Preparation and Quality Evaluation of Gan Mai Dazao Oral Liquid

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Abstract. Objective: To improve the dosage form and evaluate the quality of Gan Mai Dazao decoction. Methods: Gan Mai Dazao Oral liquid was extracted by traditional decocting method, and the quality of Jujube and Liquor ice in oral liquid was examined by TLC. Results: Gan Mai Dazao Oral liquid was clarified and odorless, which accords with the requirements of Chinese pharmacopoeia of 2015 edition for oral liquid. The TLC results were clear, well separated, highly specific and negative without interference. Conclusion: In the study the quality of Gan Mai Dazao Oral liquid prepared conforms to the requirements of the oral liquid of the pharmacopoeia, and provides a basis for further developing Gan Mai Dazao decoction.

1. Introduction

Ganmai Dazao Decoction is a classical prescription composed of Liquorice, wheat and jujube. It was first recorded in the Synopsis of the Golden Chamber [1]. The combination of three Chinese herbs has the characteristics of nourishing heart and regulating liver and making heart qi filling. It has the effect of nourishing the mind and soothing the mind, moderate, mild and urgent, softening the liver and relieving the urgency. It is mainly used to treat dysphoria of the viscera in women caused by over-thinking, impaired heart yin, loss of liver-qi and dryness of the viscera [2]. Ganmai Dazao Decoction is widely used in the treatment of depression, with good results and few side effects. Traditional Chinese medicine oral liquid is improved and developed on the basis of Traditional Chinese medicine decoction [3].Generally, it has the following advantages: (1) it can comprehensively extract various active ingredients from the decoction pieces to ensure the comprehensive efficacy of the preparation. (2) It absorbs and works quickly like as the decoction. (3) It overcomes the trouble of decocting and is easy to use. (4) After the concentration process, the dosage is small. The flavoring agent is added and the appearance and taste are more acceptable. (5) More suitable preservatives are added into the products, sterilized and sealed, and the quality is stable.

In this experiment, Ganmai Dazao Decoction was improved to prepare Ganmai Dazao Oral Liquid, which provided the basis for further development and research of Ganmai Dazao Decoction.

2. Materials and Methods

2.1. Experimental materials

Liquorice decoction pieces (Shaanxi Xingshengde Pharmaceutical Co., Ltd.), Liquorice reference substance (120904-200410, China Pharmaceutical and Biological Products Certification Institute). Wheat (Shaanxi Xingshengde Pharmaceutical Co., Ltd.), Jujube (Heyang of Shaanxi). Jujube reference substance (121040-201107, China Food and Drug Certification Research Institute). Ethyl acetate, Glacial acetic acid (Tianjin Tianli Chemical Reagent Co., Ltd.). Formic acid (Tianjin Kemio Chemical Reagent Co., Ltd.). N-butanol (Tianjin Sheng'ao Chemical Reagent Co., Ltd.) etc. Electronic Balance [Ohaus Instrument (Changzhou) Co., Ltd]. 101 Electric Heating Blasting Drying Box (Beijing Zhongxing Weiye Instrument Co., Ltd). Ultraviolet Osmotic Reflectometer (Shanghai Jingke Enterprise Co., Ltd). Specific Weight Bottle (Jiangsu Gaoyou Tianshan Instrument Factory). KQ-300DE Numerical Control Ultrasonic Cleaner (Ultrasound Instrument Co., Ltd. of Kunshan City). P-1 100*200 thin layer chromatographic cylinder (Shanghai Xinyi Instrument Factory Co., Ltd.). Thin layer silica gel G plate (Qingdao Ocean Chemical Co., Ltd.), LDEX-50KBS vertical pressure steam sterilizer (Shanghai Shen'an Medical Instrument Factory), etc.

2.2. Experimental method

2.2.1. Prescription. Liquorice 9 g; Wheat 15 g; Jujube 15.6g

2.2.2. Preparation of Ganmai Dazao Oral Liquid. The formulation was expanded by ten times weight. That is, 90.00 g Liquorice, 150.00 g Wheat, 100 jujube (about 156.00 g). The medicinal materials were washed, soaked for 30 minutes, decocted twice, each time 12 000 ml water, the first decoction for 2 hours, the second decoction for 1 hour. The decoction was put in a static state and precipitated overnight. The supernatant was filtered. The filtrate was concentrated to 400 ml and placed at room temperature. Sodium benzoate was added to 2.00 g and mixed. Packed into 20ml/ bottles and sterilized by steam circulation.

2.3. Quality evaluation

2.3.1. Preparation of control herbs. Liquorice: Weighed 1.50 g of Glycyrrhiza reference substance, added 5 ml water, ultrasonic extraction for 30 minutes, extracted through the pore size of 0.2μm microporous membrane and put in EP tube for reserve.

Jujube: Weighed 1.51 g jujube as control, added 5 ml water, ultrasonic extraction for 30 minutes, extracted through the pore size of 0.2μm microporous membrane and put in EP tube for reserve.

2.3.2. Preparation of negative reference substance. Negative reference materials were prepared according to the proportion of prescriptions.

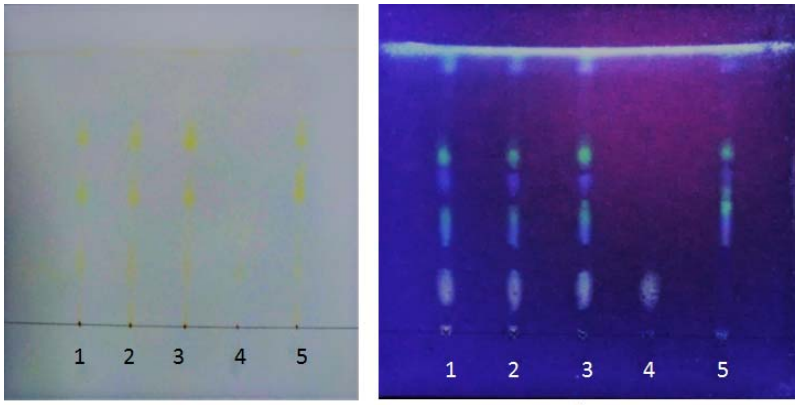
Liquorice negative control: weighed 3.05 g wheat and 2 (2.45 g) jujube, added 15 ml water, ultrasonic extraction for 30 minutes, extracted through the pore size of 0.2μm microporous membrane and put in EP tube for reserve.

Jujube negative control: weighed 1.89 g Liquorice and 3.01 g Wheat, added 15 ml water, ultrasonic extraction for 30 minutes, extracted through the pore size of 0.2μm microporous membrane and put in EP tube for reserve.

2.3.3. Thin layer chromatography (TLC)

1) Liquorice

According to the 2015 edition of the Chinese Pharmacopoeia, ethyl acetate-formic acid-glacial acetic acid-water (15:1:1:2) was the developing agent of liquorice. Three batches of oral liquid sample solution, negative reference solution and control solution were taken respectively. The sample solution, negative reference solution and control solution were about 2 μl. Pointed on the same silica gel G plate. After the thin layer plate was unfolded completely, take out, dry, spray with 10% sulfuric acid ethanol to show color. Put them into the oven at 105°C to make the spots clear. See Fig. 1 (a is the spots observed under sunlight, b is the spots observed under the UV365nm).



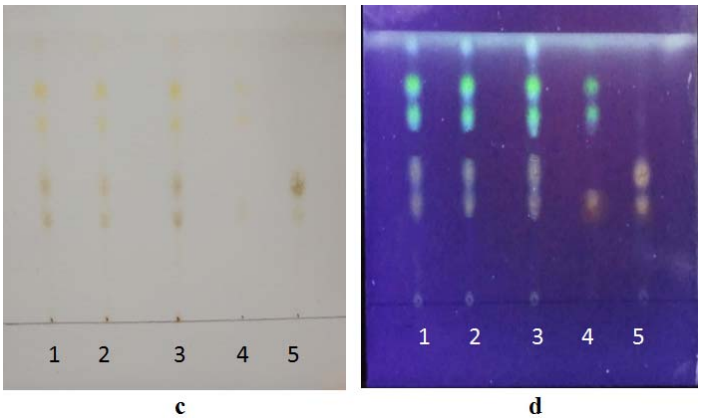
a **b**

1-3. Oral liquid sample; 4. Liquorice negative control; 5. Liquorice control

Figure 1. TLC of Liquorice

2) Jujube

According to the Chinese Pharmacopoeia of the 2015 edition, Jujube was selected toluene-ethyl acetate-glacial acetic acid (14:4:0.5) and n-butanol-glacial acetic acid-water (4:1:0.5) as the developing agent. Three batches of oral liquid sample solution, negative reference solution and reference solution were taken respectively. The sample solution, negative reference solution and control solution were about 2 μl. The samples were placed on the same silica gel G plate. After the thin layer plate was unfolded completely, the samples were taken out and dried. The samples were sprayed with 10% sulfuric acid ethanol for color rendering. The samples were placed in an oven at 105℃ until the spots were clear. The results showed that there were no obvious spots in jujube when the developing agent was toluene-ethyl acetate-glacial acetic acid (14:4:0.5), but in n-butanol-glacial acetic acid-water (4:1:0.5), the spots were obvious. Therefore, the developing system of jujube was n-butanol-glacial acetic acid-water (4:1:0.5) See Fig. 2 (c is the spots observed under sunlight, d is the spots observed under the UV365nm).



c **d**

1-3. Oral liquid sample; 4. Jujube negative control; 5. Jujube control

Figure 2. TLC of Jujube

3) Wheat

The price of wheat is cheap and the possibility of artificial fake is small. Pharmacopoeia and other related literature has not been reported by TLC, therefore, the experimental wheat does not do TLC identification.

According to the thin layer display, the chromatographic points were clear, well separated, highly specific, and negative without interference. The quality of Ganmai Dazao Oral Liquid is good if the samples, negative control and control have the same corresponding spots in the same place.

3. Quality control [3]

3.1. Quality requirements of oral liquid

The oral solution should be clarified except for other requirements. No mildew, rancidity, foreign matter, discoloration, gas or other deterioration may occur during storage, and a small amount of shaking and dispersible precipitation may be allowed.

3.2. PH value

The pH value of Ganmai Dazao oral liquid was 4.8, which accorded with the standard of pharmacopoeia. Therefore, the pH value of Ganmai Dazao oral liquid obtained by this method was qualified.

3.3. Relative density

The relative density of Ganmai Dazao Oral Liquid was determined to be 1.10 by specific gravity bottle method, which accorded with the standard of pharmacopoeia.

3.4. Content uniformity

According to the current version of the Chinese Pharmacopoeia minimum inspection method. The content uniformity of Ganmai Dazao oral liquid is in accordance with the regulations.

3.5. Microbial limit

According to the current edition of Chinese Pharmacopoeia, the microbial limit test is used. The biological limit of Ganmai Dazao oral liquid meets the requirements.

4. Results and conclusions

The oral liquor of Ganmai Dazao is a clarified dark brown liquid with unique fragrance, no precipitation and no odor. TLC showed that the samples of oral liquid, negative control and control samples had the same corresponding chromatographic points at the same position on the TLC, and the quality of Ganmai Dazao oral liquid was good.

30 min should be soaked before decocting, so that the effective ingredients in the medicinal herbs are easier to dissolve. After the decoction is precipitated one night, the supernatant is taken out and filtered again, so as to remove the insoluble impurities with large particle size in the liquid without affecting the taste of the oral liquid. During the thickening process, it should be condensed slowly with slow fire to avoid burnt paste and destroy the active ingredients in the liquid. Preservatives should be added to the 0.2%~0.5% of concentrated liquid, too much will affect the taste.

The Ganmai Dazao Oral Liquid prepared in this experiment has a good appearance and the quality meets the requirements of the current edition of the Chinese Pharmacopoeia. It provides a basis for further development and utilization of Ganmai Dazao Oral Liquid.

Acknowledgements

This work was supported by Shaanxi Project (Grant no. 2015KTCL03-14, 2012 KCT-20, 15JF001, 2015FWPT-01, 2018TD-005, 2018SF-285); Shaanxi Education Finance ((2013)171); and College Students' Innovative Entrepreneurial Training Programme (Grant no. 201710716010).

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