Design of Intelligent Near Infrared Spectroscopy Monitoring in the Production Process of Traditional Chinese Medicine Tablets

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Abstract—Traditional Chinese medicine tablets are very common in clinical application, and the market demand is large. Traditional Chinese medicine tablets are the most common dosage forms of traditional Chinese medicine. Its advantages are convenient and safe to take, easy to carry, accurate dose, and stable quality. In the production process of solid preparations of traditional Chinese medicine, due to the complexity of the components of traditional Chinese medicine, strict verification is needed to improve the quality control of the process to support the continuous and stable production of traditional Chinese medicine preparations. If the process technology is not mature, it will bring many unstable factors to the production of solid preparations of traditional Chinese medicine, such as tablet loosening, cracking, disintegration and so on. In order to improve the quality of traditional Chinese medicine tablets and ensure the smooth progress of production, in view of the common quality problems in the production of traditional Chinese medicine tablets, this paper designs near-infrared spectroscopy monitoring to improve the quality of traditional Chinese medicine tablets.

Keywords- Near infrared spectroscopy, Chinese medicine tablets, intelligent monitoring design

1 Introduction

With the continuous development of China 's medical industry, people 's requirements for the quality of drugs are getting higher and higher. It is no longer a simple pursuit of curative effect, but also more concerned about the quality of drugs. Nowadays, Chinese medicine preparations still encounter some technical problems in the production process that need to be solved urgently.

For example, the hardness of the tablet has a great influence on the post-production process of the tablet. If the hardness of traditional Chinese medicine tablets is not enough, it is easy to crack in packaging and transportation. If the hardness of traditional Chinese medicine sugar-coated tablets is not enough before coating, it is easy to appear fragments and pockmarks during coating[1].

ICPDI 2023, September 01-03, Chongqing, People's Republic of China

DOI 10.4108/eai.1-9-2023.2338798

2 Analysis of the causes of problems in traditional Chinese medicine tablets

In terms of materials, the particles are too dry, and the particles lose too much water during the drying process, which makes it difficult to combine during the pelletizing process. There are many subdivisions of particles. Due to the large proportion of subdivisions in the particles, the texture of the sheet is loose after forming to form a lobe.

In terms of equipment, the pressure of the tablet press is insufficient, and the tablet has just been formed without hardness. The rotating speed of the tableting machine is too fast, and the time for the particles to press first and then maintain the pressure is short, resulting in loose tablets. The pre-press wheel of the tableting machine did not work, and there was no pre-pressure exhaust to cause loose sheets. There are long and short errors in individual upstroke, resulting in some loose pieces.

In terms of drying, the drying temperature is too high, and the drying time is too long, which affects the particles to be too dry, too hard, and causes increased pressure, thus affecting the degree of disintegration. The particles are not sufficiently dried or not enough time, resulting in too strong viscosity.

3 Basic principle of production process monitoring system of traditional Chinese medicine tablets

3.1 The principle of near infrared spectroscopy

Near-infrared light is an electromagnetic wave between visible light and mid-infrared light. The American Society for Materials and Testing defines its wavelength range as 780-2500 nm. Near-infrared spectroscopy is mainly based on the frequency doubling and combined frequency absorption of organic compounds. It is a fast and non-destructive analysis technique. The near-infrared spectrum is mainly due to the anharmonic vibration of molecular vibration, which is generated when the molecular vibration transitions from the ground state to the high energy level. The most commonly observed bands in the near-infrared region are hydrogen-containing groups. The anharmonic constants of C-H, N-H, O-H, S-H and C = O, C = C stretching vibrations are very high. Schematic diagram of the near-infrared wavelength range is shown in Table 1.

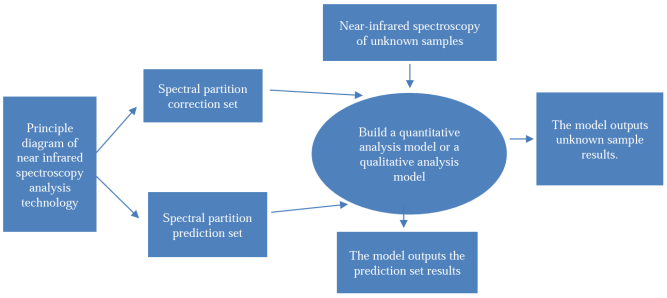

Fig.1 Principle diagram of near infrared spectroscopy analysis technology

Table 1 The schematic diagram of near-infrared wavelength range

Wavelength range	spectral classification	Spectral effect
200-400nm	UV	element
400-700nm	Vis	Appearance
700-2500nm	NIR	Principal component
2500-25000nm	IR	Functional

Many pharmaceutical companies have used NIRS for the acceptance of raw materials, quality analysis before feeding, on-line detection of mixing, drying, tableting, coating and other processes, and non-destructive analysis of end products. Infrared spectroscopy has the characteristics of strong penetration, no damage to the sample, environmental protection, suitable for qualitative and quantitative analysis, and long-distance online detection through optical fibers. The schematic of the NIR spectroscopy technique is shown in Figure 1.

3.2 The content of near infrared spectroscopy monitoring in the production of traditional Chinese medicine tablets

The general preparation process of traditional Chinese medicine tablets is as follows : processing of Chinese medicine raw materials, addition of excipients, mixing, granulation, drying, granulation, tableting (coating), quality inspection, packaging.

3.2.1 Chinese medicine raw materials

There are many kinds of raw materials of traditional Chinese medicine, such as plant medicine, animal medicine, mineral medicine and so on. Medicinal materials are the source of research and development and production of new traditional Chinese medicines, and their quality is a key factor affecting the safety, effectiveness and quality control of new traditional Chinese medicines. If there are common problems such as dyeing weight gain and adulteration of medicinal materials, research should be strengthened according to the needs of risk management. In addition, the study of exogenous pollutants in medicinal materials should be strengthened. According to the use of pesticides, veterinary drugs, fumigants, etc.in the production process of medicinal materials, as well as the risk of contamination by heavy metals and harmful elements, mycotoxins, etc.

3.2.2 Adhesives

The selection of adhesives plays an important role in the production of traditional Chinese medicine tablets. Improper use of adhesives or insufficient dosage, insufficient stirring, and poor adhesion between materials are the main factors leading to loose particles and excessive fine powder. The adhesive with strong toughness has a higher degree of plastic flow, which can improve the brittleness. Therefore, selecting the appropriate adhesive, appropriately increasing the concentration and dosage of the adhesive, and appropriately extending the stirring time are all methods to solve the unqualified hardness of traditional Chinese medicine tablets caused by it. The commonly used adhesives are starch slurry, starch and dextrin mixed slurry, syrup, molasses, etc.

3.2.3 Moisture of particles

Water is also the adhesive in the tablet. The decrease of water can reduce the elasticity, enhance the plasticity of the particles, and produce cohesion to help the tablet. After the particles are dried, if the moisture is too low, the elasticity of the particles will increase, the plasticity will decrease, and the hydrophilic adhesive will lose its adhesion to cause the pine. The water content in the granules is too high, which will cause adhesion, loose tablets, etc., so that the hardness of the tablets is reduced. The water content in the granules is controlled in different ranges due to different varieties, and the water content of the Chinese medicine granules should be controlled at 2 % -7 %[2].

4 System architecture implementation

The relevant monitoring of the production process of Chinese medicine tablets is shown in Figure 2.

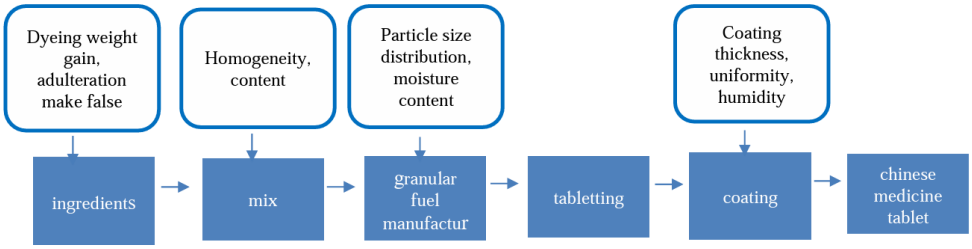

Fig.2 Monitoring related to the production process of traditional Chinese medicine tablets

4.1 The quality identification of traditional Chinese medicine raw materials by near infrared chromatography

Chinese medicinal materials are complex mixed systems. The measured infrared spectrum is the superposition of the absorption spectra of all the compounds contained in it. It is difficult to analyze the complexity. In addition, the main components of most medicinal materials are similar, and the spectra have certain similarities. It is of great significance to study the appropriate method of extracting spectral feature information to improve the stability and accuracy of the calibration model. The development and promotion of infrared spectrum processing software, such as chemometrics software and comparison software, will greatly promote the application of infrared spectrum in the quality control of raw materials of traditional Chinese medicine.

The application of infrared spectroscopy combined with chemometrics in the quality control of traditional Chinese medicine, including the use of derivative correction, standard normal transformation, multivariate signal correction, wavelet transform, data smoothing and other methods to process the original infrared spectrum, improve the signal-to-noise ratio of the spectrum, and improve the quality of the analysis signal. Using orthogonal partial least squares discriminant analysis, principal component analysis, partial least squares and other correction methods to process infrared spectral data, can quickly and accurately identify traditional

Chinese medicine and quantitatively analyze the active ingredients of traditional Chinese medicine.

4.2 Mixing process monitoring

The near-infrared spectrometer is used to monitor the uniformity of on-line mixing, which is fast, efficient and accurate. It can monitor the state of the sample in real time and understand the mixing status of the powder material in real time. The instrument is directly installed on the mixer and rotates with the mixer. The instrument monitors the uniformity of the mixture in real time online through the sapphire window. The data is transmitted through wireless WIFI. The analysis results are displayed in the form of mixture trend map and mixture sample spectrum. The mixing uniformity in the mixing process is clear at a glance, which greatly shortens the mixing time and improves the mixing efficiency.

In the production of traditional Chinese medicine tablets, specific technologies need to be used to monitor the mixing process to ensure the quality of the product. NIRS combined with the corresponding chemometrics algorithm can realize the online monitoring of the physical and chemical properties of the mixture, and can predict the mixing uniformity of the independent mixture samples produced under different process conditions, so as to predict the optimal mixing end point[3-5].

4.3 Coating process monitoring

Near-infrared spectroscopy was used to identify the end point of tablet coating and analyze the coating process.

4.3.1 Establish a model to determine the end point of coating

The partial least squares discriminant analysis model was used to monitor the coating process of tablet film coating and determine the coating end point. When establishing the partial least squares discriminant analysis model of all the spectra and the orthogonal partial least squares discriminant analysis model of all the spectra, the near-infrared spectral data of the film coating standard sheet including its chip core, film coating intermediate sheet and film coating end sheet were collected and standardized. The spectral data obtained after standardization were imported into the modeling software, and the principal components were extracted for modeling[6].

4.3.2 Coating eligibility discrimination performance was calculated.

According to the modeling conditions, the qualitative model and consistency test model based on principal component analysis and confidence interval proposed in this study were established respectively, and the discrimination performance of coating eligibility was calculated. Subsequently, the qualified rate at the coating end point was obtained by internal cross-validation, which was used as the discrimination threshold of the coating end point. Finally, the above model is used to calculate the model parameters and prediction qualification rate of each batch of the test set for the discrimination and process analysis of the coating end point.

5 Conclusion

The application of infrared spectroscopy in the quality control of traditional Chinese medicine is an important aspect of the application of infrared spectroscopy in recent years. The identification of traditional Chinese medicine by infrared spectroscopy is far more characteristic than other physical and chemical methods. It is a simple and specific identification method, which will become the main identification method of traditional Chinese medicine. Moreover, with the coordinated development of infrared spectroscopy hardware and software technology, infrared spectroscopy technology has been pushed to a new stage, making the technology more and more mature, the application scope more and more extensive, the information obtained more and more accurate, and adapt to various needs.

References

[1] Beer TD，Burggraeve A，Fonteyne M，et al. Near infrared and Raman spectroscopy for the in-process monitoring of pharmaceutical production processes [J]. Int J Pharm，2011， 417(1)：32-47

[2] Otsuka M，Tanabe H. Stability test for amorphous materials in humidity controlled 96-well plates by near-infrared spectroscopy [J]. Drug Dev Ind Pharm，2012，38(3)：380-385.

Podani, J. (1994) Multivariate Data Analysis in Ecology and Systematics. SPB Publishing, The Hague.

[3] Wahl PR，Georg F，Stephan S，et al. PAT for tableting：in line monitoring of API and excipients via NIR spectroscopy [J]. Eur J Pharm Biopharm，2014，87(2)：271-278.

[4] Aruna K, Bhaskar P , Viraj T , Gautam S. Development of Inline Near-Infrared Spectroscopy Method for Real-Time Monitoring of Blend Uniformity of Direct Compression and Granulation-Based Products at Commercial Scales. AAPS PharmSciTech.2022 Aug 24;23(7):235

[5] Sameer Talwar , Pallavi Pawar, Huiquan Wu. NIR Spectroscopy as an Online PAT Tool for a Narrow Therapeutic Index Drug: Toward a Platform Approach Across Lab and Pilot Scales for Development of a Powder Blending Monitoring Method and Endpoint Determination. AAPS J2022 Sep 28;24(6):103.

[6] Kim DW，Park JB，Lee SH，et al. Development of a Pro cess Analytical Technology(PAT)method using near-infrared spectroscopy system for evaluating an active coating process for a low-dose drug [J]. J Drug Deliv Sci Tec，2017，39(1)： 8-15.