Principles of Differentiation and Prescription for Vitiligo in Traditional Chinese Medicine Based on a Literature Investigation

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Key Words
Principles of differentiation · Prescription · Traditional Chinese medicine · Vitiligo · Literature investigation · Logistic multiple regression

Abstract
Background/Aims: Vitiligo is a common disorder of depigmented skin. Traditional Chinese medicine (TCM) has been proved to be effective for the treatment of vitiligo, but the standard differential syndromes and effective formulas and herbs are still controversial. The aim of this study is to analyze the principles of differentiation and prescription in treating vitiligo in TCM based on a large-scale literature investigation. Methods: Articles about vitiligo treatment using TCM were searched in three databases, including China National Knowledge Infrastructure (1979–2014), China Science Periodical Database (1990–2014) and PubMed (1984–2014). The frequency of differential syndromes, formulas and herbs was analyzed using a metrological method and logistic multiple regression analysis. Results: Five syndromes account for the major differential categories in vitiligo: liver and kidney deficiency, Qi stagnation and blood stasis, liver depression and Qi stagnation, disharmony between Qi and blood, and blood conflicting with wind. The common formula prescriptions most frequently used were Tong-Qiao-Huo-Xue decoction, Xiao-Yao powder and Si-Wu decoction. The most frequently prescribed herbs were Angelica sinensis, Ligusticum wallichii, Tribulus terrestris, Polygonum multiflorum, Fructus psoraleae, Radix Paeoniae Rubra, Rehmannia glutinosa, Glossy Privet Fruit, Eclipta alba, Salvia miltiorrhiza, Liquorice, and Angelica dahurica, which shows that the treatment principles of vitiligo are tonifying the liver and kidney, activating blood and expelling wind. Conclusion: The most frequent syndromes of vitiligo are liver and kidney deficiency, Qi stagnation and blood stasis. Most TCM doctors prefer prescribing herbs with efficacy in tonifying the liver and kidney, activating blood and expelling wind in treating vitiligo.
Introduction

Vitiligo is a disorder of pigmentation characterized by the presence of depigmented skin macules due to the chronic and progressive loss of melanocytes from the cutaneous epidermis [1]. Vitiligo affects approximately 0.5–1% of the world’s population [1]. People with this disorder can experience emotional stress, particularly if vitiligo develops on visible areas of the body [2]. The cause of vitiligo remains unknown, and the treatment also remains difficult [3]. A number of therapies, including corticosteroids, topical immunomodulators, photo(chemo)therapy and surgery, have proven to be partially successful but show various side effects [4].

Traditional Chinese medicine (TCM), the most common complementary and alternative medicine, has been widely used over 1,000 years in China. There are three Chinese medical terms whose descriptions match vitiligo, namely Bai-Dian, Bai-Bo-Feng or Ban-Bo [5]. TCM could be effective in stopping progression of the disease and achieving repigmentation, which has been a popular treatment for vitiligo in China [6]. However, with different classifications of the etiology and pathogenesis of vitiligo, generations of TCM physicians have prescribed various herbal formulas with distinct differential syndromes [7]. A large-scale literature investigation regarding the widely accepted differentiation of and effective formulas and herbs for vitiligo is still lacking [8].

The aim of this study is to analyze the principles of TCM differentiation and prescription for treating vitiligo based on a large-scale literature investigation, using a metrological method and logistic multiple regression analysis. Our data could provide useful information about vitiligo treatment in TCM.

Materials and Methods

Data Resources and Study Sample

A literature search was conducted to record TCM differentiations, formulas and herbs prescribed for treating vitiligo in databases, including China National Knowledge Infrastructure (1979–2014), China Science Periodical Database (1990–2014) and PubMed (1984–2014). The following keywords and subject terms were searched: ‘traditional Chinese medicine’ and ‘vitiligo’, or ‘Chinese herbs’ and ‘vitiligo’. Two authors independently assessed study eligibility and methodological quality and extracted data. The final decision on unclear criteria in the literature was made by the two authors after thorough discussion. Studies were included or excluded in the analysis depending on the following standards.

Inclusion Criteria

Studies were included in the analysis if they (1) were clinical randomized controlled studies, clinical reports, case reports or medication experience of renowned TCM doctors; (2) had clear diagnoses complying with diagnostic criteria of vitiligo, and (3) contained specific syndrome classifications or descriptions.

Exclusion Criteria

We excluded the following: (1) studies focusing on an adverse reaction or toxic effect of TCM herbs; (2) studies in which TCM herbs acted as adjuvant therapy for vitiligo; (3) studies in which TCM herbs were among various remedies and could not be confirmed as the main effective medication; (4) studies on patients without vitiligo, or if the outcome indicator did not comply with the inclusion criteria; (5) studies containing apparent errors or overlapping data; (6) studies based on animal experiments, and (7) reviews of literature.
Statistical Analysis

A statistical analysis of the frequency of syndromes and herbal formulas for the treatment of vitiligo was conducted using binary logistic stepwise regression. Patterns were set as the dependent variable, and herbs were the independent variable. For analyzing one typical pattern, the target pattern was set as 1 and the other ones were set as 0. In the analysis of each herb, the prescribed herb was set as 1, and herbs not appearing in the formulas were set as 0. By the likelihood ratio, score and Wald tests, the pattern-herb model was established (p < 0.001). Statistical significance was considered at p < 0.05 for each pattern-herb regression equation. All data were stored and analyzed using SPSS software (version 21.0 for Windows). The names of Chinese herbs in the literature were standardized according to the 2010 Chinese Pharmacopoeia [9].

Results

The Syndromes of Vitiligo

Of the 218 records initially identified from three databases after removing duplicates, 134 studies were discarded because, after reviewing the titles and abstracts, it was clear that these articles did not meet the inclusion criteria. A total of 84 studies were assessed in full text for eligibility, of which 6 were excluded for the following reasons: duplicated data (n = 2), review articles (n = 2) and insufficient information (n = 2). Finally, 78 articles including 163 formulas with 15 syndrome types of TCM were available for analysis.

Among the 15 syndrome types of TCM in vitiligo, 5 syndromes accounted for the major differential categories. The syndrome of liver and kidney deficiency was the most frequent differentiation pattern, with 49 formulas accounting for 30.06%, followed by the syndrome of Qi stagnation and blood stasis with 26 formulas accounting for 15.95%. The syndrome of liver depression and Qi stagnation with 17 formulas accounted for 10.43%. Eleven formulas were proscribed for the syndrome of disharmony between Qi and blood, which accounted for 6.75%. Finally, the syndrome of blood conflicting with wind with 9 formulas accounted for 5.52%.

The Herbal Formulas for Treating Vitiligo

The 3 most frequently prescribed herbal formulas for treating vitiligo among the 163 formulas were Tong-Qiao-Huo-Xue decoction, Xiao-Yao powder and Si-Wu decoction. The 9 most commonly used herbal formulas among 112 formulas in the 5 syndromes for vitiligo are illustrated in Table 1.

Table 1. The 9 most frequently prescribed herbal formulas for treating vitiligo

<table>
<thead>
<tr>
<th>Order</th>
<th>Herbal formulas</th>
<th>Syndromes</th>
<th>Total frequency (n = 112)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>liver and kidney deficiency</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Tong-Qiao-Huo-Xue</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>Xiao-Yao powder</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Si-Wu decoction</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Chai-Hu-Shu-Gan</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Liu-Wei-Di-Huang</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>Ba-Zhen decoction</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>Er-Zhi pill</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>Bai-Bo decoction</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>Wu-Zi-Yan-Zong pills</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
### Table 2. The 12 most frequently prescribed Chinese herbs for treating vitiligo

<table>
<thead>
<tr>
<th>Chinese herb</th>
<th>Appearance, n</th>
<th>Frequency, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Angelica sinensis</em> (Dang-gui)</td>
<td>74</td>
<td>66.07</td>
</tr>
<tr>
<td><em>Ligusticum wallichii</em> (Chuan-xiong)</td>
<td>63</td>
<td>56.25</td>
</tr>
<tr>
<td><em>Tribulus terrestris</em> (Ji-li)</td>
<td>52</td>
<td>46.43</td>
</tr>
<tr>
<td><em>Polygonum multiflorum</em> (He-shou-wu)</td>
<td>51</td>
<td>45.54</td>
</tr>
<tr>
<td><em>Fructus psoraleae</em> (Bu-gu-zhi)</td>
<td>49</td>
<td>43.75</td>
</tr>
<tr>
<td>Radix Paeoniae Rubra (Chi-shao)</td>
<td>47</td>
<td>41.96</td>
</tr>
<tr>
<td><em>Rehmannia glutinosa</em> (Shu-di-huang)</td>
<td>42</td>
<td>37.5</td>
</tr>
<tr>
<td>Glossy Privet Fruit (Nv-zhen-zi)</td>
<td>39</td>
<td>34.8</td>
</tr>
<tr>
<td><em>Eclipta alba</em> (Han-lian-cao)</td>
<td>38</td>
<td>33.9</td>
</tr>
<tr>
<td><em>Salvia miltiorrhiza</em> (Dan-shen)</td>
<td>37</td>
<td>33.0</td>
</tr>
<tr>
<td>Liquorice (Gan-cao)</td>
<td>36</td>
<td>32.1</td>
</tr>
<tr>
<td><em>Angelica dahurica</em> (Bai-zhi)</td>
<td>33</td>
<td>29.5</td>
</tr>
</tbody>
</table>

**The Herbs Prescribed for Treating Vitiligo**

The 12 most frequently prescribed Chinese herbs for vitiligo are summarized in table 2. These herbs are *Angelica sinensis* (Dang-gui in Chinese), *Ligusticum wallichii* (Chuan-xiong), *Tribulus terrestris* (Ji-li), *Polygonum multiflorum* (He-shou-wu), *Fructus psoraleae* (Bu-gu-zhi), Radix Paeoniae Rubra (Chi-shao), *Rehmannia glutinosa* (Shu-di-huang), Glossy Privet Fruit (Nv-zhen-zi), *Eclipta alba* (Han-lian-cao), *Salvia miltiorrhiza* (Dan-shen), Liquorice (Gan-cao) and *Angelica dahurica* (Bai-zhi). The frequencies of Chinese herbs prescribed for vitiligo in the 5 most common patterns are illustrated in table 3.

**Differences in Herbs Prescribed for Syndromes Analyzed by Multiple Logistic Regressions**

To analyze specifically prescribed herbs for each syndrome, multiple logistic regression analysis was used. In the following, logistic regression equations of herbs are shown for each syndrome, and the statistical data are illustrated in tables 4–8.

**Syndrome of Liver and Kidney Deficiency**

logit(P) = –1.288 to 1.466 A. (Dang-gui) + 1.735 P. multiflorum (He-shou-wu) + 1.769 F. psoraleae (Bu-gu-zhi) + 1.612 R. glutinosa (Shu-di-huang) + 1.775 Glossy Privet Fruit (Nv-zhen-zi) – 1.911 *Carthamus tinctorius* (Hong-hua) – 1.632 *Bupleurum chinense* (Chai-hu) – 23.101 *Radix Saposhnikoviae* (Fang-feng) – 21.468 *Codonopsis pilosula* (Dang-shen).

**Syndrome of Qi Stagnation and Blood Stasis**

logit(P) = –2.478 to 5.409 T. terrestris (Ji-li) + 3.33 Radix Paeoniae Rubra (Chi-shao) + 3.378 A. dahurica (Bai-zhi) + 4.331 C. tinctorius (Hong-hua) – 5.978 Radix Saposhnikoviae (Fang-feng) – 23.101 Rhizoma Atractylodis Macrocephalae (Bai-zhu) – 21.468 *Codonopsis pilosula* (Dang-shen).

**Syndrome of Liver Depression and Qi Stagnation**

logit(P) = –6.071 to 3.468 R. glutinosa (Shu-di-huang) – 5.931 A. dahurica (Bai-zhi) + 4.448 B. chinense (Chai-hu) + 3.754 Paonia lactiflora (Bai-shao) + 4.859 Radix Curcumae (Yu-jin).

**Syndrome of Disharmony between Qi and Blood**

logit(P) = –3.123 to 20.825 Barbary Wolfberry Fruit (Gou-qi-zi) + 1.809 Caulis Spatholobi (Ji-xue-teng) + 4.093 C. pilosula (Dang-shen).

**Syndrome of Blood Conflicting with Wind**

logit(P) = –4.566 + 1.925 Radix Rehmanniae (Sheng-di-huang) + 3.812 Herba Schizonepetae (Jin-jie) + 3.086 Cortex Dictamni (Bai-xian-pi).
Table 3. Frequencies of Chinese herbs prescribed for vitiligo in 5 patterns

<table>
<thead>
<tr>
<th>Order</th>
<th>Syndromes</th>
<th>Liver and kidney deficiency</th>
<th>Qi stagnation and blood stasis</th>
<th>Liver depression and Qi stagnation</th>
<th>Disharmony between Qi and blood</th>
<th>Blood conflicting with wind</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Polygonum multiflorum</td>
<td>33 (67.35)</td>
<td>20 (76.92)</td>
<td>15 (88.24)</td>
<td>9 (81.82)</td>
<td>7 (77.78)</td>
</tr>
<tr>
<td>2</td>
<td>Glossy Privet Fruit</td>
<td>32 (65.31)</td>
<td>19 (73.08)</td>
<td>15 (88.24)</td>
<td>9 (81.82)</td>
<td>7 (77.78)</td>
</tr>
<tr>
<td>3</td>
<td>Fructus psoraleae</td>
<td>32 (65.31)</td>
<td>19 (73.08)</td>
<td>15 (88.24)</td>
<td>9 (81.82)</td>
<td>7 (77.78)</td>
</tr>
<tr>
<td>4</td>
<td>Eclipta alba</td>
<td>29 (59.18)</td>
<td>17 (65.38)</td>
<td>11 (64.71)</td>
<td>6 (54.55)</td>
<td>6 (66.67)</td>
</tr>
<tr>
<td>5</td>
<td>Rehmannia glutinosa</td>
<td>28 (57.14)</td>
<td>15 (57.69)</td>
<td>11 (64.71)</td>
<td>6 (54.55)</td>
<td>6 (66.67)</td>
</tr>
<tr>
<td>6</td>
<td>Angelica sinensis</td>
<td>26 (53.06)</td>
<td>14 (53.85)</td>
<td>10 (58.82)</td>
<td>5 (45.45)</td>
<td>5 (55.56)</td>
</tr>
<tr>
<td>7</td>
<td>Tribulus terrestris</td>
<td>25 (51.02)</td>
<td>12 (46.15)</td>
<td>7 (41.18)</td>
<td>5 (45.45)</td>
<td>5 (55.56)</td>
</tr>
<tr>
<td>8</td>
<td>Semen Cuscutae</td>
<td>20 (40.82)</td>
<td>10 (38.46)</td>
<td>7 (41.18)</td>
<td>4 (36.36)</td>
<td>3 (33.33)</td>
</tr>
<tr>
<td>9</td>
<td>Ligusticum wallichii</td>
<td>19 (38.78)</td>
<td>8 (30.77)</td>
<td>5 (29.41)</td>
<td>4 (36.36)</td>
<td>3 (33.33)</td>
</tr>
<tr>
<td>10</td>
<td>Barbary Wolfberry Fruit</td>
<td>19 (38.78)</td>
<td>10 (38.46)</td>
<td>5 (29.41)</td>
<td>4 (36.36)</td>
<td>3 (33.33)</td>
</tr>
<tr>
<td>11</td>
<td>Liquorice</td>
<td>18 (36.73)</td>
<td>7 (26.92)</td>
<td>5 (29.41)</td>
<td>4 (36.36)</td>
<td>3 (33.33)</td>
</tr>
<tr>
<td>12</td>
<td>Radix Astragali</td>
<td>16 (32.65)</td>
<td>7 (26.92)</td>
<td>5 (29.41)</td>
<td>4 (36.36)</td>
<td>3 (33.33)</td>
</tr>
</tbody>
</table>

Values are expressed as frequencies with percentages in parentheses.

Table 4. Syndrome of liver and kidney deficiency

<table>
<thead>
<tr>
<th>Herbs</th>
<th>β</th>
<th>SE</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angelica sinensis</td>
<td>−1.466</td>
<td>0.683</td>
<td>4.614</td>
<td>0.032</td>
<td>0.231</td>
</tr>
<tr>
<td>Polygonum multiflorum</td>
<td>1.735</td>
<td>0.654</td>
<td>7.027</td>
<td>0.008</td>
<td>5.668</td>
</tr>
<tr>
<td>Fructus psoraleae</td>
<td>1.769</td>
<td>0.693</td>
<td>6.518</td>
<td>0.011</td>
<td>5.866</td>
</tr>
<tr>
<td>Rehmannia glutinosa</td>
<td>1.612</td>
<td>0.678</td>
<td>5.652</td>
<td>0.017</td>
<td>5.013</td>
</tr>
<tr>
<td>Glossy Privet Fruit</td>
<td>1.775</td>
<td>0.611</td>
<td>8.447</td>
<td>0.004</td>
<td>5.900</td>
</tr>
<tr>
<td>Carthamus tinctorius</td>
<td>−1.911</td>
<td>0.763</td>
<td>6.283</td>
<td>0.012</td>
<td>0.148</td>
</tr>
<tr>
<td>Bupleurum chinense</td>
<td>−1.632</td>
<td>0.763</td>
<td>4.579</td>
<td>0.032</td>
<td>0.195</td>
</tr>
</tbody>
</table>
According to the regression equation of the classification of medication, *P. multiflorum* (*He-shou-wu*), *F. psoraleae* (*Bu-gu-zhi*), *R. glutinosa* (*Shu-di-huang*) and Glossy Privet Fruit (*Nv-zhen-zi*) were specifically used for the deficiency of liver and kidney syndrome of vitiligo. Radix *Paeoniae Rubra* (*Chi-shao*), *C. tinctorius* (*Hong-hua*) and *A. dahurica* (*Bai-zhi*) were typically prescribed for Qi stagnation and blood stasis. Radix *Curcumae* (*Yu-jin*), *Radix Bupleuri* (*Chai-hu*) and *Radix Paeoniae Alba* (*Bai-shao*) were often used for the syndrome of liver depression and Qi stagnation. *C. pilosula* (*Dang-shen*) and *Caulis Spatholobi* (*Ji-xue-teng*) were used for the deficiency of Qi and blood. Radix *Rehmanniae* (*Sheng-di-huang*), Herba *Schizonepetae* (*Jin-jie*) and Cortex *Dictamni* (*Bai-xian-pi*) were most likely to be used for treating patients with the syndrome of blood conflicting with wind.

Table 5. Syndrome of Qi stagnation and blood stasis

<table>
<thead>
<tr>
<th>Herbs</th>
<th>β</th>
<th>SE</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tribulus terrestris</em> (<em>Ji-li</em>)</td>
<td>-5.409</td>
<td>1.653</td>
<td>10.709</td>
<td>0.001</td>
<td>0.004</td>
</tr>
<tr>
<td>Radix <em>Paeoniae Rubra</em> (<em>Chi-shao</em>)</td>
<td>3.330</td>
<td>0.986</td>
<td>11.416</td>
<td>0.001</td>
<td>27.935</td>
</tr>
<tr>
<td><em>Angelica dahurica</em> (<em>Bai-zhi</em>)</td>
<td>3.378</td>
<td>1.161</td>
<td>8.464</td>
<td>0.004</td>
<td>29.326</td>
</tr>
<tr>
<td><em>Carthamus tinctorius</em> (<em>Hong-hua</em>)</td>
<td>4.331</td>
<td>1.406</td>
<td>9.493</td>
<td>0.002</td>
<td>76.056</td>
</tr>
<tr>
<td>Radix <em>Saposhnikoviae</em> (<em>Fang-feng</em>)</td>
<td>-5.978</td>
<td>2.019</td>
<td>8.769</td>
<td>0.003</td>
<td>0.003</td>
</tr>
<tr>
<td>Rhizoma <em>Atractylodis Macrocephalae</em> (<em>Bai-zhu</em>)</td>
<td>-23.101</td>
<td>7,774.266</td>
<td>0.000</td>
<td>0.998</td>
<td>0.000</td>
</tr>
<tr>
<td><em>Codonopsis pilosula</em> (<em>Dang-shen</em>)</td>
<td>-21.468</td>
<td>9,390.897</td>
<td>0.000</td>
<td>0.998</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 6. Syndrome of liver depression and Qi stagnation

<table>
<thead>
<tr>
<th>Herbs</th>
<th>β</th>
<th>SE</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Rehmannia glutinosa</em> (<em>Shu-di-huang</em>)</td>
<td>-3.468</td>
<td>1.813</td>
<td>3.660</td>
<td>0.056</td>
<td>0.031</td>
</tr>
<tr>
<td><em>Angelica dahurica</em> (<em>Bai-zhi</em>)</td>
<td>-5.931</td>
<td>2.337</td>
<td>6.439</td>
<td>0.011</td>
<td>0.003</td>
</tr>
<tr>
<td><em>Bupleurum chinense</em> (<em>Chai-hu</em>)</td>
<td>4.448</td>
<td>1.587</td>
<td>7.852</td>
<td>0.005</td>
<td>85.474</td>
</tr>
<tr>
<td><em>Paonia lactiflora</em> (<em>Bai-shao</em>)</td>
<td>3.754</td>
<td>1.423</td>
<td>6.964</td>
<td>0.008</td>
<td>42.689</td>
</tr>
<tr>
<td><em>Radix Curcumae</em> (<em>Yu-jin</em>)</td>
<td>4.859</td>
<td>1.677</td>
<td>8.397</td>
<td>0.004</td>
<td>128.900</td>
</tr>
</tbody>
</table>

Table 7. Syndrome of disharmony between Qi and blood

<table>
<thead>
<tr>
<th>Herbs</th>
<th>β</th>
<th>SE</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Barbary Wolfberry Fruit</em> (<em>Gou-qi-zi</em>)</td>
<td>-20.825</td>
<td>6,942.424</td>
<td>0.000</td>
<td>0.998</td>
<td>0.000</td>
</tr>
<tr>
<td><em>Caulis Spatholobi</em> (<em>Ji-xue-teng</em>)</td>
<td>1.809</td>
<td>0.836</td>
<td>4.676</td>
<td>0.031</td>
<td>6.102</td>
</tr>
<tr>
<td><em>Codonopsis pilosula</em> (<em>Dang-shen</em>)</td>
<td>4.093</td>
<td>1.245</td>
<td>10.802</td>
<td>0.001</td>
<td>59.946</td>
</tr>
</tbody>
</table>

Table 8. Syndrome of blood conflicting with wind

<table>
<thead>
<tr>
<th>Herbs</th>
<th>β</th>
<th>SE</th>
<th>Wald</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Radix Rehmanniae</em> (<em>Sheng-di-huang</em>)</td>
<td>1.925</td>
<td>1.033</td>
<td>3.476</td>
<td>0.062</td>
<td>6.856</td>
</tr>
<tr>
<td><em>Herba Schizonepetae</em> (<em>Jin-jie</em>)</td>
<td>3.812</td>
<td>1.110</td>
<td>11.790</td>
<td>0.001</td>
<td>45.256</td>
</tr>
<tr>
<td><em>Cortex Dictamni</em> (<em>Bai-xian-pi</em>)</td>
<td>3.086</td>
<td>1.313</td>
<td>5.522</td>
<td>0.019</td>
<td>21.887</td>
</tr>
</tbody>
</table>
Discussion

Vitiligo is a relatively common dermatologic finding which has been observed since ancient times [10]. TCM herbs have been used as effective anti-vitiligo agents for over 1,000 years in China [11]. However, the published literature on the differentiation of vitiligo and herbal formulas for its treatment is controversial and inconclusive [12]. To analyze standard differentiation of and effective formulas and Chinese herbs for vitiligo, we performed a large-scale literature investigation regarding the differentiation of syndromes and herbal formulas for vitiligo. According to our statistical data, 5 syndromes account for the major differential categories among a total of 15 syndromes in vitiligo. They are the syndrome of liver and kidney deficiency, Qi stagnation and blood stasis, liver depression and Qi stagnation, disharmony between Qi and blood, and blood conflicting with wind. The 12 most frequently prescribed Chinese herbs for vitiligo are *A. sinensis* (Dang-gui), *L. wallichii* (Chuan-xiong), *T. terrestris* (Ji-li), *P. multiflorum* (He-shou-wu), *F. psoraleae* (Bu-gu-zhi), Radix Paeoniae Rubra (Chi-shao), *R. glutinosa* (Shu-di-huang), Glossy Privet Fruit (Nv-zhen-zi), *E. alba* (Han-lian-cao), *S. miltiorrhiza* (Dan-shen), Liquorice (Gan-cao) and *A. dahurica* (Bai-zhi). Most of these frequently used herbs have functions of nourishing the liver and kidney, dispelling wind and activating blood. Based on an analysis of herb frequency, we found that Chinese herbs with the function of nourishing the liver and kidney appear in every syndrome of vitiligo, which suggests that the key treatment principle for vitiligo is nourishing the liver and kidney.

Moreover, our data shows that *A. dahurica* (Bai-zhi) and *T. terrestris* (Ji-li), two herbs with the function of expelling wind, are most commonly prescribed by TCM doctors. This could be explained by the ancient classification of the pathogenesis of vitiligo in TCM, which was ascribed to ‘wind evil’ [13]. Ancient TCM doctors called vitiligo *Bai-Bo-Feng, Feng* meaning wind, which indicates that ‘wind evil’ is thought to play an important role in the development of vitiligo [14]. Chinese herbs with efficacy of dispelling the wind, therefore, are frequently used in TCM formulas for vitiligo [13].

In TCM, interestingly, physicians often prescribe black or dark herbs in treating disorders with white or pale symptoms [15]. White or pale symptoms are thought to be caused by deficiency of Qi or kidney; yet, black herbs nourish the kidney, which is the theory of the herb color-effect phenomenon in TCM [16]. Vitiligo, which is characterized by depigmented white macules in the skin, therefore, is often treated with black herbal medication. Our data show that many of the most frequently prescribed herbs are black, including *P. multiflorum* (He-shou-wu), *R. glutinosa* (Shu-di-huang), *F. psoraleae* (Bu-gu-zhi), Glossy Privet Fruit (Nv-zhen-zi) and *S. miltiorrhiza* (Dan-shen). These herbal medications are effective in nourishing the kidney, complying with the treatment principles of vitiligo.

References
