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Study on the Medication Rules of Traditional Chinese Medicine (TCM) in Treating Hepatitis B Cirrhosis in the Compensated Stage Based on Data Mining

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Abstract: ***Objective:*** ***To apply data mining techniques to study the medication rules of Traditional Chinese Medicine (TCM) in the treatment of compensated hepatitis B cirrhosis. This research aims to provide clinical insights for the further development of TCM treatment for compensated hepatitis B cirrhosis.*** ***Methods:*** ***Using the keywords "hepatitis B cirrhosis compensated stage," "liver involvement," and "Traditional Chinese Medicine," searches were conducted on platforms such as CNKI and Wanfang Database. Articles published from January 2008 to 2023 related to the compensated stage of liver cirrhosis were selected to create a database. The included TCM prescriptions were then analyzed for frequency, association rules, and clustering using software tools like Excel 2021, SPSS Modeler 18, and SPSS 26.0.*** ***Results:*** ***A total of 44 prescriptions comprising 158 herbal medicines were selected. The five most frequently used herbs were Fuling (Poria), Danshen (Salvia miltiorrhiza), Chaihu (Bupleurum), Baishao (Paeonia lactiflora), and Baizhu (Atractylodes macrocephala).*** ***Conclusion:*** ***This study summarizes the medication rules for the treatment of compensated hepatitis B cirrhosis, aiming to standardize clinical medication practices.***

Keywords: Traditional Chinese Medicine, Hepatitis B Cirrhosis Compensated Stage, Accumulation and Aggregation, Medication Rules**.**

1. Introduction

Hepatitis B is one of the most prevalent infectious diseases in China. If left untreated or mismanaged, it can easily progress to liver cirrhosis and even liver cancer. Hepatitis B cirrhosis refers to the late stage of chronic hepatitis B caused by long-term chronic inflammation after infection with the Hepatitis B virus (HBV) [1]. Complications during the later stage of liver cirrhosis significantly decrease survival rates, making it especially important to intervene during the compensated stage to slow down the progression of cirrhosis [2]. Currently, Western medicine lacks effective antifibrotic drugs, mainly focusing on antiviral nucleoside analogs, which can have side effects like drug resistance. Based on the long-standing understanding and experience of TCM in treating cirrhosis, the combination of TCM and Western medicine in the treatment of hepatitis B cirrhosis shows distinct advantages. TCM plays a significant role in reducing viral replication, improving liver function, lowering serological indicators of liver fibrosis, and alleviating symptoms, thus addressing the limitations of Western medicine treatment [3]. To further study the medication rules for the compensated stage of hepatitis B cirrhosis and the empirical treatment methods used by renowned TCM masters, this paper utilizes modern data mining techniques to analyze and summarize the composition rules of prescriptions for treating this condition, providing a theoretical basis for future TCM treatments in hepatitis B cirrhosis.

2. Materials and Methods

2.1 Data Sources

Using the keywords "Traditional Chinese Medicine," "Hepatitis B Cirrhosis Compensated Stage," "Accumulation," and "Medication Rules," literature was searched on platforms such as CNKI and Wanfang Database. Articles published between January 2008 and 2023 related to hepatitis B cirrhosis in the compensated stage were selected to create a database. A total of 105 articles were retrieved.

2.2 Inclusion Criteria

This study selected prescriptions or case records that explicitly diagnosed "Hepatitis B Cirrhosis in the Compensated Stage" from the retrieved literature. The selected records included expert experiences, theoretical discussions, or clinical trials. Prescriptions required that the names of the herbal medicines be complete.

2.3 Exclusion Criteria

Literature without a clear diagnosis of "Hepatitis B Cirrhosis in the Compensated Stage." Animal experiment-related literature. Literature where Western medicine was the primary treatment, with TCM as a supplementary therapy. Literature where prescriptions were administered in external forms such as enemas or plasters. Literature where the prescriptions contained fewer than three herbs. In cases where multiple prescriptions shared the same name and herbal composition, only one was selected.

2.4 Data Standardization

The names of the herbal medicines in the selected data were standardized according to the "Pharmacopoeia of the People's Republic of China" (2020 Edition) before being entered into the system. For example, "Yunling" was standardized as *Fuling* (Poria), "Wushan" as *Shegan* (Belamcanda chinensis), and "Zaoti" as *Chonglou* (Veratrum nigrum).

2.5 Data Entry and Verification

The data of the 44 eligible prescriptions were entered into Excel 2021. After data entry, manual verification was conducted to identify and correct any errors that occurred during the entry process, ensuring the authenticity and reliability of the study.

2.6 Data Mining and Analysis

The created database of Chinese herbal medicines was analyzed using data mining techniques in Excel 2021 and SPSS Modeler 18.0, including drug frequency analysis and association rule analysis. Clustering analysis was performed using SPSS 26.0.

3. Results

3.1 Medication Frequency Statistics

A total of 44 prescriptions for the treatment of hepatitis B cirrhosis in the compensated stage using Traditional Chinese Medicine were collected, comprising 158 herbal medicines. The five most frequently used herbs were *Fuling* (Poria), *Danshen* (Salvia miltiorrhiza), *Chaihu* (Bupleurum), *Baishao* (Paeonia lactiflora), and *Baizhu* (Atractylodes macrocephala), with a frequency greater than 18%. The specific frequency of usage was more than 15 times, as shown in Figure 1.

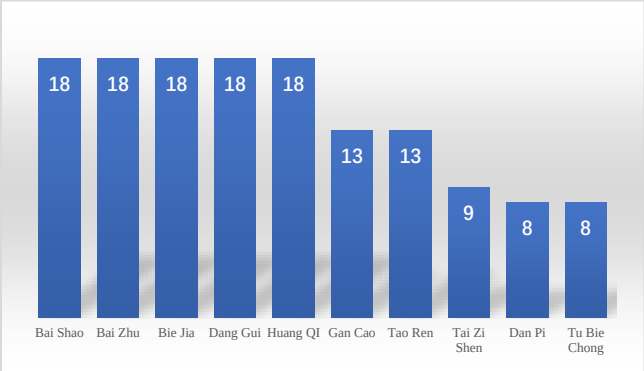

Figure 1: Frequency statistics of medicinal ingredients appearing more than 8 times in prescriptions for compensated hepatitis B cirrhosis

2.2 Association Rule-Based Prescription Pattern Analysis

An association rule analysis was conducted on all herbal medicines using SPSS Modeler 18.0. The maximum value for the antecedent was set to 2, with the "support count" for the combination of three herbs set at 18. For two-herb associations, the "support count" was set at 14. Association rules with a confidence level above 0.8 were selected for display. A total of 18 association rules were identified. The results of the associations are presented in Tables 1 and 2. Further visualization of the association rules was carried out, where the strength of the associations between herbs is represented by the thickness and darkness of the lines (Figure 2). The study shows that the core herbal medicines with the highest usage frequencies mainly include *Fuling* (Poria), *Chaihu* (Bupleurum), *Baishao* (Paeonia lactiflora), *Tubi Chong* (Eupolyphaga sinensis), and *Taoren* (Prunus persica).

Table 1: Three-drug Association Frequency with a Support Count of 5 for the Treatment of Compensated Hepatitis B Cirrhosis (Confidence Greater Than 0.8)

No.	Consequent Item	Antecedent Items	Instances	Confidence
1	Fu Ling	Bai Shao, Chai Hu	12	83%
2	Chai Hu	Bai Shao, Fu Ling	12	83%
3	Bai Shao	Chai Hu, Fu Ling	11	90%
4	Chai Hu	Tu Bie Chong, Fu Ling	8	87%
5	Chai Hu	Bai Shao, Dang Gui	8	87%
6	Fu Ling	Bai Shao, Dang Gui	8	87%
7	Fu Ling	Bai Zhu, Bai Shao	7	85%
8	Fu Ling	Bai Zhu, Chai Hu	7	85%
9	Chai Hu	Tu Bie Chong, Tao Ren	6	83%
10	Tu Bie Chong	Tao Ren, Chai Hu	6	83%
11	Chai Hu	Gan Cao, Bai Shao	6	83%
12	Bai Shao	Gan Cao, Chai Hu	6	83%
13	Bai Shao	Gan Cao, Dang Gui	5	80%
14	Fu Ling	Gan Cao, Dang Gui	5	80%
15	Fu Ling	Tai Zi Shen, Dan Shen	5	80%
16	Tao Ren	Tu Bie Chong, Dang Gui	5	80%
17	Chai Hu	Tu Bie Chong, Dang Gui	5	80%
18	Fu Ling	Bai Zhu, Dang Gui	5	80%

Table 2: Two-drug Association Frequency with a Support Count of 6 for the Treatment of Compensated Hepatitis B Cirrhosis (Confidence Greater Than or Equal to 0.8)

No.	Consequent Item	Antecedent Item	Instances	Support
1	Fu Ling	Bai Shao	12	27%
2	Chai Hu	Bai Shao	12	27%
3	Bai Shao	Chai Hu	11	25%
4	Chai Hu	Tu Bie Chong	8	18%
5	Chai Hu	Bai Shao	8	18%
6	Fu Ling	Bai Shao	8	18%
7	Fu Ling	Bai Zhu	7	15%
8	Fu Ling	Bai Zhu	7	15%
9	Chai Hu	Tu Bie Chong	6	13%
10	Tu Bie Chong	Tao Ren	6	13%
11	Chai Hu	Gan Cao	6	13%
12	Bai Shao	Gan Cao	6	13%

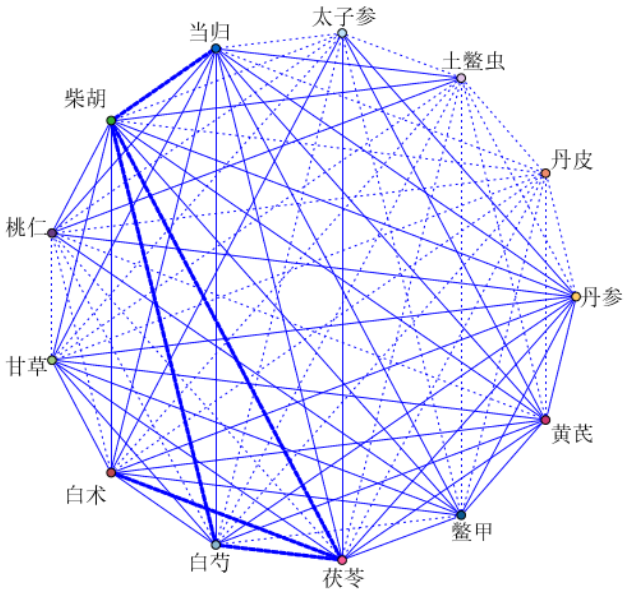

Figure 1: High-Frequency Drug Association Network for the Treatment of Compensated Hepatitis B Cirrhosis

3.3 Cluster Analysis

Cluster analysis was performed on 13 high-frequency herbal

medicines that appeared more than 15 times. Based on the dendrogram, the high-frequency medicines formed three core herbal pairs (Figure 2). The pair *Fuling* (Poria) - *Baizhu* (Atractylodes macrocephala) - *Gancao* (Licorice) - *Chaihu* (Bupleurum) - *Baishao* (Paeonia lactiflora) corresponds to the etiology of liver qi stagnation and spleen deficiency in hepatitis B cirrhosis compensated stage. The pair *Danggui* (Angelica sinensis) - *Danshen* (Salvia miltiorrhiza) - *Huangqi* (Astragalus membranaceus) - *Biejia* (Soft-shelled Turtle Shell) - *Taizishen* (Pseudostellaria heterophylla) corresponds to the etiology of liver and kidney yin deficiency, while the pair *Taizishen* (Pseudostellaria heterophylla) - *Taoren* (Prunus persica) - *Biejia* (Soft-shelled Turtle Shell) - *Danpi* (Moutan Cortex) corresponds to the etiology of liver qi stagnation and blood stasis.

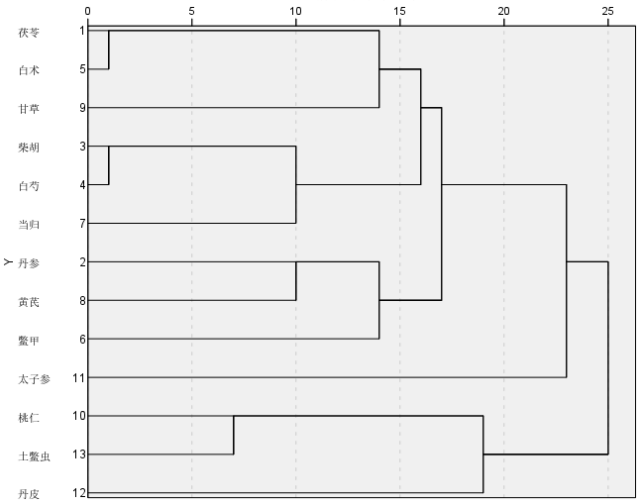

Figure 2: Clustering Dendrogram of High-Frequency Chinese Medicinal Herbs for the Treatment of Compensated Hepatitis B Cirrhosis

4. Analysis and Discussion

Hepatitis B cirrhosis manifests different main symptoms and diagnostic focuses at various stages of the disease, leading to different diagnoses. In Traditional Chinese Medicine (TCM), hepatitis B cirrhosis generally falls under categories such as "hypochondriac pain," "accumulation," "distension," and "jaundice." The *Maijing*: *Ping Wuzang Jiju Mai Zhen* (Pulse Classic: Diagnosis of Accumulation and Pulse Symptoms in the Five Zang Organs) states: "Diagnosed as liver accumulation, the pulse is string-like and fine, with pain in both hypochondria." The body lacks moisture. "The nails have become black and dry" [4]. This suggests that cirrhosis is an accumulative disease primarily characterized by right hypochondriac pain, lumps under the ribs, abdominal distention, poor appetite, and symptoms of liver stasis. Modern TCM considers the compensated stage of hepatitis B cirrhosis to fall under the category of "accumulation syndrome." "Accumulation" refers to a chronic disease of the blood, often severe in nature, with palpable abdominal masses and fixed pain [5]. Therefore, traditional TCM understanding of chronic hepatitis cirrhosis mainly focuses on blood stasis obstructing the meridians. TCM internal medicine suggests: "The primary treatment principle is to invigorate blood and resolve stasis, commonly used in practice." *Practical TCM Internal Medicine* notes, "The disease lies in the blood, and the basic treatment method is to invigorate blood, resolve stasis, soften hard masses, and disperse nodules." *Ling Shu: Bai Bing Shi Sheng* (The Spiritual Pivot: The Beginning of All Diseases) states, "Internal injury from worry and anger causes qi to reverse, obstructing the six meridians." The blood coagulates internally and fails to disperse. "All accumulation becomes stagnant" [6]. *Zhu Bing Yuan Hou Lun* (On the Origins of Diseases) suggests that the formation of accumulation generally involves a gradual development process: "When external pathogens invade the organs, initially, they do not form accumulation. If they stagnate and fail to resolve, they eventually lead to accumulation" [7]. Throughout the perspectives of medical masters across generations, accumulation is mainly caused by external cold, emotional stagnation, irregular diet, improper lifestyle, or excessive physical exertion. The pathogenesis mainly involves qi stagnation in the liver meridian, leading to poor blood circulation, stagnation, and blood stasis obstructing the vessels, resulting in dampness and phlegm accumulation, which gradually forms hardened masses. Clinical manifestations of the disease primarily present in four aspects: qi stagnation, damp obstruction, blood stasis, and deficiency damage. This formation follows a chronic and continuous process, a slow development from qi stagnation to blood stasis, with a mixture of deficiency and excess. Factors such as damp-heat, excessive alcohol consumption, and emotional stagnation over time contribute to poor blood and qi circulation, leading to blood stasis and obstruction in the hypochondrium, causing hypochondriac pain. The failure of water to flow downward into the bladder leads to abdominal distension and a protruding navel, representing "blood not moving results in water retention." As the disease originates in the blood and affects water metabolism, resolving blood stasis is key to treating cirrhosis [8]. The *Su Wen Zhi Zhen Yao Da Lun* (Basic Questions: The Great Treatise on True Essentials) states, "All damp swelling and fullness are related to the spleen" [9]. The spleen is the organ responsible for regulating water metabolism. When spleen function is impaired, water and dampness accumulate, leading to cirrhosis. Therefore, treatment should focus on strengthening the spleen and replenishing qi. If damp-heat persists, it can eventually lead to the depletion of yin fluids in the liver and kidneys, causing blood stasis and water retention. At this stage, the treatment should focus on nourishing yin and promoting diuresis. Currently, the main treatment principles for hepatitis B cirrhosis in the compensated stage are regulating qi, strengthening the spleen, resolving stasis, and nourishing yin.

4.1 Medication Frequency Analysis

Using Excel 1, SPSS Model 18, and SPSS software, a prescription database for the compensated stage of hepatitis B cirrhosis was established. Several aspects were examined to summarize the medication patterns in Traditional Chinese Medicine (TCM) for treating hepatitis B cirrhosis in the compensated stage, including medication frequency, association rule-based prescription patterns, the degree of association between herbs, the association network of high-frequency medicines, and cluster analysis of high-frequency herbs. In terms of medication frequency, the top 10 most frequently used herbs were *Fuling* (Poria), *Danshen* (Salvia miltiorrhiza), *Chaihu* (Bupleurum), *Shaoyao* (Paeonia lactiflora), *Baizhu* (Atractylodes macrocephala), *Biejia* (Soft-shelled Turtle Shell), *Danggui* (Angelica

sinensis), *Huangqi* (Astragalus membranaceus), *Gancao* (Licorice), and *Taoren* (Prunus persica). The medicinal effects of these herbs primarily focus on soothing the liver and relieving stagnation, strengthening the spleen and promoting qi circulation, resolving stasis and dispersing accumulations, and nourishing yin and tonifying the kidneys. These effects align with the pathogenesis of liver qi stagnation and spleen deficiency, liver and spleen blood stasis, and liver and kidney yin deficiency in the compensated stage of hepatitis B cirrhosis, as shown in Table 1.

4.2 Drug Analysis

The high-frequency drugs identified in this study primarily exhibit effects such as strengthening the spleen, promoting diuresis, soothing the liver, promoting qi circulation, nourishing yin, and resolving stasis. The selection of these drugs is based on the pathogenesis and disease progression of the condition. In the compensated stage of hepatitis B cirrhosis, liver qi stagnation and spleen deficiency are the primary etiologies. In the early stages of compensated cirrhosis, damp-heat toxins often obstruct the liver and gallbladder. Over time, the liver becomes overactive, affecting the spleen, leading to liver qi stagnation and spleen deficiency, characterized by a combination of both deficiency and excess. In the later stages of the disease, prolonged illness depletes the vital qi, preventing the spleen from nourishing the liver, ultimately leading to the deficiency of both liver and spleen. *Baishao* (White Peony) softens the liver, nourishes yin, and alleviates pain, making it an essential herb in treating liver cirrhosis. *Chaihu* (Bupleurum) strengthens the spleen and replenishes qi, while *Baizhu* (Atractylodes macrocephala) strengthens the spleen and supplements qi. *Fuling* (Poria) promotes diuresis and strengthens the spleen, while *Danshen* (Salvia miltiorrhiza) activates blood and promotes circulation. *Gancao* (Licorice) harmonizes the effects of all other herbs. In the compensated stage of liver cirrhosis, symptoms like pain or distention in the hypochondriac region, fatigue, and poor appetite are prominent. Many practitioners classify this condition under the category of “accumulation.” This condition is often the result of prolonged invasion by damp-heat toxins, leading to obstruction of the liver and gallbladder. Over time, this harms the spleen and stomach, disrupting the flow of qi and causing blood stasis. Eventually, it results in the formation of accumulations. The key pathogenesis is qi stagnation and blood stasis. The treatment principle is to focus on resolving blood stasis and promoting blood circulation. *Danfang* (Moutan Cortex) can nourish blood and replenish yin, while *Biejia* (Soft-shelled Turtle Shell) and *Taoren* (Peach Kernel) activate blood and resolve stasis, reduce swelling, and dissipate masses. The combined use of these herbs can strengthen the spleen, support the upright qi, expel pathogenic factors, and resolve blood stasis. In his *Yi Gui Tong Yuan Lun*, Ming Dynasty physician Li Zhongzi discussed the academic idea of “liver and kidney share the same source, treated together,” emphasizing the mutual influence between the liver and kidneys in both physiological and pathological contexts. *Tubiechong* (Ground Beetle) nourishes yin and strengthens the kidneys, while *Biejia* nourishes yin, clears heat, reduces steaming, softens masses, and dissipates nodules. The effects of the commonly used herbs in this study correspond to pathologies such as qi stagnation, spleen deficiency, liver depression, blood stasis, and yin deficiency, as shown in Figure 2.

Based on the analysis of the core herbal pairs frequently used in this study, the top 10 most frequently used herb pairs were: *Fuling* (Poria), *Danshen* (Salvia miltiorrhiza), *Chaihu* (Bupleurum), *Baishao* (White Peony), *Baizhu* (Atractylodes macrocephala), *Biejia* (Soft-shelled Turtle Shell), *Danggui* (Angelica sinensis), *Huangqi* (Astragalus membranaceus), *Gancao* (Licorice), and *Taoren* (Peach Kernel). These herb pairs mainly possess the functions of strengthening the spleen and promoting diuresis, activating blood and resolving stasis, and nourishing yin and clearing heat. It is evident that practitioners select herbs based on the different etiologies and pathogenesis of the compensated stage of hepatitis B cirrhosis. From the cluster analysis, three new formulas for treating the compensated stage of hepatitis B cirrhosis were identified: *Fuling* (Poria) - *Baizhu* (Atractylodes macrocephala) - *Gancao* (Licorice) - *Chaihu* (Bupleurum) - *Baishao* (White Peony) - *Danggui* (Angelica sinensis) - *Danshen* (Salvia miltiorrhiza) - *Huangqi* (Astragalus membranaceus), *Biejia* (Soft-shelled Turtle Shell) - *Taizishen* (Pseudostellaria), *Taoren* (Peach Kernel), and *Tubiechong* (Ground Beetle) - *Danpi* (Moutan Cortex). These formulas can provide reference for clinical applications and the practice of TCM in the treatment of this condition. However, there are limitations in this study. The selection of prescriptions is relatively small and only focuses on herbal formulas, so some expert experiences may have been overlooked due to the limitations of the research methods. Therefore, further improvements in research skills and technical algorithms are needed to better summarize and inherit the treatment experiences of renowned physicians. In conclusion, this study summarizes the medication patterns in Traditional Chinese Medicine for the compensated stage of hepatitis B cirrhosis in China. The effects of the drugs primarily focus on strengthening the spleen and promoting qi circulation, activating blood and resolving stasis, and nourishing yin and clearing heat. The selected prescriptions align with the etiologies of hepatitis B cirrhosis in the compensated stage. This study is beneficial for improving the efficacy of TCM in treating this condition and provides ideas for standardized and rational clinical treatment, ultimately reducing the burden on patients and improving their quality of life.

5. Conclusion

The key to treating the compensated stage of hepatitis B cirrhosis is to delay the progression of cirrhosis. Traditional Chinese Medicine (TCM) plays a significant role in reducing viral replication, improving liver function, decreasing fibrosis, and alleviating patient symptoms, thereby largely compensating for the shortcomings of Western medicine in treating this disease. Therefore, in clinical practice, the application of TCM should be promoted. Patients in the compensated stage of hepatitis B cirrhosis are commonly affected by key pathologies such as qi stagnation, spleen deficiency, damp-heat, and yin deficiency. In treating these patients, the treatment strategy should focus on identifying the causes based on these patterns and addressing them with appropriate herbal remedies. This approach can help slow the disease’s progression.

References

[1] Zhang Huan. Summarize the rule of differentiation and treatment of compensatory hepatitis B cirrhosis with traditional Chinese medicine through digging clinical medical records [D]. Shangdong University of Traditional Chinese Medicine, 2023.
[2] Yu Youxin; Tie Shenghua; Chen Siqing; Lan Ping. A discussion on the syndrome differentiation and treatment of hepatitis B cirrhosis in decompensated period [J]. Clinical Journal Of Chinese Medicine, 2023, 15(28): 122-125.
[3] Wang Lianying. The study of medication on rule of Professor Zhang Junchang based on data mining in the treatment of Hepatitis B cirrhosis compensation period [D]. Guangzhou University of Traditional Chinese Medicine, 2019.
[4] Zhang Jiazeng. Clinical Study of Jiawei Xia Yu Xue Formula Combined with the Blood Pricking Therapy in the Treatment of Hepatitis B Cirrhosis in Compensated Stage (Blood Stasis Blocking Collateral Type) [D]. Guangxi University of Traditional Chinese Medicine, 2023.
[5] Zhang Xu. Clinical study of Jiawei Gexia Zhuyu Granule in the treatment of hepatitis B cirrhosis in compensated stage (blood stasis blocking collateral type) [D]. Guangxi University of Traditional Chinese Medicine,2022.
[6] Wei Cuiting. Clinical research of Chaihu Guizhi Ganjiang Decoction and Danggui Shaoyao Decoction in thetreatment of hepatitis B liver cirrhosis in the compensatory phase [D]. Guangxi University of Traditional Chinese Medicine,2022.
[7] Zhu Qianxin; He Jingsong; Li Mingshun; Zhong Peiling; Chen Yingjie. Clinical Study on Ruangan Granules Combined with Entecavir for Treatment of Active Compensation Period of Hepatitis B Cirrhosis[J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2020,37(06):1024-1029.
[8] Zhang Jialing. The clinical study of Rougan Sanjie Pills combined with Entecavir in the treatment of hepatitis B liver cirrhosis in the compensatory phase (blood stagnation syndrome) [D]. Guangxi University of Traditional Chinese Medicine, 2021.
[9] Peng Mengnan. Clinical Study of Integrated Traditional Chinese and Western Medicine in The Treatment of Compensated Hepatitis B Cirrhosis Based on “Liver and Spleen Related” Theory. [D]. Guangzhou University of Traditional Chinese Medicine, 2020.