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Neo4j-Based Analysis of Traditional Chinese Medicine Clinical Patterns Used to Treat Irritable Bowel Syndrome

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Abstract: ***Objective: To apply Neo4j to construct a knowledge graph to explore the medication pattern of clinical treatment of irritable bowel syndrome, and to provide a new basis for the treatment of irritable bowel syndrome by Chinese medicine. Methods: By searching, collecting and screening the clinical type of literature on Chinese medicine treatment of irritable bowel syndrome in the database of China Knowledge Network in the past 5 years, using the prescriptions that meet the criteria in these literatures to establish an Excel database, and then applying the PHP 5.4 program code to the statistics of evidence type, frequency of Chinese medicine, frequency of use of Chinese medicine, as well as Chinese medicine operation. Results: The final results were visualized using Javascript with the Echarts v5.3.2 drawing plug-in. A total of 298 valid data were included, of which the IBS-D high-frequency syndrome was liver depression and spleen deficiency, and the use of Chinese medicines was mainly based on spleen-strengthening medicines, Rhizoma Atractylodis Macrocephalae and Poria cocos ranked the first in terms of the "pairwise correlation", while the IBS-C high-frequency syndrome was liver depression and Qi stagnation, and the use of Chinese medicines was mainly based on regulating Qi, and the highest "pairwise correlation" was Hojiblasta chinensis and Radix Angelicae Sinensis. Hovenia Citri reticulatae and Angelica sinensi had the highest "pairwise correlation". Conclusion: Irritable bowel syndrome (IBS) is centered on liver stagnation, and the main principle of treatment is to regulate qi and dredge the liver.***

Keywords: Irritable bowel syndrome, Knowledge map, Clinical patterns, Neo4j, Chinese medicine**.**

1. Introduction

Irritable bowel syndrome (IBS), a complex bowel dysfunction disorder, is characterized by diarrhea or constipation, which may be predominant or alternating (categorized as diarrheal IBS-D, constipated IBS-C, or mixed IBS-M, respectively), accompanied by abdominal pain, bloating, and altered bowel habits [1]. According to an epidemiological survey [2], approximately 10-15% of the world population is affected by IBS, and the number of patients is increasing every year. Because its pathogenesis and pathophysiological mechanisms are still unclear, the current clinical treatment of IBS is mainly based on targeted treatment, often using antidiarrheal drugs, antispasmodics, laxatives, probiotics, gastrointestinal dynamics, psychotropic drugs [3], but the long-term efficacy of treatment is not obvious, and the recurrence rate is high. Relevant clinical studies have shown that, compared with the single application of Western drugs, TCM can improve intestinal hypersensitivity by reducing the level of 5-HT [4] and inhibiting the NF-κB signaling pathway to protect the intestinal mucosa [5]. Therefore, in this study, we will search for patients with IBS who have been treated with TCM with significant effects in the past 5 years on the China Knowledge Network (CNN), and find out the intrinsic regularities by studying the combination and symptoms of each class of drugs, so as to provide new ideas for the clinical diagnosis and treatment of IBS.

Knowledge graph is a kind of formalized description of real-world things and their relationships through text extraction, data fusion, knowledge reasoning and other techniques, finally in the form of a graph [6]. Among them, Neo4j as a high-performance non-relational database, which not only provides a complete set of graph query language, but also can effectively support most of the graph data, so it has good scalability and security. Wang Jingwei et al [7] first constructed a knowledge graph of *typhoid fever* by storing the knowledge of the provisions of *typhoid fever*, which lays a solid foundation for the subsequent visualization study. In this study, we start from the nodes of evidence type, traditional Chinese medicine (TCM), and TCM operation to explore and generalize the laws of TCM treatment of IBS at multiple levels.

2. Information and Methods

2.1 Data Sources

"Irritable bowel syndrome," "traditional Chinese medicine," "combination of Chinese and Western medicine," and "combination of acupuncture and medicine" were used as subject terms for the search. The Knowledge Network database was used to collect and screen literature in the clinical research category of using Chinese medicine to treat irritable bowel syndrome in the past 5 years (April 1, 2019 to November 1, 2024).

2.2 Inclusion Criteria

(1) Literature that meets the diagnostic criteria of *Expert Consensus Opinions on Chinese Medicine Diagnosis and Treatment of Irritable Bowel Syndrome (2017)* [8]; (2) Clinical medicine as the subject of research journals or papers; (3) Clinical program design is reasonable and effective; (4) There is a treatment group and a control group, and a complete prescription of traditional Chinese medicine in the treatment

group.

2.3 Exclusion Criteria

(1) Literature that does not meet the diagnostic criteria of "irritable bowel syndrome"; (2) Literature that is not Linchuan research or the clinical therapeutic effect is not clear; (3) Literature that the research subjects are animals; (4) Literature that the main treatment is mainly Western medicine; (5) Literature that is published repeatedly.

2.4 Standardization of Data

According to the *Pharmacopoeia of the People's Republic of China [9] and the Chinese Pharmacopoeia* [10], the terms of Chinese medicine evidence and traditional Chinese medicine involved in the literature that met the inclusion criteria were standardized. For example, "Jiang Hanxia, Zhi Hanxia, Fa Hanxia" were standardized as Hanxia, and when there were big differences in properties, such as the drugs of Radix et Rhizoma Glycyrrhizae and Radix et Rhizoma Glycyrrhizae, Radix et Rhizoma Dioscoreae and Radix Rehmanniae, etc., the data were recorded separately.

2.5 Database Construction and Data Analysis

1) Data collection: collect 298 valid data that meet the criteria of inclusion, exclusion and observation of efficacy, and standardize them; 2) Database establishment: take the standardized 298 data as the research object, and use Excel to establish a data table to record the information of evidence type, traditional Chinese medicine and Chinese medicine operation. Run the JavaJDK environment, according to the two-layer frequency-weighted shearing algorithm for weight calculation, the results of the analysis were imported into the Neo4j Community3.5.25 to construct the graph database to generate the weight mapping, respectively. 3) Statistical analysis: Generate the overall relationship mapping in Neo4j, and use Python3.8.6 for descriptive analysis, statistics on the frequency and frequency of evidence type, Chinese medicine and Chinese medicine operation. The frequency and frequency of evidence type, Chinese medicine and Chinese medicine operation were counted by PHP5.4 program code; the relationship between evidence type and Chinese medicine, Chinese medicine and Chinese medicine, and evidence type and Chinese medicine operation were limited to the minimum support degree of 0.05 and the minimum confidence degree of 0.45, and the antecedent word was set as the antecedent event, and the posterior word was set as the concomitant event, and the confidence degree and weight were calculated respectively. Calculation of Weights: The ratio of the frequency of occurrence of a Chinese medicine or evidence type in the nodes of the hierarchy to the total frequency of occurrence of the Chinese medicine or evidence type in all nodes. For example, if the frequency of occurrence of "Rhizoma Atractylodis Macrocephalae" in the node "Liver Depression and Spleen Deficiency" is 115, and the frequency of occurrence of "Rhizoma Atractylodis Macrocephalae" in all nodes is 235, then "Rhizoma Atractylodis Macrocephalae" is in the node "Liver Depression and Spleen Deficiency". The weight of "Bai Zhu" in the node of "Liver Depression and Spleen Deficiency" is 0.48. In this study, the weight reflects the correlation between a certain type of evidence and traditional Chinese medicine within a certain range, and the correlation is positively correlated with the size of the weight. The calculated results were output, and the final results were visualized using Javascript language with Echarts v5.3.2 drawing plug-in [11].

3. Results

3.1 Frequency Statistics

In this paper, a total of 298 valid data that met the screening conditions were collected to generate the overall knowledge map of evidence types in Neo4j. Among them, there were 10 herbs with frequency of occurrence ≥ 25%, namely Rhizoma Atractylodis Macrocephalae, Poria cocos, Radix Paeoniae Alba, Tangerine peel, Codonopsis pilosula, Roasted licorice, Windbreak, Bupleurum chinense, Licorice, Aucklandia, as shown in Table 1, and there were two evidence types with frequency of occurrence ≥ 10%, namely Liver Depression and Spleen Deficiency, and Spleen and Kidney Yang Deficiency.

Table 1: Distribution of traditional Chinese medicine for treatment of IBS with frequency ≥ 25% (top 10)

Serial Number	traditional Chinese medicine	Frequency	Frequency
1	Rhizoma Atractylodis Macrocephalae	235	78.8591
2	Poria cocos	179	60.0671
3	Radix Paeoniae Alba	176	59.0604
4	Tangerine peel	158	53.0201
5	Codonopsis pilosula	141	47.3154
6	Roasted licorice	139	46.6443
7	Windbreak	122	40.9396
8	Bupleurum chinense	118	39.5973
9	licorice	80	26.8456
10	Aucklandia	76	25.5034

3.2 Calculation and Statistics of Confidence Level

Using PHP 5.4 program code to analyze the confidence level of evidence type and Chinese medicine, Chinese medicine and Chinese medicine, etc., the minimum support degree is set to 0.05, and the minimum confidence level is set to 0.45. The degree of support is the ratio of the frequency of the simultaneous occurrence of the antecedent events and the concomitant events to the total number of events, and the confidence level is the probability of the concomitant events occurring in the presence of the antecedent events. The circle in the pattern represents the node, and the arrow represents the relationship, specifically: "a→b", where "a" is the postposition, i.e., the accompanying event, and "b" is the antecedent, i.e., the antecedent event, the number of the parameter is the confidence level of "a" for "b". For example, in Figure 1, "Windbreak→diarrhea type", the probability of "Windbreak" being used together with "diarrhea type" is 86.93%, and the probability for the rest of the entries is the same. In summary, the results showed that the high-frequency Chinese medicines used in the treatment of IBS-C were Hovenia Citri Reticulatae and Angelica Sinensis, and the high-frequency Chinese medicines used in the treatment of IBS-D were Rhizoma Atractylodis Macrocephalae, Poria, Paeonia lactiflora and Pericarpium Citri Reticulatae, as shown in Figure 1. The high-frequency clinical syndromes of IBS were spleen and kidney Yang deficiency syndromes, liver depression and spleen deficiency syndromes, and the corresponding syndrome-Chinese medicine relationships are

shown in Figure 2. The high-frequency drug pairs of 26 entries were summarized in Figure 3. 2 plotting plug-in, the resulting data were plotted in Sankey diagram. See Figure 4, Figure 5 and Figure 6. The significance of Sankey diagram in this study is that the thicker the connecting line between the nodes, the higher the confidence level.

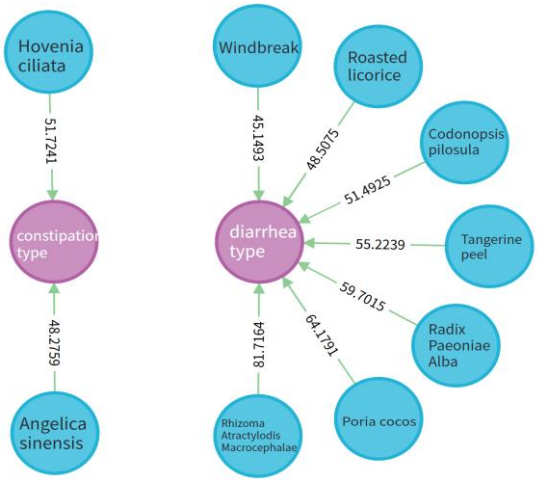

Figure 1: Relationship mapping of herbs in IBS-D and IBS-C with ≥45% confidence level

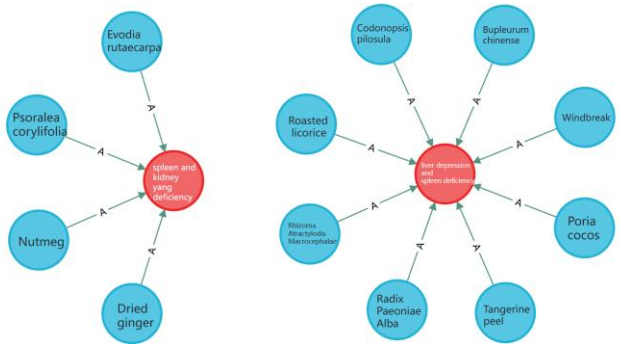

Figure 2: Plot of evidence-herbal medicine relationship with confidence level ≥45% in IBS treatment

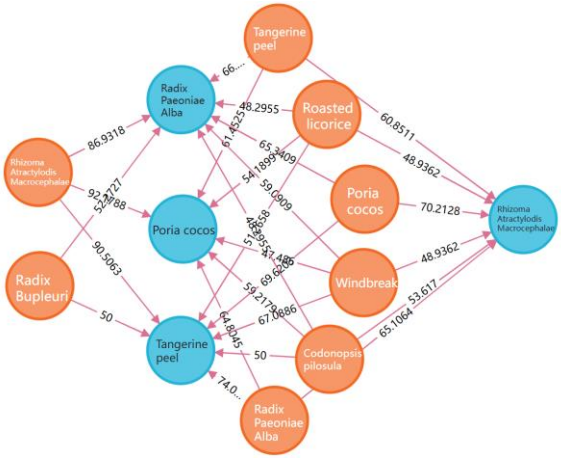

Figure 3: Plot of TCM-herbal medicine relationship with confidence level ≥45% in IBS treatment

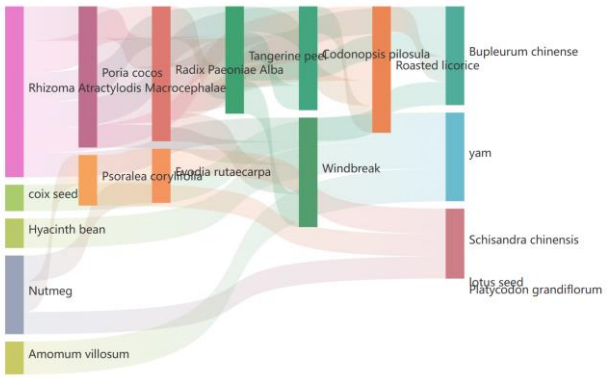

Figure 4: IBS Chinese medicine treatment prescription in Chinese medicine - Chinese medicine relationship Sankey diagram

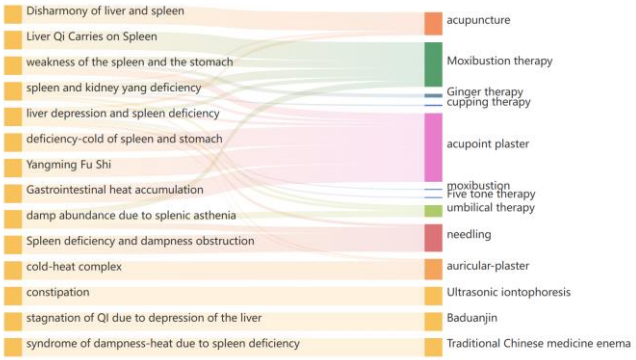

Figure 5: IBS Chinese medicine treatment in evidence type-Chinese medicine operation relationship Sankey diagram

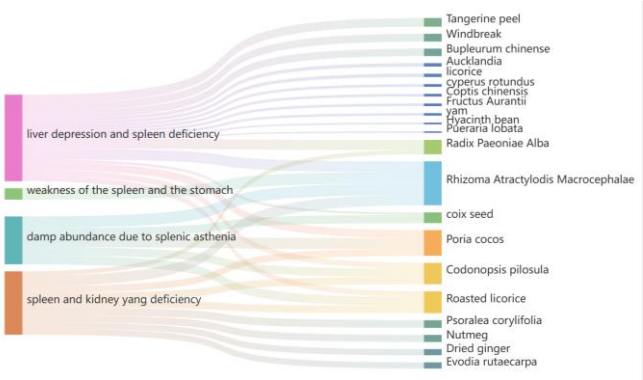

Figure 6: IBS Chinese medicine treatment in the evidence type - Chinese medicine relationship Sankey diagram

3.3 Statistics of Structural Relationship Graph

By using nodes to indicate semantic symbols and arrows to indicate the relationship between semantics, a "multi-relationship graph" can be obtained, such as Figure 7. For example, in Figure 7, the brown node represents the entity of "TCM operation", and the red node represents the entity of "certificate type", e.g, The certificate type of "Weakness of Spleen and Stomach" can be selected during the treatment period by using the TCM operation of "Acupuncture, Acupuncture Point Patching and Ginger Therapy", and in addition to "Weakness of Spleen and Stomach", "Acupressure" is also used in the treatment of "Deficiency of Liver, Spleen and Gastrointestinal Heat Accumulation", and so on, and the same applies to the rest of the entries.

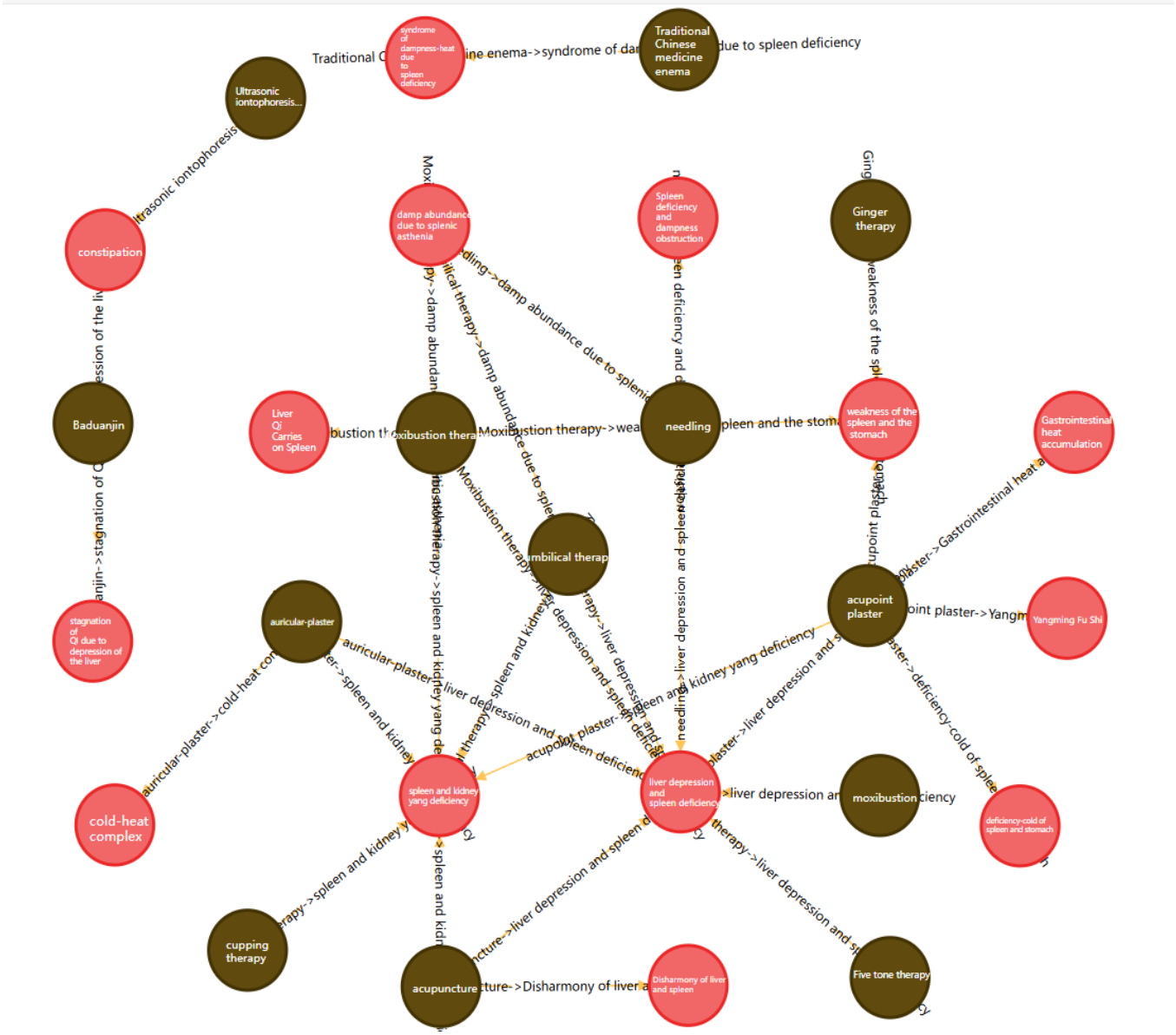

Figure 7: IBS evidence type-TCM operation-related knowledge mapping

The results of the current study showed that the IBS clinics were dominated by IBS-C and IBS-D. The most common disease pattern of IBS-C was liver depression and qi stagnation pattern, and the HF herbs used in treatment were Hovenia ciliata and Angelica sinensis; and the HF pattern of IBS-D was liver depression and spleen deficiency, and spleen and kidney yang deficiency. In Chinese medical theory, the liver is responsible for detoxification and regulation of qi. When the liver qi is depressed and the elimination and excretion are out of order, it can affect the transportation function of the spleen and stomach, as well as the conduction function of the large intestine. According to Prof. Fang Heqian, a master of national medicine, the stagnation of liver qi, the loss of its discharge and excretion, and the weakness of the spleen and stomach, the loss of their ascending and descending of turbidity, can cause the dregs of dregs of the liver to be misdirected and secreted into the interior, resulting in constipation [12].”*Suwen Lifting Pain Theory*” once said: “Anger is qi reversal, or even vomit blood and supper leakage.” Anger is the will of the liver, liver qi stagnation, excretion is not normal, can affect the spleen qi ascension and clear function. If the spleen qi does not ascend, the water and grain essence cannot be transported and transferred normally, but goes down to the large intestine, and diarrhea may occur. Combined with the clinical situation, it can be seen that a long-term state of liver depression can affect the normal function of the patient’s brain-intestinal axis. In the case of liver depression, the body’s emotional state such as anxiety and depression may be aggravated, which in turn affects the nervous system’s regulation of the intestine. Such emotional factors can affect the motor, secretory, and sensory functions of the intestine through the neuroendocrine pathway. Treatment is basically based on the use of methods such as dredging the liver and regulating the liver and spleen. In terms of frequency of medication, the first four tastes of Chinese herbal medicines commonly used in spleen-kidney yang deficiency syndrome were Psoralea corylifolia, Nutmeg, Evodia rutaecarpa, Dried ginger. Clinical studies have shown [13] that Psoralea corylifolia, Nutmeg, Evodia rutaecarpa have a multi-component, multi-target, and multi-pathway mechanism of action in the treatment of spleen-kidney yang deficiency in irritable bowel syndrome, and play a role in improving the metabolism of the gastrointestinal mucosa, regulating the response of key pathways, and enhancing the

therapeutic effect. Although the specific mechanism of action of dried ginger is not clear in the existing references, it is hypothesized from the perspective of Chinese medicine theory that it may have the effect of warming yang and dispersing cold and improving gastrointestinal function in the treatment. Among them, Psoralea corylifolia-Nutmeg is a commonly used clinical pair of drugs to warm the spleen and kidney, and the formula, called Er Shen Wan, is derived from *Puji Ben Fang* (a traditional Chinese medical text). It is often combined with Schisandra powder (Schisandra chinensis, Evodia rutaecarpa) to form the famous formula Si Shen Wan for the treatment of renal ejaculation due to deficiency of Yang in the spleen and kidneys. The first eight tastes of Chinese medicine commonly used in liver depression and spleen deficiency are Rhizoma Atractylodis Macrocephalae, Radix Paeoniae Alba, Pericarpium Citri Reticulatae, Poria cocos, Codonopsis pilosula, Radix Saposhnikoviae, Radix Bupleuri, roasted licorice, and the clinical treatment of liver depression and spleen deficiency is usually in accordance with the therapeutic principle of "treating the middle jiao as if in balance, and it is not flat. The most commonly used drug is Rhizoma Atractylodis Macrocephalae, which is sweet and bitter in taste, warm in nature, and belongs to the Spleen and Stomach meridians. Its main effects are to strengthen the spleen and benefit the qi, dry up dampness and diuresis, stop sweating and stabilize the fetus. In the *Materia Medica*, Rhizoma Atractylodis Macrocephalae, is "the key medicine for supporting the spleen and stomach, dispersing dampness and removing paralysis, eliminating food and removing lumps". From the theory of traditional Chinese medicine, Rhizoma Atractylodis Macrocephalae, is especially suitable for water-dampness internal diseases caused by spleen deficiency, because of its sweet and warm nature can nourish the spleen and stomach, and bitter and warm nature can dry dampness, by strengthening the spleen to transport water-dampness, to achieve the purpose of eliminating dampness. Research [14] showed that Rhizoma Atractylodis Macrocephalae has a bidirectional regulation of gastrointestinal function, and its volatile oil fraction, water-eluting liquid fraction and polysaccharide fraction can promote gastrointestinal peristalsis, while petroleum ether fraction and alcohol-eluting liquid fraction play the opposite role. Clinically, Rhizoma Atractylodis Macrocephalae can be adjusted to achieve the therapeutic purpose by adjusting the drug dosage of Rhizoma Atractylodis Macrocephalae and drug pairing. For example, Prof. Yuan [15] based on the new formula of Hovenia aristata Tang to treat irritable bowel syndrome, and the therapeutic efficacy was remarkable. This formula is characterized by the reuse of Rhizoma Atractylodis Macrocephalae, adjusting the dosage of Citrus aurantium and Rhizoma Atractylodis Macrocephalae from 1:2 to 1:5, which is intended to enhance yang and benefit qi, and strengthen the spleen and regulate the intestines to restore the normal function of the intestines and stomach. Based on Neo4j analysis, high-frequency pairs were found to be Rhizoma Atractylodis Macrocephalae → Windbreak, Rhizoma Atractylodis Macrocephalae → Poria cocos, Rhizoma Atractylodis Macrocephalae → Poria cocos, Tangerine peel → Rhizoma Atractylodis Macrocephalae → Radixeiaeoniae Alba, and Roasted licorice, etc. Among them, the confidence level of "Rhizoma Atractylodis Macrocephalae → Windbreak" was 94.3%. Rhizoma Atractylodis Macrocephalae → Windbreak" had a confidence level of 94. 3%, Rhizoma Atractylodis Macrocephalae for tonifying qi and strengthening the spleen of the key drugs, Windbreak for the wind medicine in the humectant, there is the effect of qi activation of blood and blood stasis, the two with both tonifying the spleen and benefiting the qi, but also can get rid of the evil out of the evil, to eliminate the complementary to the evil evil of the disadvantages. Clinical experimental studies have also proved that Rhizoma Atractylodis Macrocephalae - Windbreak has a synergistic protective effect on the intestinal mucosal barrier [16]. The confidence level of Rhizoma Atractylodis Macrocephalae and Poria cocos is 93%, and the combination of the two can eliminate phlegm and water in the chest and abdomen and tonify the spleen and qi, which is widely used in the *Treatise on Miscellaneous Diseases of Typhoid Fever*, mainly to treat a class of diseases with abnormal water-liquid metabolism. Depending on the location of the disease where water and drink are internally arrested, the composition of the ling-ju remedy is correspondingly different [17]. If it stops below the heart or in the chest, use Ling Gui Zhu Gan Tang; if it stops above or below the surface, use Wu Ling San. "Tangerine Peel → Bupleurum chinense and Windbreak are also closely related. Tangerine peel has the effect of regulating qi and strengthening the spleen, Bupleurum chinense detoxifies the liver and resolves depression, reconciles the Shaoyang, and Windbreak is pungent, warm and detoxifies the epidermis. The combination of the three can regulate the spleen and stomach and elevate the spleen and qi.

4. Conclusion

Neo4j is a high-performance graph database. It integrates data from different systems and formats into a graph structure. It clearly demonstrates the existence of complex interrelationships among clinical data. This facilitates the in-depth mining of potential knowledge in clinical data. It also provides new ideas and methods for clinical medication [18]. This study explored the law of TCM medication in IBS, analyzed the high-frequency patterns of the disease, TCM and medication pairs, and visualize the traditional Chinese medicine operations corresponding to different syndrome types. This clearly showed the relationship between different factors and provided certain references for the clinical treatments or related research studies. However, there are still many shortcomings, such as the lack of drug dosage in the selected formulas and the lack of extraction and analysis of tongue and pulse, etc. In the future, the clinical features will be further summarized to provide new ideas and methods for the diagnosis and preventive treatment of irritable bowel syndrome.

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