Acta Pharmaceutica Sinica B 2014;4(3):182–192

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

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REVIEW

Application of near infrared spectroscopy to the analysis and fast quality assessment of traditional Chinese medicinal products

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Received 17 October 2013; revised 2 December 2013; accepted 10 February 2014

KEY WORDS

Near infrared spectroscopy;
Traditional Chinese medicine;
Quality control;
Fast inspection

Abstract Near infrared spectroscopy (NIRS) has been widely applied in both qualitative and quantitative analysis. There is growing interest in its application to traditional Chinese medicine (TCM) and a review of recent developments in the field is timely. To present an overview of recent applications of NIRS to the identification, classification and analysis of TCM products, studies describing the application of NIRS to TCM products are classified into those involving qualitative and quantitative analysis. In addition, the application of NIRS to the detection of illegal additives and the rapid assessment of quality of TCMs by fast inspection are also described. This review covers over 100 studies emphasizing the application of NIRS in different fields. Furthermore, basic analytical principles and specific examples are used to illustrate the feasibility and effectiveness of NIRS in pattern identification. NIRS provides an effective and powerful tool for the qualitative and quantitative analysis of TCM products.

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Peer review under responsibility of Institute of Materia Medica, Chinese Academy of Medical Sciences and Chinese Pharmaceutical Association.

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http://dx.doi.org/10.1016/j.apsb.2014.04.001
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1. Introduction

Chinese herbs and patent drugs are important parts of traditional Chinese medicine (TCM), the use of which is considerable not only in China but all over the world. Despite this widespread use, there are many confusing aspects related to TCM such as the fact that many similar TCMs produce different pharmacodynamic effects, one TCM can have two or more names and one name can apply to more than one TCM. These problems lead to difficulty in the quality control (QC) of TCM and call for urgent attention[1].

In comparison with the Chinese Pharmacopoeia 2005 (ChP2005), drug standards and test methods for TCM have been considerably improved and extended in the Chinese Pharmacopoeia 2010 (ChP2010). Common methods now include histological and morphological examination, thin layer chromatography (TLC), high-performance liquid chromatography (HPLC), gas chromatography (GC), liquid chromatography–mass spectrometry (LC–MS) and gas chromatography–mass spectrometry (GC–MS)[2–4]. This more authoritative and comprehensiveness coverage of TCM in the ChP is critical for improving the QC of TCM. However, there are still deficiencies such as the time period of inspection in the ChP is longer than the 28 days recommended by the Institute for Drug Control (IDC) in China.

Another problem is that TCM components are often pretreated by physical or chemical processes before being tested. These procedures are complex and multifarious and some of them such as morphological identification lack accuracy since the results depend on the experience and expertise of the TCM pharmacist undertaking the test[5]. Thus, for objectivity, rapidity and accuracy of testing, more rational methods are needed.

Since the 1990s, the application of near infrared spectroscopy (NIRS) in fields involving drugs, food, agriculture, the petroleum industry and environmental protection has developed rapidly[6,7]. NIRS has many advantages in relation to QC and inspection[8] and allows classification, qualitative analysis and quantitative analysis of TCM products. The further development of NIRS will serve to strengthen quality supervision and control of TCM products and regulate markets[9].

2. Advantages of NIRS technology

The advantages of NIRS are many with rapidity of analysis being one of the most important[10]. Thus NIRS combined with appropriate mathematical models and pattern recognition techniques allows analysis of a wide variety of sample types rapidly. Second, NIRS is a non-destructive technique which avoids complex sample preparation by chemical or physical processes. In fact, both solid and liquid samples in different types of packaging stored under different conditions can all be tested without complex pretreatment[11] because of the better penetrability of fiber optics used in NIRS. Third, it provides acceptable accuracy in both qualitative and quantitative analysis to meet the requirements of QC and preliminary screening[12].

3. Identification of TCM by NIRS

3.1. Qualitative identification

TCM herbs and animal products are subject to numerous complex problems in clinical use. For example, herbs are often adulterated with or replaced by non-therapeutic plants of similar appearance[13–15] because the ability to identify a particular herb is very dependent on the experience of the TCM pharmacist.

Identification based on microscopic examination is frequently applied to TCM powders by looking for the presence of microstructures[16–18]. In addition, it is used to examine slices of TCM plant cells. The ChP2005 recorded 620 items requiring identification by microscopy and the number increased to 1253 in the ChP2010[19]. However, identification using microscopy still depends on the experience of the TCM pharmacist whereas NIRS provides a more reliable non-subjective method to identify TCM products. For example, 269 samples of Bai-Zhi (Radix Angelicae Dahuricae) and 350 samples of wild or cultivated Dan-Shen (Radix et Rhizoma Salviae Miltiorrhizae) were identified and classified by NIRS with a accuracy rates of 99% and 95%, respectively[20].

Some species of TCM are grown in different regions of China where differences in weather conditions and soil environments lead to variations in quality[21]. NIRS can then be used to locate the source of a particular sample. For example, Jin-Yin-Hua (Flos Lonicerae Japonicae) is widely planted in the provinces of Henan, Hebei, Hunan, Shandong and Guangxi. Qualitative analysis by NIRS not only identified 22 samples as coming from Henan province with 100% accuracy but also correctly sourced 68 samples from other provinces and sourced only 9 samples incorrectly[22].

The use of genuine medicinal materials is very important to the integrity of TCM (Table 1). However, many rare and expensive TCM herbs are often adulterated[23]. For example, the adulteration of Dong-Chong-Xia-Cao (Cordyceps), one of most important and precious TCM herbs, is a serious problem. Fortunately, NIRS provides a rapid and convenient method to identify Dong-Chong-Xia-Cao with an accuracy rate greater than 95%[24]. In contrast, Hong-Qu (Rubrum Fermentum) is not a rare material but a commonly used food additive in China and many Asian countries[25]. The problem here is that many substances are similar in appearance to Hong-Qu making identification by microscopy difficult. In this case, NIRS in combination with cluster analysis was successful in classifying Hong-Qu effectively[26,27].

Grinding is frequently used in the preparation of TCM as part of the extraction and purification of desired components from crude materials. As a result, TCM herbs and animal products in the form of powders lose their significant characteristics making identification difficult. In addition, different TCM herbs have similar shape, color and microscopic features[28]. For example, Bai-Zhi (Radix Angelicae Dahuricae), Ye-Ge (*Puerariae Lobatae*), Cang-Zhu (Rhizoma Atractylodis), Bai-Shao (Radix Paeoniae Alba) and Dang-Gui (Radix Angelicae Sinensis) display only subtle differences in appearance[29] and, after grinding, become even more difficult to distinguish. However, using principal component analysis (PCA) and cluster analysis to classify NIRS data allowed TCM powders with indistinguishable appearance to be identified and classified as accurately as by HPLC. NIRS is now considered the technique of choice for the QC of Chinese patent medicines[30–32].

3.2. Pattern recognition technology

A NIR spectrum incorporates a large amount of information and includes overlapping and interconnected signals. As a result, pattern recognition is an important approach to reduce the number of variables. Pattern recognition is classified as either unsupervised or supervised[33]. Cluster analysis, PCA and discriminant analysis

Table 1 Quantitative analysis of TCM products by near infrared spectroscopy.

Province	Genuine medicinal material	Province	Genuine medicinal material
Sichuan and Chongqin	Chuan-Bei-Mu (Bulbus Fritillariae Cirrhosae)	Hubei, Anhui and Jiangsu	Ban-Xia (Rhizoma Pinelliae)
	Chuan-Xiong (Rhizoma Chuanxiong)		Ge-Gen (Radix Puerariae Lobatae)
	Huang-Lian (Rhizoma Coptidis)		Cang-Zhu (Rhizoma Atractylodis)
	Fu-Zi (Radix Aconiti Lateralis Praeparata)		Tai-Zi-Shen (Radix Pseudostellariae)
	Chuan-Wu (Radix Aconiti)		Dang-Shen (Radix et Rhizoma Salviae Miltiorrhizae)
Guangzhou, Guangxi and Hainan	Sha-Ren (Fructus Amomi)	Shandong, Hebei, Shanxi and Shǎnxi	Dang-Shen (Radix et Rhizoma Salviae Miltiorrhizae)
	Guang-Huo-Xiang (Herba Pogostemonis)		Huang-Qi (Radix Astragali)
	Chuang-Xin-Lian (Herba Andrographis)		Chai-Hu (Radix Bupleuri)
	Jin-Qian-Cao (Herba Lysimachiae)		Huang-Qin (Radix Scutellariae)
	Luo-Han-Guo (Fructus Siraitiae)		Bai-Zhi (Radix Angelicae Dahuricae)
Yunnan	San-Qi (Radix et Rhizoma Notoginseng)	Hunan, Jiangxi, Fujian and Taiwan	Bai-Bu (Radix Stemonae)
	Mu-Xiang (Radix Aucklandiae)		Wei-Ling-Xian (Radix et Rhizoma Clematidis)
	Chong-lou (Rhizoma Paridis)		Xu-Chang-Qing (Radix et Rhizoma Cynanchi Paniculati)
	Fu-Ling (Poria)		Ze-Xie (Rhizoma Alismatis)
	Tian-Ma (Rhizoma Gastrodiae)		Zhi-Shi (Fructus Aurantii Immaturus)
Guizhou	Tian-Dong (Radix Asparagi)	Neimenggu	Suo-Yang (Herba Cynomorii)
	Huang-Jing (Rhizoma Polygonati)		Gan-Cao (Radix et Rhizoma Glycyrrhizae)
	Ba-Ji (Rhizoma Bletillae)		Ma-Huang (Herba Ephedrae)
	Du-Zhong (Cortex Eucommiae)		Rou-Cong-Rong (Herba Cistanches)
	Wu-Zhu-Yu (Fructus Euodiae)		Yin-Yang-Huo (Folium Epimedii)
He'nan	Huai-Di-Huang (Radix Rehmanniae)	Xizang	Hu-Huang-Lian (Rhizoma Picrorhizae)
	Huai-Niu-Xi (Raix Achyranthis bidentatae)		Zang-Mu-Xiang (Radix Aucklandiae)
	Huai-Shan-Yao (Rhizoma Dioscoreae)		Xue-Lian-Hua (*Saussurea Involucrata*)
	Huai-Ju-Hua (Flos Chrysanthemi)		Mao-He-Zi (Fructus Terminaliae Billericae)
	Tian-Hua-Feng (Radix Trichosanthis)		She-Xiang (Rhizoma Belamcandae)
Zhejiang	Zhe-Bei-Mu (Bulbus Fritillariae Thunbergii)	Xinjiang	Xue-Lian-Hua (Saussurea Involucrata)
	Bai-Zhu (Rhizoma Atractylodis Macrocephalae)		A-Wei (Resina Ferulae)
	Yan-Hu-Suo (Rhizoma Corydalis)		Zi-Cao (Radix Arnebiae)
	Shan-Zhu-Yu (Fructus Corni)		Gan-Cao (Radix et Rhizoma Glycyrrhizae)
	Hang-Bai-Ju (Flos Chrysanthemi)		Zi-Ran (Cuminum Cyminum)
Heilongjiang, Jilin and Liaoning	Ren-shen (Radix et Rhizoma Ginseng)	Drug from sea	Zhen-Zhu (Margarita)
	Xi-Xin (Radix et Rhizoma Asari)		Shi-Jue-Ming (Concha Haliotidis)
	Fang-Feng (Radix Saposhnikoviae)		Hai-Piao-Qiao (Endoconcha Sepiae)
	Wu-Wei-Zi (Fructus Schisandrae chinensis)		Mu-Li (Concha Ostreae)
	Long-Dan (Radix et Rhizoma Gentianae)		Hai-Ma (Hippocampus)
Gansu and Ningxia	Da-Huang (Radix et Rhizoma Rhei)	Import from abroad	Xi-Yang-Shen (Radix Panacis quinquefolii)
	Dang-Gui (Radix Angelicae sinensis)		Ru-Xiang (Olibanum)
	Qin-Jiao (Radix Gentianae macrophyllae)		Chen-Xiang (Resinatum Aquilariae Lignum)
	Qiang-Huo (Radix et Rhizoma Notopterygii)		Pang-Da-Hai (Semen Sterculiae Lychnophorae)
	Gou-Qi-Zi (Fructus Lych)		Mo-Yao (Myrrha)

belong to the unsupervised class whereas latent projection, k-nearest neighbor algorithm (KNN), Fisher linear discriminant analysis (KLDA) and artificial neural networks (ANNs) belong to the supervised class.

3.2.1. Cluster analysis

Cluster analysis is frequently used to identify and classify TCM products[34]. Based on groups of variables, samples can be classified to different resources[35,36]. TCMs are multicomponent systems and, in the case where the components in samples give distinct differences in NIR spectra, samples can be classified using cluster analysis[37,38]. In fact, cluster analysis is a convenient method to simplify data from multicomponent systems for data analysis and data mining.

3.2.2. Principal component analysis

The large number of variables in TCM makes their analysis difficult[39]. PCA is a mathematical procedure to reduce the dimensions of data by linear fitting[40]. It produces a group of new variables which represent the primary information of the original variables without any data loss[41]. For example, in the NIR spectra of Jin-Yin-Hua (Flos Lonicerae Japonicae) and Huang-Qin (Radix Scutellariae), the two main raw materials in Yin-Huang oral liquid and Shuang-Huang-Lian oral liquid are a large number of signals from baicalin, chlorogenic acid and other components. To simplify the analysis, dimensions of the data were linearly reduced to calculate cumulative contribution rates and score plots[42]. Results presented on two- or three-dimensional maps effectively demonstrated differences in quality.

3.2.3. k-Nearest neighbor algorithm

k-Nearest neighbor algorithm (KNN) is a non-parametric method to classify objects based on closest training examples in the feature space. It ranks the contributions of neighbors in terms of their closeness to the object. In applying a combination of NIRS and KNN to samples of Dang-Shen (Radix et Rhizoma Salviae Miltiorrhizae), a common TCM herb in China, a mathematical model was established which was able to classify samples from different resources with an accuracy rate of 94%[43].

3.2.4. Latent projection

Methods based on quantitative calibration and pattern recognition are established on the basis of latent projection. Partial least squares (PLS)[44], partial least-squares discriminant analysis (PLS-DA)[45] and soft independent modeling of class analogy (SIMCA)[46] were all developed from latent projection. Latent projection has been used in the identification and classification of TCM products by NIRS. For instance, PLS-DA was applied to classify 600 samples of Bing-Lang (Semen Arecae) processed by six different methods[45]. Moreover, SIMCA and PLS-DA combined with NIRS have been used to identify Ci-Wu-Jia (Radix et Rhizoma Acanthopanacis Senticosi Seu Caulis)[46] grown in different geographical areas.

3.2.5. Artificial neural networks

ANNs are a new information processing method applied to TCM[47,48]. Many simple neurons connected to each other make up a complex network that can compute values by feeding information through the network[49]. The radial basis function ANN (RB-ANN)[50,51] and back-propagation ANN (BP-ANN) [52] are common applications used to overcome some of the disadvantages of NIRS such as broad spectral range, poor signal strength and overlapping signals[53]. ANN reduces interference and noise and has good nonlinear conversion capability to effectively avoid prediction error[54]. The combination of NIRS and ANN is particularly useful for the identification of TCMs with indistinguishable features[55].

3.2.6. Specific spectrum method

Direct comparison of a sample spectrum with the spectrum of an authentic specimen is an important method for qualitative analysis of a TCM product. It is similar to fingerprinting as applied in chromatography and spectroscopy[56–58]. Identification of signals characteristic of a particular component can then be applied in the QC of TCM[57–59]. NIRS provides just as much information as HPLC and is superior in that it can be applied to most drug preparations with minimal sample preparation, even to the extent of allowing analysis in aluminum–plastic packaging[60]. Using appropriate wavelength ranges and optimization methods are important in establishing specific spectral features for use in QC.

4. Quantitative analysis of TCM products

Both qualitative and quantitative analysis by NIRS require the development of a mathematical model. For medicines with relatively simple composition containing high purity components, establishing a mathematical model for NIRS is relatively straightforward[61] and provides good results in quantitative analysis[61–64]. However, for analysis of TCM by NIRS, establishing a model is more difficult because they contain many components at low concentration. Thus, quantitative analysis of TCM by NIRS is still in the development and validation stage[65,66].

4.1. Model establishment

Quantitative analysis by NIRS requires sufficient spectra to make sample measurement sets and validation sets. Sample measurement sets are used to establish the mathematical model after which validation sets are used to test and verify the accuracy of the model. The model is also optimized using samples with known composition[67,68]. General steps (Fig. 1) include: (1) pre-quantitative analysis for target compositions, collecting and analyzing sample measurement sets by NIRS; (2) establishing a quantitative model for target compositions and then optimizing the model by NIRS; and (3) using validation sets to verify the accuracy and repeatability of the model.

Having collected sufficient spectra, the two major steps involve selecting the wavelength range and pre-treating spectra[69]. Selecting a limited wavelength range is important because information derived from the full wavelength range is enormous and the absence of signals in certain regions of the spectra may influence the accuracy of results. Thus it is important to select the wavelength range of positive correlation and reject the range of negative correlation.

Pre-treating spectra is a procedure to optimize data and avoid disturbance due to a changing baseline. Common pretreatments include averaging, smoothing and normalizing using first and second derivative spectra[70]. The first derivative can eliminate shift errors and the second derivative can eliminate tilt (or rotation) errors[71]. Other methods to extract information from spectra are also available including multiplicative scatter correction (MSC), Savitzky–Golay method (SG) and standard normal variate (SNV)[72].

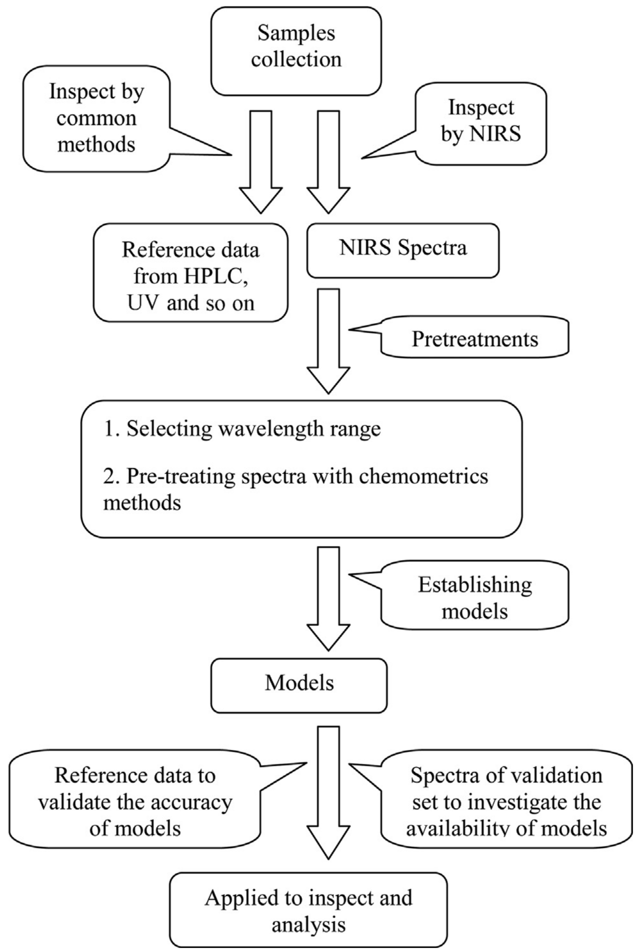

Figure 1 A brief summary of the processes involved in model establishment in qualitative and quantitative analysis of TCM products by NIRS.

Improving the model by correction methods is crucial for accurate quantitative analysis. Correction based on multiple linear regression[73] and chemical stoichiometry[74] is useful to obtain maximum information. Commonly used methods of multiple linear regression are principal component regression (PCR)[75], partial least-squares discriminant analysis (PLS-DA) and partial least squares regression (PLS)[76]. In recent years, optimization methods used for quantitative analysis of TCM by NIRS are shown in Table 2.

4.2. *Quantitative analysis of TCM products by NIRS*

4.2.1. *Single or multiple component systems*

Most quantitative tests for TCM follow the ChP and use HPLC or GC. Any new test method intended to replace an existing method must show some advantage and guarantee accuracy. Examples of the use of NIRS for quantitative analysis include determinations of baicalin in Huang-Qin (Radix Scutellariae)[85], phillyrin in Lian-Qiao (Fructus Forsythiae)[86] and berberine in Huang-Bai (Cortex Phellodendri Chinese)[84], In all cases, results were compared with those obtained by HPLC and shown to be accurate.

TCM products generally contain either a single or more than one TCM herb. The former is exemplified by Dan-Shen injection which contains only Dan-Shen (Radix et Rhizoma Salviae Miltiorrhizae) whereas an example of the latter is Fu-Fang-Dan-Shen dripping pills which contain extracts of both Dan-Shen and San-Qi (Radix Notoginseng). The extraction process involves decoction with water, separation, purification and extraction with water, alcohol and other chemical reagents[93].

Single component TCM products such as paclitaxel injection[94] are readily analyzed by HPLC, UV or NIRS but NIRS has advantages in the QC of such products. It also simplifies test procedures and reduces technical barriers in quantitative analysis[77]. For example, assay of lutein and β-carotene in cabbage[95] and of pinene, methyl salicylate and eugenol in safflower oil[96] (commonly used to treat traumatic injury) all gave satisfactory results by NIRS. A more complex example is Tan-Re-Qing injection, a TCM product made up of Huang-Qin (Radix Scutellariae), Xiong-Dan-Fen (Bear gall powder), Shan-Yang-Jiao (Cornu Caprae Hircus), Jin-Yin-Hua (Flos Lonicerae Japonicae) and Lian-Qiao (Fructus Forsythiae). In this case, NIRS spectra of 120 samples were collected[97] and the content of chlorogenic acid, caffeic acid, luteoloside, baicalin, ursodesoxycholic acid and chenodeoxycholic acid were determined and shown to be accurate by HPLC.

Stability of the mathematical model dictates the accuracy of quantitative analysis by NIRS. It is influenced by a series of factors such as the accuracy of chemical reference values, the number of spectra representative of the model, equipment factors and human factors. A sufficient number of representative samples, strict control of experimental conditions and adoption of appropriate data-processing methods all impact on chemical reference values and accuracy. If sufficient spectra are obtained and there is no perturbation, quantitative analysis of multicomponent systems can be achieved by NIRS. For example, in the analysis of the therapeutically active components in Shan-Zhu-Yu (Fructus Corni), astilbin (regulating the immune system) and ursolic acid (sedation and antibacterial effects)[98], NIRS spectra in the wavelength ranges 4638–7659 cm^{-1} and 8197–9441 cm^{-1} provided abundant information to give accurate results as confirmed by HPLC.

4.2.2. *TCM extracts*

Extracts of TCM herbs are the intermediate stage between the original plant and an isolated active component[99]. In order to reduce any deterioration in therapeutic activity, TCM formulations should be as close to the original plant as possible. However, in practice, physical and chemical pretreatments are required to remove unwanted impurities which can affect the pharmacodynamic effects of the active components. In China, out of more than 5000 TCM products, only 47 extracts are recorded in the ChP2010 including those of hawthorn leaf, scutellaria, gingko leaf, total phenolic acids of salvia, asiatic moonseed and forsythia.

In the extract of Yin-Xing (*Ginkgo biloba*), flavonoids are important pharmacodynamic constituents[100]. According to the ChP, total flavonoids are made up of the sum of the total flavonol glycosides and total terpene lactones as determined by HPLC. Total flavonol glycosides are then made up of the sum of the amounts of quercetin, kaempferide and isorhamnetin and total terpene lactones of the amounts of bilobalide, ginkgolide A, ginkgolide B and ginkgolide C. Quality assessment of the extract is a complex task which is accomplished more simply and conveniently by NIRS than by HPLC. Using the wavelength range 1100–2500 nm, pre-treating spectra by SNV and evaluating different regression methods (PCR, PLS and modified PLS) produced an assay with acceptable absolute and relative errors and a reliable accuracy rate[101]. Another example using NIRS and a PLS algorithm in the regression model is the quantitative analysis of the total phenolic acids

Table 2 NIRS analysis of the partial genuine medicinal materials in China.

Drug	Component	Wavelength range (cm^{-1})	Pretreatment method	Reference
Taxol injection	Taxol	9000–4400	Minus a straight line	77
Acanthopanax Senticosus Injection	Chlorogenic acid Syringin Eleutheroside E	8927–8735, 6800–5400, 4700–4300	First derivative+vector normalization	78
Acanthopanax Senticosus powder	Syringin	4601–4246	First derivative+multiple scattering correction	79
Cordyceps Sinensis (Berk) Sacc	Glu Arg Asp Total amino	10000–3970 9420–3950 9050–3855 8500–3800	First derivative+Savitzky–Golay	80
Eucommiae Unloads	Pinoresinol diglucoside	7502–4597	First derivative+minus a straight line	81
Yiqing Granule	Baicalin	6749–4987	First derivative+multiple scattering correction	82
Semen Thlaspi	Sinigrin	7502–5446	Maximum and minimum normalization	83
Phellodendron Chinese Schneid	Berberine	8000–4000	Second derivative	84
Radix Scutellariae	Total Flavonoids Baicalin	8015–5446 6105–4242	Maximum and minimum normalization First derivative	85
Forsythiae Suspensa	Phillyrin	9002–4103	First derivative	86
Ophiopogon Japonicus	Polysaccharides	4000–4900, 5100–6900, 7050–10000	First derivative+Savitzky–Golay+multiple scattering correction	87
Ligusticum Chuanxiong Hort	Ferulic acid	7501–6799, 4424–4246	First derivative	88
Rehmannia Glutinosa Libosch	Catalpol	6102–4597	First derivative+multiple scattering correction	89
Dioscorea Zingiberensis C.H.	Extracts by ethanol	5476–7466	First derivative+standard normalization variate	90
Rhizoma Dioscoreae	Polysaccharide	7513–4597	First derivative+vector normalization	91
Rhizoma Dioscoreae	Extracts by water Extracts by ethanol	8717–5446, 4613–4242	First derivative+vector normalization	92
Bear Gall powder extracts	Ursodesoxycholic acid Chenodeoxycholic acid Ursolic acid	4500–8500	First derivative+Savitzky–Golay	10

in the extracts of Huang-Qi (Radix Salvia) and Dan-Shen (Radix et Rhizoma Salviae Miltiorrhizae)[102]. NIRS with a PLS model was also applied to analyze the major pharmacodynamic components (polysaccharides and triterpenoids) in the extract of Ling-Zhi (Ganoderma lucidum) and Hei-Ling-Zhi (Ganoderma atrum) and gave accurate results[103]. Research into the quantitative analysis of the total alkaloids in the extract of Huang-Bai (Cortex Phellodendri) also revealed the superiority and practicality of NIRS[104].

5. Analysis of illegally additives in TCM products

The presence of illegal additives in drugs, health care products and cosmetics is a perennial problem that can affect quality and lead to potential harm[105–107]. In the case of TCM products, coloring agents are often added. Examples include the addition of golden orange II to Hong-Hua (Flos Carthami)[108] to enhance its red color and hide moldiness and discoloration and the addition of auramine O to Huang-Qin (Radix Scutellariae) and Pu-Huang (Pollen Typhae) to enhance their yellow color[109]. Another example is the addition of abietic acid to Ru-Xiang (Olibanum) and Mo-Yao (Myrrha) to enhance their characteristic smell[110].

TCM health care products are widely used in China. Compared with drugs, the supervision of TCM health care products is much less rigorous. For example, sildenafil citrate, sildenafil and phenolphthalein are frequently added to TCM health care products to enhance an effect against male sexual dysfunction[111–114]. Also, in cosmetics TCM products aiming to improve effects of treating acne and whitening face, hormones and similar substances are often added[115,116]. Similar compounds are often added to Chinese patent drugs. For example, prednisone acetate and dexamethasone acetate are commonly found in preparations for treating cough and asthma[117].

TLC is frequently used to assess the presence of illegal additives in TCM products. However, as a technique, it suffers from poor sensitivity and reproducibility. As a result, it often requires HPLC or HPLC–MS to further confirm the presence of illegal additives. In principle, NIRS can detect illegal additives based on correlation coefficient analysis. Spectra are compared to calculate the similarity and characteristic range after which the appropriate threshold of correlation coefficient is adjusted to investigate the correlation[118,119].

TCM health care products aimed at invigorating kidney function and strengthening "Yang" are used extensively in China. Lu-Rong (Cornu Cervi Pantotrichum), Rou-Cong-Rong (Herba Cistanches), Yin-Yang-Huo (Folium Epimedii), Tu-Si-Zi (Semen

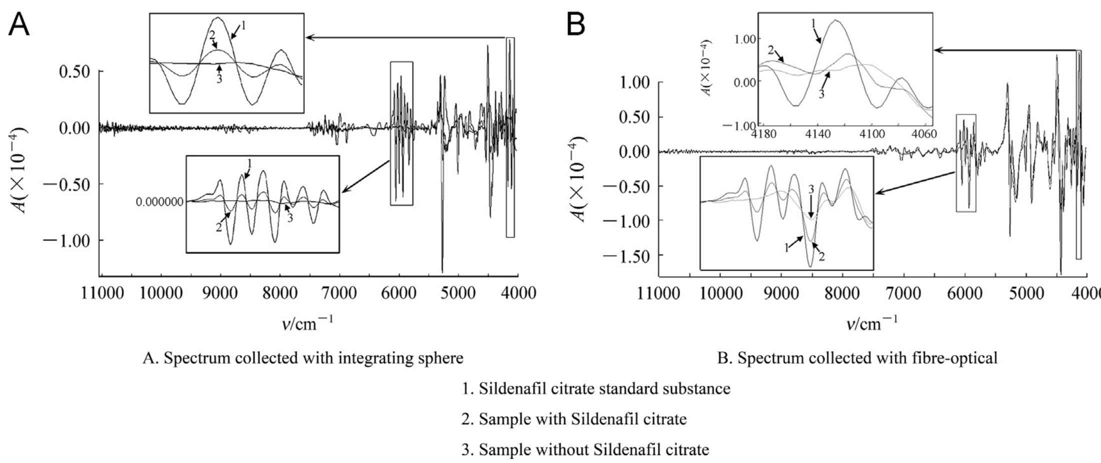

Figure 2 Analysis of sildenafil citrate illegally added to TCM products by derivative NIRS.

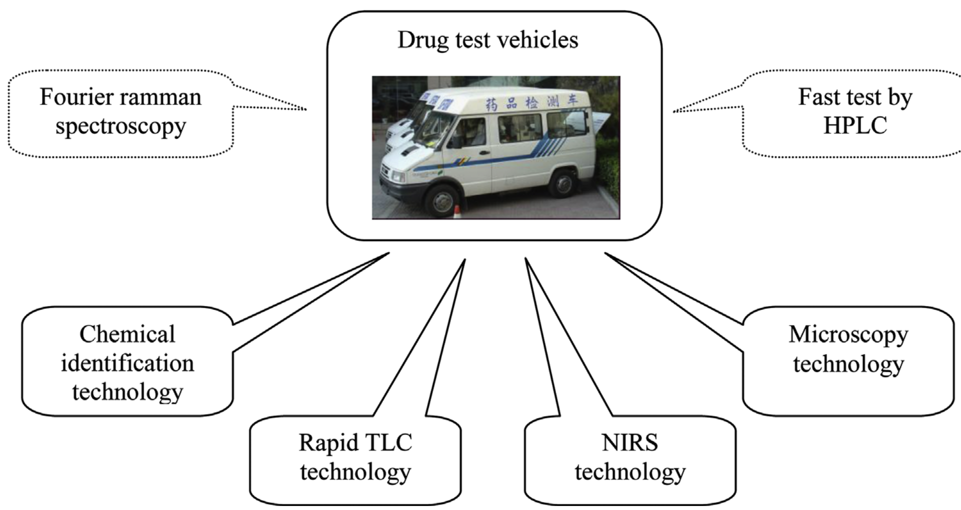

Figure 3 The main components that make up a fast inspection platform. Chemical identification, TLC, NIRS and microscopy are basic technologies in a drug test vehicle. In some parts of China, because of special requirements, Fourier-transform Raman spectroscopy and HPLC are also included.

Cuscutae), Ba-Ji-Tian (Radix Morindae Officinalis) are also popular TCM products that aim to strengthen male sexual function. However, because their efficacy takes considerable time, drugs, most commonly sildenafil citrate, are often added. To police this phenomenon, NIRS with correlation coefficient analysis is used for rapid screening[119]. Spectra of sildenafil citrate and samples testing positive and negative for the drug in the wavelength ranges 6070–5800 cm^{-1} (Fig. 2) and 4170–4070 cm^{-1} were subject to second derivative and vector normalization. Correlation coefficients of 70% for integrating sphere and 65% for fiber-optical were satisfactory and analysis by LC–MS indicated an accuracy as high as 90%. NIRS can also be used to investigate the presence of illegal additives in foods such as in the control of melamine in milk[120].

6. Application of NIRS to fast inspection

A platform for fast inspection is based on drug identification and other information produced by NIRS, rapid TLC, chemical identification and microscopy. It aims to control the quality of drugs through random inspection (Fig. 3)[121,122] carried out by personnel operating a drug testing vehicle. Mobility and rapidity are key features of the fast inspection platform in TCM supervision[123,124].

During a surprise inspection, the advantages of NIRS are important to overcome problems of small sample size, a prolonged testing period and high cost. It can be applied without destroying aluminum packing and to a wide range of formulations including powders, tablets and capsules[125]. However, NIRS has some serious disadvantages for fast inspection such as poorer sensitivity and stability compared with HPLC. It also suffers from environmental effects, unreliable sampling and poor technical ability on the part of the operatives. Nevertheless, on the whole the accuracy of NIRS is satisfactory for routine analysis[126].

Because adulteration of TCM is becoming an increasing problem, attention has been focused on the safety of TCM products on the market. Microscopy, chemical reaction tests, TLC, Fourier-transfer Raman spectroscopy and NIRS can all form part of a fast inspection platform but individual techniques still have problems to overcome. Thus, TLC is useful to back-up the results of NIRS[127] but in practice it poses difficulties not only in selecting the best type of plate, solvent system and developing agent but in obtaining clear and well resolved spots. Similarly, chemical reaction tests lack specificity and can only identify the class of substance, *e.g*., flavonoids and saponins. It also is only useful to support the results obtained by NIRS.

NIRS is more reliable than TLC and chemical reaction tests but accuracy depends on the quality of the model[78]. In routine screening, a sample which fails an NIRS test should be examined according to the official ChP method. False positives always appear in practice but further inspection following the ChP2010 prevents the problem. False positive results suggest that a model established by NIRS may be flawed and requires improving by enlarging the sample size and sampling region or changing the wavelength region[128]. This should then improve the stability and applicability of the model.

7. Conclusions

Experience in testing and maintaining the quality of TCM products has developed continuously as their use has grown. To improve and apply routine inspection technologies, higher efficiency of test methods is vital. NIRS has many advantages relevant to daily inspection of TCM products such as its rapidity and non-destructive nature. NIRS technology is developing and improving continuously and its wider application to the quantitative and qualitative analysis of TCM products will certainly improve their quality control and safety in clinical use.

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