ISSN 2618-1584 Vol. 5, Issue 6: 99-105, DOI: 10.25236/FMSR.2023.050616

Analysis of Characteristics and Regularity of Chinese Patent Medicine for the Treatment of Irregular Menstruation Included in Chinese Pharmacopoeia Based on Data Mining

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Abstract: *The aim of this study was to explore and analyze the characteristics and patterns of Chinese patent medicine for treating irregular menstruation, as included in the Chinese Pharmacopoeia, using data mining techniques. We established an Excel database based on the prescriptions for irregular menstruation in the Pharmacopoeia of China, and used the TCM Inheritance Assistance Platform (TCMISS V3.0) software to analyze the data. After selecting medicines that met the criteria, we established a prescription database and conducted a statistical analysis of medication frequency, prescription rules, cluster analysis, and the distribution of herbs according to the four qi, five flavors, and meridians.Seventy-one Chinese patent medicines met the inclusion criteria, containing a total of 235 individual herbs. The most common dosage forms were pills and capsules. There were 10 primary flavors, including Angelica sinensis, Ligusticum wallichii, prepared Rehmannia root, Radix paeoniae alba, Poria cocos, Radix liquiritiae, Codonopsis pilosula, motherwort, vinegar with incense, and donkey-hide gelatin. These herbs are mainly used to tonify the blood, promote blood circulation, relieve pain, and warm the body. They are commonly attributed to the liver meridian and have a sweet taste. Using cluster analysis, we identified three groups of core drugs. Group 1 included Angelica, Ligusticum chuanxiong, and Rehmannia; Group 2 included white peony root, Poria cocos, and Dangshen; Group 3 included licorice, gelatin, motherwort, and vinegar with incense. The treatment of irregular menstruation in the Chinese Pharmacopoeia mainly involves blood tonics, blood-moving agents, and analgesics, providing an objective basis for the clinical use of Chinese patent medicine in the treatment of irregular menstruation.*

Keywords: *Data-mining, Irregular menstruation, Chinese patent medicine, Medication rule*

Irregular menstruation is a common symptom of clinical gynecology, irregular menstruation mainly refers to the occurrence of abnormal menstrual periods, cycles, and amounts of menstruation in women. Clinical irregular menstruation is also called menstrual disorders which have complex causes [1], such as cold stimulation, emotional disorders ,drug abuse, smoking and alcoholism,fatigue and dieting. Common manifestations include abnormal menstrual cycle, abnormal menstrual volume, dysmenorrhea, irregular bleeding and so on. With the fast pace of the development of life, women also face various pressures of study, work and life, which has caused a serious impact on women's physical and mental health. Many women in the face of these pressures, first in irregular menstruation, will bring the corresponding pain, long-term will also cause organic lesions. Furthermore, many gynecological diseases are related to women's feelings, if treatment is lost or mistreated, it can lead to the development of the disease and further affect their quality of life.

Menstrual irregularities were first described in the "Urgent Gold Prescription", at that time it was realized that irregular menstruation could be divided into two types: irregular menstrual cycles and abnormal menstrual volume. It was initially thought that the cause of irregular menstruation was a combination of external and internal injuries. After the Ming Dynasty, there was a clear understanding that irregular menstruation could be caused by a variety of factors [2], including external factors such as sex and love, internal injuries, irregular diet, and abnormal daily routines. Zhang Zhongjing proposed that irregular menstruation could be caused by cold, deficiency, qi injury, blood cold accumulation,

ISSN 2618-1584 Vol. 5, Issue 6: 99-105, DOI: 10.25236/FMSR.2023.050616

cold injury, and meridian problems. Nowadays, irregular menstruation is classified into four types: excessive bleeding, prolonged bleeding, scanty bleeding, and amenorrhea. The treatment of irregular menstruation is based on syndrome differentiation and can be divided into two categories: treatment of qi and blood and treatment of zang-fu organs. Treatment methods include nourishing qi, nourishing blood, invigorating blood circulation, treating qi and relieving pain, relieving liver, relieving depression, and tonifying kidney and regulating menstruation. There are various classification forms, treatment methods, and prescription forms, among which the most common syndrome types are cold syndrome, heat syndrome, deficiency syndrome, and empirical syndrome. This paper mainly studies Chinese patent medicines for the treatment of irregular menstruation in the 2020 Pharmacopoeia of China and analyzes data from the TCM Inheritance Assistance platform (TCMISS V3.0) to provide effective treatment methods for the clinical treatment of irregular menstruation in gynecology.

1. Data and methods

The source of this information is the "Chinese Patent Medicine Prescription for the Treatment of Irregular Menstruation" in the 2020 Pharmacopoeia of China.

The inclusion criteria for the drugs were that they had one or more effects related to irregular menstruation, such as promoting menstruation, reducing menorrhagia, treating amenorrhea, dysmenorrhea, early or late menstruation, and leakage. Chinese patent medicines with the same composition but different dosage forms were classified as a single variety.

The names of TCM decoction pieces referred to the records in the Pharmacopoeia. To avoid reducing the frequency of variables and affecting correlation analysis, all TCM decoction pieces were counted according to the students.

The data were processed and analyzed using the TCM Inheritance Assistance platform (TCMISS V3.0) software, which was provided by the Institute of Traditional Chinese Medicine at the China Academy of Chinese Medical Sciences.

Database establishment and data analysis: The existing drug information that met the volume and discharge standards was summarized into Excel and recorded into the prescription management module of the TCM inheritance auxiliary system one by one. The data were checked and reviewed again to ensure accuracy.

Statistical analysis: Statistical analysis was carried out using the data analysis system and statistical report system in the TCM inheritance auxiliary platform. The analysis included frequency statistics, grouping rules, cluster analysis, four qi, five flavors, and meridian distribution.

2. Result

2.1 Analysis of medication frequency

Table 1: Frequency 14 Drug frequency table

Traditional Chinese medicine name	Frequency	Percentage
Angelica sinensis	48	67.61%
Ligusticum wallichii	34	47.89%
Prepared rehmannia root	33	46.48%
Radix paeoniae alba	30	42.25%
Poria cocos	24	33.80%
Radix liquiritiae	19	26.76%
Codonopsis pilosula	18	25.35%
Motherwort	17	23.94%
Vinegar with incense	16	22.54%
Donkey-hide gelatin	14	19.72%

In the analysis of medication frequency for the 235 recorded Chinese medicines, the results showed a total frequency of 821 times for 10 medicines, including Angelica, xiong, Ligusticum, white peony root, Poria, licorice, Dangshen, herb, motherwort,vinegar, and gelatin, as shown in Table 1.

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2.2 Four qi, five flavors and classics of Traditional Chinese medicine

The distribution of the four qi, five flavors, and meridians of Chinese medicine were analyzed through prescription statistics. Refer to Tables 2, 3, and 4 for the details of each distribution.

Table 2: Frequency table of drug four

Four properties	Frequency	Percentage
Warm	248	30.21%
Flat	158	19.24%
Micro cold	113	13.76%
Tepor	83	10.11%
Cold	63	7.67%
Cool	13	1.58%
Heat	12	1.46%
Severe heat	9	1.10%
Severe cold	0	0.00%

Table 3: Frequtable of five drugs

Five tastes	Frequency	Percentage
sweet	354	43.12%
Pungent	300	36.54%
bitter	267	32.52%
Sour	55	6.70%
Micro bitter	36	4.38%
Salty	33	4.02%
Puckery	28	3.41%
Light	26	3.17%
Micro sweet	9	1.10%
Micro salty	1	0.12%
Micro pungent	0	0.00%
Slightly sour	0	0.00%
Slightly astringent	0	0.00%

Table 4: Frequency table of drug consumption

Channel tropism	Frequency	Percentage
Liver	400	48.72%
Spleen	335	40.80%
Kidney	246	29.96%
Heart	221	26.92%
Lungs	175	21.32%
Stomach	139	16.93%
Gallbladder	57	6.94%
Pericardium	42	5.12%
Large intestine	39	4.75%
Triple energizer	23	2.80%
Bladder	16	1.95%
Small intestine	4	0.49%

2.3 Cluster analysis of traditional Chinese medicine

Cluster analysis of the 71 Chinese prescriptions was conducted using the Euclidean distance method and longest distance type method, as shown in Figure 1. With a distance greater than 5.5, the TCM can be divided into three groups. The specific grouping is as follows: Group 1: Angelica, Chuanxiong, and cooked Rehmannia; Group 2: white peony root, Poria cocos, and Dangshen; Group 3: licorice, gelatin, motherwort, and vinegar incense.

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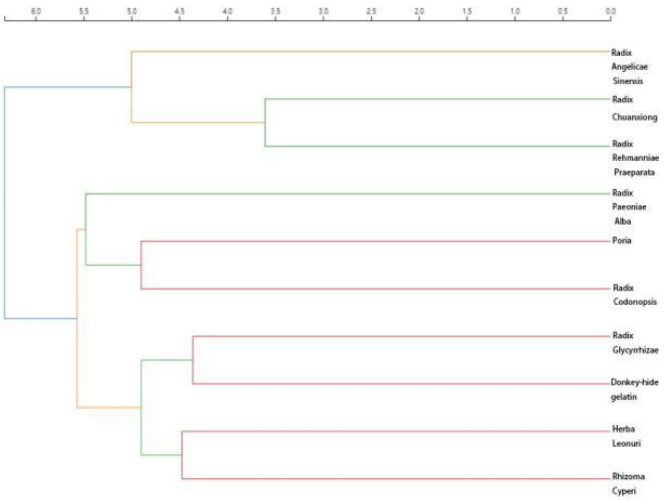

Figure 1: Cluster analysis plots

2.4 Complex network analysis

Table 5: Drug association table

Traditional Chinese medicine	Traditional Chinese medicine	Support	Confidence level	Elevation degree	Co-occurrence degree
Angelica sinensis	Ligusticum wallichii	0.44	0.65	1.36	31
Ligusticum wallichii	Angelica sinensis	0.44	0.91	1.35	31
Angelica sinensis	Prepared rehmannia root	0.39	0.58	1.25	28
Prepared rehmannia root	Angelica sinensis	0.39	0.85	1.26	28
Ligusticum wallichii	Prepared rehmannia root	0.38	0.79	1.7	27
Prepared rehmannia root	Ligusticum wallichii	0.38	0.82	1.71	27
Angelica sinensis	Radix paeoniae alba	0.37	0.54	1.28	26
Radix paeoniae alba	Angelica sinensis	0.37	0.87	1.29	26
Poria cocos	Angelica sinensis	0.25	0.75	1.11	18
Ligusticum wallichii	Radices paeoniae alba	0.24	0.5	1.18	17
Radices paeoniae alba	Ligusticum wallichii	0.24	0.57	1.19	17
Poria cocos	Prepared rehmannia root	0.23	0.67	1.44	16
Motherwort	Angelica sinensis	0.21	0.88	1.3	15
Liquorice	Angelica sinensis	0.21	0.79	1.17	15
Radices paeoniae alba	Prepared rehmannia root	0.21	0.5	1.08	15
Vinegar with incense	Angelica sinensis	0.2	0.88	1.3	14
Liquorice	Radices paeoniae alba	0.2	0.74	1.75	14
Liquorice	Ligusticum wallichii	0.2	0.74	1.55	14
Codonopsis pilosula	Angelica sinensis	0.2	0.78	1.15	14

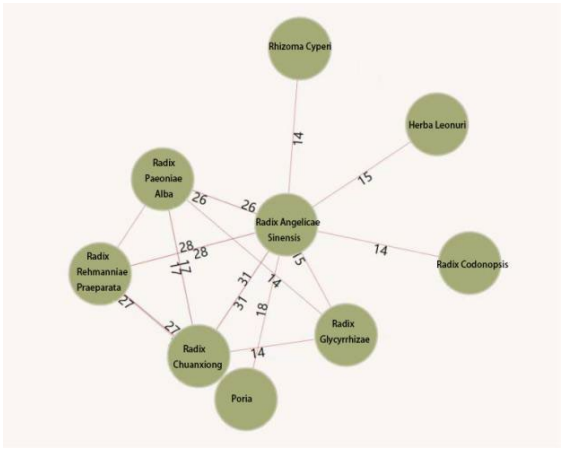

Figure 2: Drug association plot

Confidence is the probability of the occurrence of the former, the support is the probability of the

ISSN 2618-1584 Vol. 5, Issue 6: 99-105, DOI: 10.25236/FMSR.2023.050616

occurrence of the two; the confidence is the ratio of the probability of the latter, and the higher the relationship, the higher the positive correlation. Set confidence 0.50 and support 0.2, the drug association analysis is shown in Table 5. Drug association plots are shown in Figure 2.

3. Conclusion

From the analysis of drug frequency, it can be seen from Table 1 that in high-frequency Chinese medicine, Angelica, Chuanxiong, cooked Rehmannia, white peony root and Poria cocos occupy the top five in drug frequency. Modern pharmacology shows that these drugs can achieve menstrual regulation through various ways. Angelica [3], is sweet, xin, and warm. It returns to the liver, heart, and spleen and is typically used in doses of 6g to 12g. Angelica can invigorate blood circulation and menstruation, and provide pain relief. Experimental studies have shown that Angelica can have a bidirectional effect on the uterus. Depending on the state of uterine function, Angelica can cause uterine smooth muscle relaxation through volatile oil and ferulic acid, or uterine smooth muscle contraction through water-soluble or alcohol-soluble substances. Angelica's ferulic acid content has a nourishing effect on the blood and promotes blood circulation. The mechanism behind Angelica's ability to treat irregular menstruation is related to its anticoagulant, analgesic, and anti-inflammatory effects. Chuanxiong [4], is xin and warm and returns to the liver, gallbladder, and pericardium. The common dosage is 3g to 10g. Chuanxiong can promote blood circulation, promote qi, dispel wind, and relieve pain. The volatile oil found in Chuanxiong provides sedative analgesia and improves blood flow. The combination of Chuanxiong and Angelica has a significant effect in the treatment of dysmenorrhea. Among them, the ratio of Chuanxiong and Angelica at 2:3 has a blood-nourishing effect, while a ratio of 1:1 can promote blood circulation and alleviate blood stasis[5]. Mature Rehmannia is sweet and slightly warm and returns to the liver and kidney meridians. The common dosage is 6g to 15g, and it can nourish Yin and fill the pulp. Mature Rehmannia also enhances the immune regulation function of the blood system. Research has found that mature Rehmannia can improve estrogen levels [6], which is consistent with modern clinical treatment of menstrual diseases. White peony root is bitter, acidic, and slightly cold and belongs to the liver and spleen meridians. The common dosage is 6g to 15g, and it can nourish the blood and Yin and alleviate liver pain. When combined with other herbs, such as Fried White peony root and peony total side, it has a liver-protecting and analgesic effect [7]. White peony root, peony florin, and peony within side can regulate bone marrow hematopoiesis, which is consistent with the function of White peony root in the treatment of irregular menstruation[8]. Poria cocos is sweet, light, and flat and belongs to the heart, lung, spleen, and kidney meridians. The common dosage is 10g to 15g, and it can promote water permeation, strengthen the spleen, and calm the heart. Poria cocos mainly contains polysaccharides and Poria acid[9], Poria acid has anti-tumor, anti-inflammatory effect, and has the active ingredient of good health function. The first four high-frequency Chinese medicines, namely Angelica, Chuanxiong, cooked Rehmannia, and white peony root, are components of Siwu soup. Siwu soup is an empirical prescription for enriching blood and regulating menstruation and is regarded as a basic prescription in the treatment of irregular menstruation[10]. In the clinical application of Siwu soup, it is necessary to add or reduce ingredients based on syndrome differentiation [11], and flexibly use various herbs to achieve the desired effects of nourishing the blood, promoting circulation, and removing blood stasis. This approach can also help reduce adverse drug reactions. The therapeutic effect of Siwu soup combined with pure Western medicine is remarkable, and it can be used as a first-line prescription for the clinical treatment of irregular menstruation.

From the perspective of the four qi, five flavors, and meridians, warm and flat herbs are mainly used to regulate menstruation, while sweet and spicy herbs are also commonly used. Commonly-used herbs are attributed to the liver, spleen, and kidney. Traditional Chinese medicine believes that the treatment of irregular menstruation should target its underlying cause, and focus on regulating the liver, spleen, and kidney, which are closely related to menstruation. In clinical practice, irregular menstruation is classified into three categories: kidney deficiency, liver depression, and spleen deficiency [12]. In treatment, it generally starts from tonifying the kidney, liver and spleen to regulate the palace. In the treatment of irregular menstruation, the focus is on tonifying the kidney, liver, and spleen to regulate the uterus. Traditional medicine believes that the production of menstruation is closely related to the health of the kidneys, which are responsible for water metabolism. Therefore, the fundamental approach to regulating menstruation is to tonify the kidneys, replenish the essence and blood, and balance the qi and blood to ensure smooth menstruation. The spleen plays a crucial role in transporting and transforming nutrients and is the source of vital energy and blood. Nourishing the spleen and stomach can promote the production of blood and strengthen the spleen to invigorate Yang. Additional treatment methods may include dehumidification[13]. The liver is considered the sea of blood,

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and many female diseases are related to liver health. The liver is responsible for regulating the flow of qi and blood, and stagnation of liver qi can lead to dysmenorrhea, irregular menstruation, and excessive or insufficient bleeding. To address these issues, it is important to relieve liver stagnation and nourish the liver to ensure its proper function.

Cluster analysis revealed that the C1 drug combination included angelica, Chuanxiong, and cooked Rehmannia, which are all ingredients in Siwu soup. Angelica promotes blood circulation and nourishes the blood, while also relieving pain and regulating the meridians. Chuanxiong is considered a "qi medicine in the blood" that promotes blood movement, removes stagnation, and nourishes the blood and pulp. All three herbs have a blood-nourishing and menstruation-regulating effect and are commonly used to treat menstrual disorders caused by blood deficiency.The C2 drug combination included white peony root, Poria cocos, and Dangshen. White peony root can nourish the blood and soften the liver, and has an analgesic effect. Poria cocos is sweet and warm, and can strengthen the spleen and stomach, promote the transport of qi and blood, and serve as the basis for blood circulation. Dangshen is a qi-tonifying herb that can enhance the spleen and qi, making it an effective complement to white peony root[14]. These three flavors work together to promote qi and blood circulation. The C3 drug combination included licorice, gelatin, motherwort, and vinegar. Licorice has a sweet taste and can replenish qi, relieve pain, and harmonize the effects of various herbs. It is often used as a blood tonic. Gelatin can nourish Yin and tonify qi and blood, making it effective in treating conditions such as Yin and blood deficiency. Motherwort is known for promoting blood circulation and regulating menstruation. Adding vinegar to the mixture can enhance its effectiveness in promoting blood circulation[15], motherwort is the most commonly used drug in gynecology, commonly used in dysmenorrhea and abnormal uterine bleeding [16]. Vinegar can relieve liver stagnation and pain, and promote the effects of blood-moving herbs. Studies have shown that vinegar can inhibit uterine contractions and has astringent properties [17], These findings can be useful in clinical practice when treating menstrual disorders.

From the complex network analysis, the rules of 71 prescriptions were analyzed, in which Angelica and Chuanxiong appeared each other most frequently 31 times; Angelica and cooked Rehmannia bleeding each other 28 times; Chuanxiong and cooked ground appeared each other 27 times; and Angelica and white peony root appeared each other 26 times.

Irregular menstruation refers to gynecological disorders characterized by abnormal menstrual cycles, menstrual flow, and duration. In treatment, patients should be advised to take medication according to their menstrual cycle and maintain good hygiene, avoid exposure to cold temperatures, avoid overworking, maintain a balanced diet, and manage their emotions. Traditional Chinese medicine has developed a proprietary treatment for irregular menstruation, which includes 71 different herbal formulas and a total of 235 different herbs. The top ten most frequently used herbs are Angelica, Chuanxiong, cooked Rehmannia, white peony root, Poria cocos, licorice, Dangshen, motherwort, vinegar, and gelatin. These herbs are mainly warm or neutral in nature, and have sweet or pungent tastes. They are commonly attributed to the liver, spleen, and kidney.Analysis of the medication rules revealed that these commonly used herbs can be divided into three groups. Group1: includes Angelica, Chuanxiong, and cooked Rehmannia; Group 2 :includes white peony root, Poria cocos, and Dangshen; Group 3 :includes licorice, ejiao (gelatin), motherwort, and vinegar. These findings provide new insights and treatment options for irregular menstruation. In recent years, traditional Chinese medicine has become increasingly popular for the treatment of irregular menstruation, as it can address both the symptoms and underlying causes of the condition, reduce adverse reactions, and regulate endocrine disorders, ultimately improving the quality of life for women[18]. However, this study has certain limitations. It only summarizes the treatment of irregular menstruation using Chinese patent medicine from the Chinese Pharmacopoeia, and the data may not be comprehensive, leading to some deviation in the research results. Therefore, it is necessary to combine these findings with clinical treatment and closely monitor the patient's condition and response to medication. This will help achieve the expected treatment goals and reduce the occurrence of irregular menstruation in women.

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