Analysis of Clinical Medication Rule of *Trigonellae* Semen Based on Data Mining

Jing-Yi Qiao¹,a, Jing Chen¹,b, Jing-Jing Shi¹,c and Ming-San Miao¹,d,*

¹Henan University of Chinese Medicine, Zhengzhou, China

a qiaojingyi618@126.com, b chenjingliuhua@163.com, c shijingjing515@126.com,
d miaomingsan@163.com

**Keywords:** Trigonellae Semen, Data mining, Medication rule

**Abstract. Objective:** To further explore the clinical medication rule of *Trigonellae* Semen and analyze the potential compatibility relationship of traditional Chinese medicine (TCM). **Method:** The clinical application literature of *Trigonellae* Semen in CNKI and Wanfang database is screened. Excel 2013 is used to establish the database of the selected prescriptions, and Apriori algorithm of SPSS Modeler 14.1 is used to analyze the association rules, mining the application rules of *Trigonellae* Semen in clinical compatibility. **Result:** Among the 71 prescriptions selected, 186 Chinese medicines are used, 730 times in total. Except *Trigonellae* Semen, the top five high-frequency Chinese medicines are Angelica, Astragalus, Epimedium, Atractylodes Macrocephala and Prepared Rhubarb. The most commonly used Chinese medicines are deficiency-Nourishing Drugs, blood-activating and Stasis-eliminating, and heat-clearing drug. Sweet, pungent and bitter in flavor, warm in nature, the three meridians of liver, kidney and spleen are the most frequently used. Fourteen highly correlated combinations of traditional Chinese medicines are obtained. Fifteen and thirteen combinations of TCM are obtained from the analysis of medication for gynecological and renal diseases. **Conclusion:** *Trigonellae* Semen has obvious compatibility relationship with TCM in the use of gynecological and kidney diseases. We should attach importance to the compatibility of *Trigonellae* Semen with Cyperi Rhizoma, Semen Litchi, Corydalis Rhizoma, Angelica, Prepared Rhubarb and Rhizoma Smilacis Glabrae in order to produce better clinical efficacy.

1. Introduction

*Trigonellae* Semen comes from the seeds of *Trigonella foenum-graecum* L. of Leguminosae Butterfly Flower Subfamily[1]. It has the function of warming the kidney, strengthening yang, etc. It is often used for kidney asthenia, abdominal coldness, small intestinal hernia. In recent years, the research on *Trigonellae* Semen is increasing day by day, and found that it has many functions such as hypoglycemia, antioxidant, anti-cancer and so on[2]. In order to expand and extend the clinical application of *Trigonellae* Semen and give full play to its medical characteristics, this paper discusses the law of clinical application of *Trigonellae* Semen in the way of data mining. It is hoped that the potential relationship between *Trigonellae* Semen and other TCM can be found from the existing medication methods, so as to expand the scope of clinical medication and provide some data reference for further in-depth study of *Trigonellae* Semen.

2. Materials and Methods

2.1. Data Sources

From January 1, 1998 to December 31, 2018, in CNKI, we selected "medical and health science and technology" category, searched "Trigonellae Semen" and "clinical" in full text, and searched "Trigonellae Semen" and "clinical" in Wanfang Journal Database.
2.2. Inclusion and Exclusion Criteria
Select the clinical research literature of compound Chinese medicine containing Trigonellae Semen, exclude repetitive literature and review, the literature of theoretical discussion, non-clinical trials, single Chinese medicine or no specific composition of TCM.

2.3. Data Processing
According to the above criteria, 71 literatures are screened out and 71 prescriptions are obtained. The names, classifications and properties of TCM included in them are unified by referring to the Chinese Pharmacopoeia (Edition 2015)\(^3\) and the Clinical Chinese Pharmacy\(^4\). The names of the diseases treated are classified according to the National Standard of the People's Republic of China, the Disease Part of the Terminology of Clinical Diagnosis and Treatment of Traditional Chinese Medicine.

2.4. Data Analysis
Excel 2013 is used to input the information of the selected Chinese medicines into the database, SPSS Modeler 14.1 statistical software is used to analyze the standard Chinese medicines, and Apriori model is used to analyze the association rules.

3. Results
3.1. High Frequency Chinese Medicine and Classification Analysis
All prescriptions used 186 kinds of TCM, involving 20 kinds of TCM, with a cumulative frequency of 730 times. Among them, 23 kinds of TCM with frequencies more than 8 are used, with a cumulative frequency of 356 times, accounting for 48.77%. Except Trigonellae Semen, Angelica, Astragalus, Epimedium, Atractylodes macrocephala and Prepared Rhubarb are the most frequently used high frequency Chinese medicines. See Table 1 below for details. The most frequently used drugs are deficiency-Nourishing, blood-activating and stasis-eliminating, heat-clearing, and then are activating medicinal materials, warm heart medicine and damp-excreting drugs, which are consistent with the use of single TCM. Sweet (325 times, 29.93%), pungent (295 times, 27.16%) and bitter (304 times, 27.99%) in tastes, warm (324 times, 44.38%) in properties, the three meridians of liver (422 times, 23.79%), kidney (354 times, 19.95%) and spleen (286 times, 16.12%) are the most frequently used.

<table>
<thead>
<tr>
<th>TCM</th>
<th>Frequency</th>
<th>Percentage</th>
<th>TCM</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigonellae Semen</td>
<td>71</td>
<td>100.00</td>
<td>Prepared Rhubarb</td>
<td>15</td>
<td>21.13</td>
</tr>
<tr>
<td>Angelica</td>
<td>30</td>
<td>42.25</td>
<td>Semen Cuscutae</td>
<td>16</td>
<td>22.54</td>
</tr>
<tr>
<td>Astragalus</td>
<td>25</td>
<td>35.21</td>
<td>Rhizoma</td>
<td>14</td>
<td>19.72</td>
</tr>
<tr>
<td>Epimedium</td>
<td>21</td>
<td>29.58</td>
<td>Radix Codonopsis</td>
<td>14</td>
<td>19.72</td>
</tr>
<tr>
<td>Atractylodes</td>
<td>16</td>
<td>22.54</td>
<td>Paeoniae Radix</td>
<td>12</td>
<td>16.9</td>
</tr>
</tbody>
</table>

3.2. Classification of Main Diseases
The diseases treated by 71 prescriptions included in the criteria are analyzed. 10 kinds of TCM diseases contain gynecological diseases (23 times, 32.39%) and kidney diseases (21 times, 29.58%) are the most common.

3.3. Analysis of High Frequency Association Rules of TCM Containing Huluba Prescription
SPSS Modeler 14.1 is used to analyze the association rules of TCM with frequency (≥8). The data flow of association rules of "data source→type→network" is established, and the compatibility relationship between TCM is further excavated by Apriori model. Under the conditions of 16% support, 90% confidence and 2 max preconditions, 14 combinations of highly correlated drugs are
excavated, and the promotion degree of all combinations is greater than 1, which indicated that the 14 combinations of TCM had statistical significance[5].

3.4. Analysis of Medication Regularity of *Trigonella* Semen for Common Diseases

3.4.1. Analysis of Drug Use in Gynecological Diseases

Fifteen Chinese herbal medicines with frequency (≥6) in the treatment of gynecological diseases are analyzed, and 15 pairs of medicines with statistical significance are obtained under the conditions of 29% support, 100% confidence and 2 max preconditions. Details are shown in Table 2.

Table 2. Analysis of Association Rules of Traditional Chinese Medicine for Gynecological Diseases

<table>
<thead>
<tr>
<th>Chinese medicine combination</th>
<th>Support Degree</th>
<th>Confidence Level</th>
<th>Lifting Degree</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trigonella</em> Semen-Angelica</td>
<td>58.33</td>
<td>100</td>
<td>1.04</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Epimedium</td>
<td>37.50</td>
<td>100</td>
<td>1.04</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Radix Morinda Officinalis</td>
<td>29.17</td>
<td>100</td>
<td>1.04</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Prepared Rhubarb</td>
<td>29.17</td>
<td>100</td>
<td>1.04</td>
</tr>
</tbody>
</table>

3.4.2. Analysis of Drug Use in Kidney Diseases

In this study, 10 kinds of Chinese herbal medicines with frequency (≥6) are used to treat kidney diseases, and 13 pairs of medicines with statistical significance are obtained under the conditions of 35% support, 100% confidence and 2 max preconditions. Details are shown in Table 3.

Table 3. Analysis of Chinese Medicine Association Rules for Kidney Diseases

<table>
<thead>
<tr>
<th>Chinese medicine combination</th>
<th>Support Degree</th>
<th>Confidence Level</th>
<th>Lifting Degree</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trigonella</em> Semen-Astragalus</td>
<td>68.18</td>
<td>100</td>
<td>1.05</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Angelica-Prepared Rhubarb</td>
<td>45.45</td>
<td>100</td>
<td>1.05</td>
</tr>
<tr>
<td>Prepared Rhubarb-Rhizoma Smilacis Glabrae</td>
<td>36.36</td>
<td>100</td>
<td>1.47</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Rhizoma Smilacis Glabrae Angelica</td>
<td>36.36</td>
<td>100</td>
<td>1.05</td>
</tr>
<tr>
<td><em>Trigonella</em> Semen-Rhizoma Smilacis Glabrae-Prepared Rhubarb</td>
<td>36.36</td>
<td>100</td>
<td>1.05</td>
</tr>
</tbody>
</table>

4. Discussion

4.1. Clinical Compatibility Analysis of *Trigonella* Semen

The most commonly used compatibilities with *Trigonella* Semen are deficiency-nourishing drugs (Angelica sinensis, Herba Epimedii, etc.), blood-activating and stasis-eliminating drugs (Ligusticum chuanxiong, Salvia miltiorrhiza, etc.), and heat-clearing drug (Radix Paeoniae Rubra, Poria glabra, etc.). The main medicinal properties are warm and calm, accounting for 64.79%. The main medicinal flavors are sweet, bitter and pungent, accounting for 85.08%. TCM is used most frequently in the liver meridian, followed by kidney and spleen. Liver governs dredging, regulating Qi and blood, liver and kidney have the same origin, liver store blood, kidney store essence, essence and blood intergrowth, and liver governs dredging and kidney govern storage. Kidney is the innate principal growth and development, spleen is the acquired principal transport, liver, spleen and
kidney are interdependent and constrained, and coordinate the balance of the body\textsuperscript{[6,7]}. Most of the TCM used in combination with Trigonellae Semen are similar to Trigonellae Semen itself in the characteristics of warmth, bitterness, tonifying kidney and tonifying yang. The diseases treated by Trigonellae Semen mostly manifest deficiency of viscera. They include 10 kinds of TCM diseases, most of which manifest deficiency of Qi and blood, weakness of organs and qi, especially gynecological diseases and kidney diseases. These two kinds of diseases are mostly related to the kidney, Trigonellae Semen belongs to the kidney meridian and the commonly used compatibility of TCM tonifying deficiency, promoting blood circulation and clearing heat are also in line with this. Fourteen combinations of TCM are obtained, most of which are compatible with Angelica, Astragalus, Prepared Rhubarb, such as Trigonellae Semen-Angelica, Trigonellae Semen-Astragalus-Angelica, Angelica-Paeoniae Radix Rubra, etc. Trigonellae Semen is mainly used in tonifying kidney-yang. It can be used with Tonifying yang, tonifying qi and promoting blood circulation drugs to enhance the effect of warming kidney, tonifying yang, dispelling cold and relieving pain.

4.2. Drug Analysis of Trigonellae Semen in the Treatment of Gynecological Diseases

Gynecological diseases mostly lie in the discord between Qi and blood, belonging to liver, spleen and kidney. Both Chong channel and Ren channel originate in the uterus and play an important role in women\textsuperscript{[8]}. The kidney controls the uterus, and kidney weakness can lead to not liver freely distributing. Women take blood as the foundation\textsuperscript{[9]}. The weakness of kidney and liver function will lead to various female diseases. Gynecological diseases are mainly caused by deficiency of liver and kidney qi, obstruction of Qi and blood, and blockage of collaterals. The principles of soothing liver and tonifying kidney, promoting blood circulation and regulating menstruation, nourishing yin and nourishing blood are followed in the treatment of gynecological diseases\textsuperscript{[10,11]}. A total of 15 combinations of TCM are obtained. The compatibility of Trigonellae Semen with tonifying deficiency drugs (Angelica, Epimedium), qi-promoting drugs (Linderae Radix, Cyperi Rhizoma), blood-activating and stasis-removing drugs (Corydalis Rhizoma, Salviae Miltiorrhizae Radix et Rhizoma ) and Qi-Regulating drugs (Semen Litchi ) should be strengthened, and the compatibility mechanism of high-frequency combination of TCM should also be studied.

4.3. Drug Analysis of Trigonellae Semen in the Treatment of Kidney Diseases

Kidney diseases are mostly caused by insufficient vital energy, external wind, cold, dampness and heat invasion, and kidney gas depletion\textsuperscript{[12,13]}. They are mostly manifested by insufficiency of Qi and blood, deficiency of yin and yang, internal obstruction of dampness and turbidity, etc. In the treatment of kidney diseases, we mostly use invigorating qi and nourishing blood, promoting blood circulation and removing stasis, invigorating spleen and eliminating dampness\textsuperscript{[14]}. A total of 13 combinations of TCM are obtained. Trigonellae Semen is often combined with deficiency-nourishing Drugs, heat-clearing drug and blood-activating drugs. Warm nature can warm the inside to disperse cold, warm the liver to disperse knots, sweet taste can supplement Qi and blood, spicy taste can promote Qi and blood, bitter taste can clear away evil. Trigonellae Semen combined with these drugs can play the role of strengthening the body, removing pathogens, clearing away heat and detoxification, activating blood circulation and removing blood stasis. Among them, Angelica, Radix Rehmanniae Praeparata and Rhizoma Smilacis Glabrae are the most widely used. Attention should be paid to the compatibility mechanism of Trigonellae Semen and these three medicines.

In this paper, the rule of clinical medication of Trigonellae Semen is preliminarily discussed, the medication characteristics of Trigonellae Semen in the treatment of gynecological and renal diseases are analyzed, and the compatibility characteristics of Trigonellae Semen in different diseases are revealed. The compatibility of Trigonellae Semen with tonifying deficiency drugs, promoting blood circulation drugs and clearing heat drugs is used for kidney weakness, liver depression and Qi stagnation, spleen dysfunction, etc. It is also widely used in gynecological
diseases and kidney diseases. The compatibility of *Trigonellae* Semen with Cyperi Rhizoma, Semen Litchi, Corydalis Rhizoma, Angelica, Prepared Rhubarb and Rhizoma Smilacis Glabrae should be emphasized in order to produce better clinical efficacy.

5. Acknowledgement

This research is financially supported by the National International Cooperation Base (2016-65), Henan Province Science and Technology Tackling (162102310181).

6. References


