. The numerical value of a loading for a given variable on a PC shows how much that variable has in common with that component is a valuable alternative to ordinary PCA as an exploratory tool as it has many advantages such as: flexibility; the possibility to differentiate between signal and baseline; and all results are always on the original scale of the data [20].

Unsupervised Pattern Recognition: Unsupervised pattern recognition differs from exploratory data analysis in that the aim of the methods is to detect similarities, whereas using EDA there is no particular prejudice as to whether or how many groups will be found. It uses a number of methods, primarily cluster analysis, to group different samples (or objects) using chemical measurements. The first step is to determine the similarity between objects. The most common and easiest tool to apply is similarity analysis (SA), which is based on the correlation coefficients 'r'. This is implemented using reference fingerprints of standardized extracts, but unfortunately they are rarely available. Alternatively, the mean or median fingerprint of the data set is usually taken.

In addition to similarity analysis based on the entire fingerprint relative retention time (RTT) and relative peak area (RPA) of characteristic peaks also can be used.

This may appear a rather subjective approach as the fingerprint is dependent on the composition and size of the data set, which may influence the outcome. Another concern is the high contribution to the similarity value for the major peaks, thus masking differences in the smaller peaks. Despite the drawbacks, similarity analysis is a fast and easy-to-use technique useful for a preliminary analysis of a data set [21]. The next step is to link the objects. The most common approach is called hierarchical cluster analysis (HCA). Hierarchical clustering techniques are based on the creation of branched structures, called dendrograms, which are qualitative in nature and permit visualisation of clusters and correlations amongst samples.

Hierarchical cluster analysis utilizes two major strategies for comparing samples. In the agglomerative strategy, each observation starts in its own individual cluster and merges with others while moving up in the hierarchy, whereas the divisive strategy starts with all samples in one cluster, which is split while moving down the hierarchy. In order to decide when clusters should be merged or split, a measure of (dis)similarity between the samples is required as well as a linkage criterion specifying the (dis)similarity between the clusters. The main objective of HCA is to display data in natural clusters showing patterns in two-dimensional space.

Supervised Pattern Recognition: In general, supervised techniques make use of calibration or training sets with a priori known information to build a classification model. The model is then tested using an independent sample set with a priori known information to validate the predictive properties of the model before using it on unknown samples. Supervised pattern recognition methods have been used intensively for the classification of data sets. The most popular techniques for the classification of herbal products include Linear Discriminant Analysis (LDA), k-Nearest Nei9ghbour (k-NN), Soft Independent Modeling of Class Analogy (SIMCA), Artificial Neural Network (ANN), Partial L east Squares–Discriminant Analysis (PLSDA) and Orthogonal Projections to Latent Structures–Discriminant Analysis (OPLS-DA).

Artificial neural networks are a powerful data-modelling tool to capture and represent complex relationships between inputs and outputs. The ANN is a supervised method of data analysis, which is particularly effective for modelling non-linear systems, and includes three interactive parts: input, data processing and output layers. The parameters required for an ANN model optimisation include a number of neurons in the middle layer, scale functions, learning rate factor, momentum factors and initial weights. There are many varieties of artificial neural network methods, among which, back-propagation ANN (BP-ANN) is the most classic feed-forward multilayer network [22].

Multivariate calibration: In multivariate calibration, a quantitative model is developed for the reliable prediction of a property of interest (y) such as total flavonoid content, anti-oxidant activity, etc., from a number of predictor variables (x1, x2) regarded as chromatographic or spectroscopic scan points. This model should describe the measured x and y data of the calibration set adequately for future application in predicting their value for this property on future samples. Regularly applied methods are the linear multivariate calibration techniques such as stepwise multiple linear regression (Step-MLR), principal component regression (PCR), partial least squares (PLS), partial robust M-regression (PRM), uninformative variable elimination PLS (UVE-PLS), uninformative variable elimination genetic algorithm PLS (UVE-GA-PLS) and orthogonal projections to latent structures [23].

PLS is a widely used technique with great predictive power, but the interpretation of the model's regression coefficients (if needed) might be complicated for complex biological samples due to the modeling of small orthogonal variations in the data matrix X. In O-PLS these orthogonal variations are removed from the data matrix prior to building a one-component PLS model. This is done by subtracting PLS components, orthogonal to y, from the original X data. The optimal number

of O-PLS components to be subtracted is determined by cross-validation. The main advantages of O-PLS are improved interpretability, because of the separation of the correlated and non-correlated variations, and the construction of simpler predictive models. The Partial Robust M-regression (PRM) method is a robust version of the partial least squares approach. The aim of this method is to construct a robust calibration model that well describes the trend represented by the majority of the data. In PRM this is achieved by introducing continuous weights for the data objects so that their possible negative influence on the regression coefficients is diminished. A major advantage of the PRM model is that outlier detection is not required before model construction.

Quality evaluation of herbal medicine: After introducing the basic concepts of NIR, chemometrics and classification methods and the commonly applied methods in handling procedure of data generated from NIRS, the application of NIRS as shown in **Fig. 1** & chemometrics in quality evaluation by herbal medicine in the field of control of raw material, taxonomic discrimination, authenticity, efficacy, consistency, **Geographic origins** [24] and safety evaluation of medicinal herbs are discussed in the following sections.

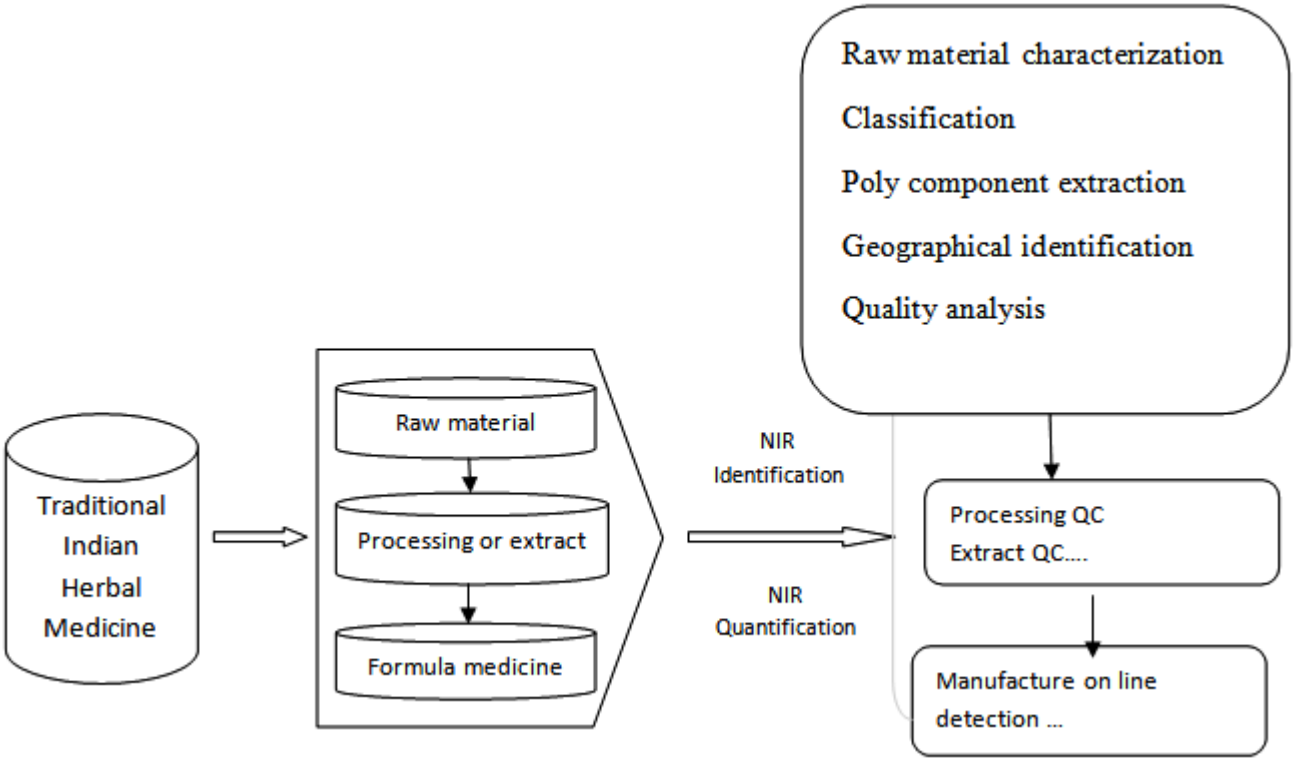

FIG. 1: FLOW DIAGRAM IF NIRS APPLICATIONS IN HERBAL MEDICINE

Control of Raw materials: NIRs have been widely used for authentication and quantification of raw materials and it also used for process quality control and or extraction monitoring[25]. Not only for single raw material, but also for complex formulas are current trends of investigation. NIRS is used not only for monitoring the secondary metabolites, but also used for determining additional parameters like fiber content, moisture etc., Compared to Chromatography no sample destruction is required for NIRS. Information can be gathered from the intact entire piece of samples. This makes NIRS preferred tool for pattern recognition of raw materials applied to classify materials into species & geographical origin, identify multi-originated raw material and quality control of quantitative analysis of ingredients [26, 27, 28].

Taxonomic discrimination: Infra-red has been applied in many studies for the analysis of different herbs and plants containing essential oils, taking GC-MS as a reference method. Applications include: the classification of different basil chemo

types utilizing PLS regression and discrimination of basil, chamomile, thyme and oregano [29]. In all the previous studies, high correlations between vibration spectroscopic data and GC reference values for the most relevant components was observed, which confirmed the utility of IR for rapid evaluation of the most important volatile substances directly in the drug as a useful alternative for the usually applied chromatography techniques.

Authenticity: Ascertaining authenticity is the first important step to assess the quality of plant medicine. Each medicinal plant contains certain characteristic constituents. Therefore, constituents including their respective chemical ratios can be analyzed to identify medicinal plants and distinguish the fakes among the identical medicinal plants. Furthermore, not only can authenticity be identified but substitutes can also be searched according to the theory that "herbs containing the same properties have similar potency" [30, 31]. For instance, comparing fingerprints of species under the monograph, and the nonofficial species by similarity analysis, one can investigate the possibility of using these nonofficial species as alternatives to the official species.

Quality and Consistency: The quality of traditional plant medicines is closely related to their chemical constituents and their concentration, and consistency might vary slightly according to differences in climate, cultivating or wilding, harvest time, possessing procedure and storage. When evaluating the recorded spectra, minor differences in concentrations might influence the quality of the plant medicines, while small differences between the spectra can discriminate between species. PCA, SA and HCA can classify and discriminate medicinal plants spectra effectively [32, 33].

The results were analyzed by SA, HCA and PCA. Each method highlighted different properties of the data matrix according to the spectra from different types of herbal medicine. Consequently, the preference ranking organization method for enrichment evaluations and Geometrical Analysis for Interactive Assistance (GAIA) and Multi-Criteria Decision Making (MCDM) methods provided the most comprehensive information for matching and discrimination of the fingerprints. The data were analyzed by chemometrics methods such as SA, PCA and HCA to classify the samples. The NIR spectra combined with chemometrics can be useful in the quality control and evaluation of Herbal medicine.

Geographic origins: Near infra-red diffuse reflection spectroscopy, Raman spectroscopy and IR spectroscopy were compared for their ability to cluster different ginsengs according to source and processing methods [28, 34]. Cluster analysis grouped the samples into four main clusters and the best results were obtained using Raman spectroscopic analysis. A combination of FT-IR with PCA, SIMCA and LDA was applied to the classification of herbal medicine according to geographical location or variety, where the best discriminatory approach was obtained by LDA.

PLS has been used in many studies to predict the active constituents, the content of caffeine and total polyphenols in tea, and SIMCA has been used to identify tea varieties from different origins Coupling NIR spectroscopy with DA and PLS-DA analysis was applied to geographical origin discrimination and content determination of baicalin, wogonoside, baicalein and wogonin in radix *Scutellaria baicalensis*. A combination of FT-IR with CDA has been applied to distinguish 70 Greek *Mentha pulegium* samples according to their geographical locations[28], where the main spectral features for the discrimination of samples among the different collection areas occur primarily in the carbonyl region and are correlated with the main volatile constituents of the extracts.

Safety: The safety issue of plant medicines has been reported to contain heavy metals, pesticide residual, mycotoxin and synthetic prescriptions or non-prescription drugs. They may originate from mineral components, contamination and adulteration determination of them is crucial to ensure the safety of the plant medicines. Trace elements such as iron, copper, zinc and manganese are known to play important roles[35,36] in biological systems and may have relationship with specific growth location and curative efficacy of the plant, so it has been studied extensively recently. In contrast, other elements, such as lead and cadmium are toxic even in trace amounts.

Therefore, it has the central importance of ascertaining the content of toxic elements.

CONCLUSIONS: The present study demonstrates that NIR can successfully be used to monitor the quality of herbal medicinal products at different steps of the manufacturing processes. They can be used routinely in the quality control laboratory to ensure that the raw material sent by the supplier fulfils the required specifications. Principal component analysis, second derivative and hierarchical analysis proved to be especially helpful in choosing representative calibration samples, a specific spectral region, and an improved spectral acquisition mode. Moreover, the study of factors affecting the spectra was found to be crucial to optimize the variability of parameters that should be included in the calibration set (frequency, supplier and particle size) and the sample presentation mode.

SA, PCA and HCA have been successfully applied for such purposes as their major advantage for distinguishing herbs is that these techniques allow the identification of the metabolic profile without necessarily identifying its chemical constituents, as well as the determination of a chromatographic discriminating region. For better understanding of the discriminating efficiency of the variables, a preliminary study based on PCA and HCA has to be carried out in spite of prior knowledge of class membership of the herb. Then to obtain suitable classification rules for assigning samples to categories, supervised pattern recognition methods can be applied. Principle component analysis has been applied to explore the distribution pattern of samples by examining the score plots.

From the loading plot the areas of the chromatograms that are significant and contribute to the largest variance in the data. In addition, loading values are very informative for screening chemical markers that have the most influence on the separation among different groups of samples. The discriminatory abilities of both supervised and unsupervised methods have been investigated in many studies. Both can discriminate closely related species of the same genus and detect adulteration based on levels of secondary metabolites or major bioactive components.

The methods also have been applied to determine whether the secondary metabolites can be used as markers for preprocessing and harvesting time of different herbs to assess their quality. Concerning geographical origins, they have been employed successfully for the classification of samples from different localities, cultivars, suppliers and even different batches from the same supplier according to their phytochemical diversity.

Supervised pattern recognition methods were investigated, such as SIMCA, LDA, PLS-DA and ANNs, which are employed to construct a discrimination model, the potential use of fast chromatograms and spectra in the construction of multivariate models relating their profiles with the biological activity of different herbs and to predict the content responsible for this activity. The PLS regression method has been applied successfully for the prediction of different secondary metabolites.

Chemometrics analysis and a robustness study are thus highly critical steps for the development of specific and robust NIR models. When comparing the outputs and benefits of NIR compared to traditional analysis methods, HPLC was found to give more informative composition results as compared to NIR spectroscopy. However, controlling that the sample is of the required identity and quantifying a small number of marker substances are often the goals for the pharmaceutical industry. In these cases, NIR is a technique of choice for the quality control of herbal medicinal remedies. In addition, it was shown that the advantages in terms of time and costs saved during the analysis are considerable compared to HPLC: NIR routine analysis is more than an order of magnitude faster, environmental friendly, and does not require highly skilled personnel.

The methods were validated according to pharmaceutical regulations and all the criteria met the recommended specifications. Qualitative methods were validated for their specificity, and quantitative methods were validated for their accuracy, precision, specificity, linearity, range, limit of quantization and robustness. The potential power of chemometrics in quality evaluation needs no further description.

In the evaluation of quality of herbs, chemometrics can be used to optimize experimental procedures, pre-treat fingerprints, extract maximum useful information, and analyze results. Chemometrics is a suitable analysis method and a useful tool for estimating medicinal plants quality.

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