Data Mining Method for Exploring the Composition Law and Therapeutic Mechanism of Chinese medicine of macroscopic

Ting-Ting Chen¹, Ya-Bo Shi²

¹First Clinical Medical College of Nanjing University of Chinese Medicine, Nanjing 210046, China; ²School of Pharmacy, Henan University of Traditional Chinese medicine, Zhengzhou 450008, China.

*Corresponding to: Ting-Ting Chen, 138 Xianlin Avenue, Qixia District, Nanjing 210046. Email: chentingtting@126.com.

Highlight:
Using the data mining method, the drug association rules and complex system entropy cluster analysis method contained in the prescription are used to analyze the drug use characteristics and prescription formation rules of the tangible "cancer toxin" for the treatment of tumors, and the new prescription (Medicated leaven, Hawthorn, Malt, Atractylodes, Poria cocos, Ginseng) generated by the system is analyzed. The drugs contained in the new prescription are mainly to nourish the acquired healthy qi, Clinical medication often adds or subtracts the flavor of drugs for dispelling evil and attacking poison on the basis of this axis prescription, so as to "dispel evil and attack poison" without harming the health.

Abstract:
Background: Based on the theory of "cancer toxin" in traditional Chinese medicine (TCM), combined with data mining method, this paper discusses the prescription and medication law of macroscopic "cancer toxin". Methods Sort out the relevant prescriptions of macroscopic "cancer toxin" and carry out correlation analysis. Results The results showed that the main therapeutic drugs for macroscopic "cancer toxin" were invigorating the spleen and Qi, regulating the Qi mechanism, eliminating toxin and pathogenic factors, eliminating dampness and swelling, promoting blood circulation and removing blood stasis, attacking toxin, softening and firmness, and dredging collaterals to relieve pain. Conclusion High frequency medicine embodies the core of tangible macroscopic "cancer toxin" treatment, and the new prescription composition embodies the fundamental treatment. At the same time, the mechanism of macroscopic "cancer toxin" was analyzed to pave the way for further clinical practice.

Key words: Macroscopic "cancer toxin"; External prescriptions; Data mining; Drug use patterns; Action mechanism

Abbreviations:
TCM, traditional Chinese medicine.

Competing interests:
The authors declare that they have no conflict of interest.

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Background

In Suwen Zhizhenyao Dalun, the application of the treatment principle of "stagnation requiring dispersion, retention requiring purgation" in the treatment of tumors reflects the characteristics of traditional Chinese medicine in the treatment of various tumors by "eliminating pathogen" [1]. With the continuous development of interdisciplinary, data mining method has been continuously applied to the field of traditional Chinese medicine, especially the application of association rules of traditional Chinese medicine compatibility is becoming more and more perfect. The excavated drug combinations have certain guiding significance for clinical medication [2]. Therefore, when seeking the medication laws of traditional Chinese medicine in the treatment of macroscopic "cancer toxin" and the corresponding clinical pathogenesis rules of traditional Chinese medicine, the drug association rules and complex system entropy clustering analysis method were used to analyze the medication characteristics and prescription rules of macroscopic "cancer toxin" in the treatment of tumors, and reveal the pathogenesis and treatment characteristics behind the medication rules, laying the groundwork for the later study of the corresponding mechanism research and clinical treatment.

Methods of collecting and analyzing prescriptions

Source of prescriptions

Screening and confirmation of prescriptions by two people, the included prescriptions mainly came from the prescriptions that met the inclusion criteria of Dictionary of tumor prescriptions [3] and Prescription Dictionary of Traditional Chinese Medicine [4] and the modern prescriptions that can be searched in CNKI (until January 2020). Combined with the characteristics of macroscopic "cancer toxin", we used "tumor", "cancer","lump" and related disease names combined with "traditional Chinese medicine", "Chinese materia medica" and "prescription" as the main search terms to query and retrieve medical records and prescriptions. A total of 1838 prescriptions were included after preliminary screening according to the topics or abstracts, composition and function of prescriptions, and final confirmation according to inclusion and exclusion criteria.

Inclusion criteria

The included prescriptions have a clear prescription composition, and mainly treat tumors and have a description of the clinical symptoms of macroscopic "cancer toxin" related diseases. Oral prescriptions, including pills, ointment, powder, soup and other formulations.

Exclusion criteria

Repeated or identical prescriptions: Prescriptions without clear compatibility meaning; Prescriptions for single drug: Prescriptions with inaccurate description of drug composition or indications; Prescriptions not suitable for treatment of tumor-related macroscopic "cancer toxin" disease: Non-oral prescriptions for external use or other uses.

Standardization of data

When entering the components of Chinese medicine involved in each group, the name of traditional Chinese medicine will be standardized and unified according to Traditional Chinese Pharmacy [6] or DICTIONARY OF TRADITIONAL CHINESE PHARMACY [5]. For example, to unify "Rhubarb Sichuan", "Huoshen" and "Chuanjun" into "rhubarb", to unify "Sparganium sinense" into "rhizoma sparganii", to unify "HuangQi" into "Astragalus mongholicus", and so on.

Data entry and analysis

Input 1838 prescriptions into the 'Traditional Chinese Medicine Inheritance Support System (V 2.5 version)' software. Through the above software "data analysis system" in the "group analysis" function for analysis, the specific steps are as follows: ① Medication frequency statistics: analysis of the use of high frequency Chinese medicine. ② Composition rule analysis: The compatibility association rules of TCM included in the composition were analyzed. The number of support was set to 100, and the confidence was set to 0.6. The combination frequency between TCMs was sorted and the association relationship between TCMs was analyzed. ③ Clustering screening of core Chinese medicine: the appropriate correlation coefficient and penalty coefficient in this analysis were selected according to experience, and the combination of Chinese medicine was extracted by clustering analysis method (the software mainly includes complex system entropy clustering and unsupervised entropy hierarchical clustering [7]) to find new prescriptions. Finally, the extracted data were analyzed and discussed.

Results

Analysis of overall medication frequency of prescriptions for macroscopic "cancer toxin" related diseases

A total of 1838 prescriptions for oral treatment of tumor-related macroscopic "cancer toxin" were recorded, including 1555 Chinese herbs, with the highest frequency of 388 times and the lowest frequency of 1 time. There were 28 Chinese herbs with...
application frequency of more than 125 times, namely rhubarb, Angelica, Aucklandia, Sparganium, licorice cinnamon, musk, areca, croton, forsythia, pinellia, frankincense, Tangerine Peel, myrrh, rhizoma zingiberis, ginseng, Atractylodes, seaweed, pericarpium citri reticulatae viride, laminaria, Scutellaria baikalensis, zedoary, Ligusticum wallichii, Coptis chinensis, sal ammoniac, Angelica dahurica, Platycodon grandiflorum, and Manis pentadactyla, with frequency of 388, 357, 282, 273, 268, 260, 215, 207, 206, 191, 186, 178, 172, 163, 161, 155, 154, 153, 146, 143, 137, 133, 127, and 126 times, respectively.

### Analysis of the overall prescription rules of macroscopic "cancer toxin" related diseases

According to the previous analysis experience, the system was debugged. Combined with the analysis results of medication frequency in 2.1, the number of support in the function of ‘ prescription rule analysis ‘ was set to 100. Ten commonly used combinations (Table 1) can be extracted from the ‘ medication mode ‘ module, involving 11 traditional Chinese medicines.

According to table 1, Myrrh and Frankincense are the most common drug combinations, followed by Angelica, Rhubarb, Sparganium, and Zedoary. Other drug combinations involving Angelica, Rhubarb, Myrrh, Aucklandia, Sparganium, Laminaria, Cinnamon, Frankincense, Areca, Seaweed, Zedoary, a total of 11 herbs. Angelica is sweet in taste, and it can replenish blood with light and pungent Qi. It can nourish blood, activate blood circulation, dredge meridians and activate collaterals. Its main treatment includes syndrome aggregation; Rhubarb has the functions of attacking stagnation, removing blood stasis and detoxification, clearing away heat and cooling blood. It is mainly used to treat abdominal pain due to stagnation, excess heat and damp heat. It can break the accumulation of symptoms, clean up the intestines and stomach, eliminate phlegm and heat in the intestines; Myrrh has the effect of dispersing blood stasis and relieving pain, detumescence and promoting muscle regeneration. It can not only treat all kinds of pain caused by blood stasis, but also treat carbuncle, swelling and sore; Aucklandia takes its functions of promoting Qi to relieve pain, strengthening spleen to eliminate food, and its main tune is to guide stagnation and eliminate the block of Qi addiction; Sparganium is mainly used for the treatment of senile mania, accumulation and caking; Laminaria is cold in nature. It has the effects of eliminating phlegm, softening firmness, dispersing nodules, promoting diuresis and detumescence. It is often used to treat gall gas tuberculosis, swelling and hardness; Cinnamon is pungent and warm. It can control all kinds of diseases, dredge blood vessels, replenish middle and Qi; Frankincense has the functions of promoting blood circulation, Qi circulation, relieving pain, detumescence and promoting muscle regeneration, and can treat abdominal pain; Areca can eliminate accumulation and phlegm, and is often combined with Aucklandia and zedoary to regulate Qi and eliminate accumulation; Seaweed can be used for softening hard and resolving masses, eliminating phlegm and promoting diuresis, and are mostly used for gall tumor, scrofula, phlegm and fluid edema and other diseases. Zedoary has the function of promoting Qi and relieving depression, breaking blood stasis and relieving pain, which is commonly used in Qi and blood stagnation and syndrome accumulation.

The 11 Chinese herbs involved in the above drug combination were introduced into the prescription assistant (http://tcm.zhongerp.com) for prescription similarity analysis. The similarity analysis showed that it was 33% similar to paconiae decoction in Suwen pathogenesis Qi Yi Bao Ming Ji, mainly clearing viscera heat, regulating Qi and blood; It is 29% similar to yanhusuo powder in Jiyin Programme. It is a blood regulating agent with the functions of regulating Qi, activating blood circulation and relieving pain; It is 29% similar to Tory Powder for Pain powder in Surgical practice. It has the functions of enriching blood, removing blood stasis and relieving pain. It can be seen from the above, the 11 traditional Chinese medicines involved in the drug combination and the traditional Chinese medicine with high frequency of frequency analysis are mainly used for promoting blood circulation and removing blood stasis, dredging collaterals and relieving pain, clearing heat and detoxifying, softening and hardening. It has certain conditioning effects on the blood stasis, phlegm and heat toxin contained in the macroscopic "cancer toxin".

<table>
<thead>
<tr>
<th>Serial number</th>
<th>Drug model</th>
<th>Frequency of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Myrrh, frankincense</td>
<td>134</td>
</tr>
<tr>
<td>2</td>
<td>Angelica, rhubarb</td>
<td>132</td>
</tr>
<tr>
<td>3</td>
<td>Sparganium, zedoary</td>
<td>117</td>
</tr>
</tbody>
</table>
Set support degree is greater than or equal to 100 and confidence is greater than or equal to 0.6, and then carry out correlation analysis on the entered prescription. Five core combinations of traditional Chinese medicine can be extracted from the ‘rule analysis’ module (Table 2). It can be seen that the correlation between Zedoary, Sparganium, Myrrh and Frankincense is the most closely related in the prescription, that is, the addition and subtraction of Scrofula-eliminating Pill in "Records of Traditional Chinese and Western Medicine in Combination". From the medication rules in the prescription medication mode, it can be concluded that the correlation combination of traditional Chinese medicine in the oral prescription of macroscopic "cancer toxin" is mainly "promoting blood circulation and eliminating accumulation, removing blood stasis and resolving stagnation, promoting Qi and relieving pain". The main treatment of drugs includes the description of macroscopic "cancer toxin" in tumors such as abdominal mass accumulation.

### Analysis of new prescription of treating macroscopic "cancer toxin" based on entropy method

Based on the number of included prescriptions, the frequency of traditional Chinese medicine and the coefficient of drug pair, the parameters in the cluster analysis were debugged, and the data of new prescriptions obtained under multiple parameters were pre-read. Finally, the correlation degree was set as 4 and the penalty degree was set as 2, and the related cluster analysis was carried out on the included prescriptions. A new prescription was excavated (Table 3), and the relationship between the six traditional Chinese medicine drugs contained in the new prescription was displayed on the network (Figure 1).

### Table 2 Correlation analysis of traditional Chinese medicines

<table>
<thead>
<tr>
<th>Serial number</th>
<th>Rule</th>
<th>Confidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zedoary -&gt; Sparganium</td>
<td>0.82</td>
</tr>
<tr>
<td>2</td>
<td>Myrrh -&gt; frankincense</td>
<td>0.82</td>
</tr>
<tr>
<td>3</td>
<td>Frankincense -&gt; Myrrh</td>
<td>0.75</td>
</tr>
<tr>
<td>4</td>
<td>Laminaria -&gt; Seaweed</td>
<td>0.73</td>
</tr>
<tr>
<td>5</td>
<td>Seaweed -&gt; Laminaria</td>
<td>0.68</td>
</tr>
</tbody>
</table>

The new prescriptions generated by the system were analyzed. Atractylodes, Poria cocos and Ginseng were combined with drugs with the functions of tonifying Qi, invigorating spleen, clearing nutrients and nourishing stomach to achieve the purpose of supporting the body's healthy Qi. The combination of Medicated leaven, Hawthorn and Malt has the effect of eliminating evil and supporting healthy. The drug contained in the new prescription is mainly to nourish the healthy Qi. Clinical medication is often based on this axis prescription to add and subtract the herbs of eliminating pathogenic factors and attacking toxins, so that 'eliminating pathogenic factors and attacking toxins' does not hurt the healthy Qi.
Table 3  New prescription list based on entropy clustering

<table>
<thead>
<tr>
<th>Number</th>
<th>New combination</th>
<th>Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>leaven_Hawthorn_Malt_Atractylodes</td>
<td>Sijunzi Soup, Bihe drinking _Poria cocos_Ginseng</td>
</tr>
</tbody>
</table>

Fig. 1  Drug association rule network map in new prescription

Discussion and thinking

With the continuous inheritance and development of the theory of "cancerous toxin", contemporary physicians believe that the occurrence of tumors is caused by deficiency of healthy Qi, retention of pathogenic Qi, dysfunction of viscera, and endogenous toxin [8], and the core pathogenesis and syndrome of "cancer caused by toxin" in traditional Chinese Medicine can be summarized as "phlegm, blood stasis, depression and toxin" [9]. From the aspects of pathogenicity and refractory of cancer, it is analyzed that cancerous toxin starts from intangible and becomes tangible [10]. In the clinical practice of tumor treatment, the stubborn characteristics of cancerous toxin make it difficult to eliminate many substantive masses. Therefore, combined with the understanding of the occurrence, development, treatment and prognosis of tumors and related diseases in modern medicine, we inherit the main therapeutic principle of "strengthening the body resistance and eliminating pathogenic factors, and consolidating the root and clearing the source" of traditional Chinese medicine [11]. According to the specific disease stage of macroscopic "cancer toxin", the overall syndrome differentiation of prescriptions is modified to seek both temporary and permanent solutions.

Pathogenesis analysis of macroscopic "cancer toxin"

"Cancer poison" is a kind of poison that often injures people. When it is found in clinic, most of them have reached the tangible stage. In the disorder of viscera function, evil poison accumulates meridians and viscera, making the body yin and yang disorders, Qi and blood dysfunction, resulting in Qi stagnation, blood stasis, phlegm coagulation, poison accumulation cementation each other, the evolution of the pathogenesis of tumor [12], combined with the pathogenic characteristics of 'cancer poison', the pathogenesis of 'cancer poison' is summarized as 'phlegm stasis depression poison, deficiency of vital Qi, corresponding to the elimination of cancer detoxification, phlegm and blood stasis', in order to eliminate external and endogenous Qi stagnation, blood stasis, phlegm coagulation, poison accumulation of 'evil' and produce tangible accumulation of 'cancer poison'.

Discussion on the overall drug use of macroscopic "cancer toxin"

A total of 1838 prescriptions were recorded, involving...
1555 kinds of traditional Chinese medicine, which can reflect the complexity and variability of the pathogenic characteristics of macroscopic "cancer toxin" from the side. There are 28 kinds of traditional Chinese medicine used more than 125 times in the prescription. The efficacy is mainly based on invigorating spleen and replenishing Qi, regulating Qi movement, eliminating toxins, drying dampness and swelling, promoting blood circulation and removing blood stasis, attacking toxins and softening hard, dredging collaterals and relieving pain. The efficacy is corresponding to the pathogenesis and treatment principles of macroscopic "cancer toxin" related diseases. According to the analysis of the pathogenesis of the disease, "strengthening healthy Qi" is the basis for the treatment of medication, and anti-cancer and detoxification are the key points for the treatment of macroscopic "cancer toxin" [13]. 'Strengthening body resistance' means tonifying deficiency, invigorating spleen and replenishing Qi, nourishing yin and middle. 'Detoxification' means softening hard mass, spreading poison, and even using poison drugs to attack "toxin" for nursing.

Analysis of medication rules and mechanism

Anti-cancer and detoxication, seeking for dialectical causes

Due to the particularity of the etiology, pathogenesis and formation process of macroscopic "cancer toxin", the selection of drug treatment in clinical syndrome differentiation not only pays attention to the basic principle of " eliminating evil and attacking toxin," but also refer to the basic pathogenesis of macroscopic "cancer toxin",so as to use phlegm, blood stasis and detoxification products according to syndrome differentiation, on the basis of strengthening spleen and replenishing Qi, strengthening body resistance and tonifying deficiency, regulating Qi and relieving depression, regulating Qi movement makes evil not easy to stay in and condense, paving the way for eliminating phlegm and dampness, clearing heat and preventing cancer to prevent and control the formation and development of macroscopic "cancer toxin", and promote the coordinated balance of local and overall state of the body.

Mediate the good and evil, and distinguish the primary and secondary

For the clinical prescription of macroscopic "cancer toxin", it is necessary to grasp the primary and secondary of the rise and fall of pathogenic factors in place, so as to not lose the prescription in dialectical medication. When the disease is in the early stage, "cancer toxin" is deeply hidden and difficult to detect, and if the evil toxin is not removed,it is easy to damage the vitality, yin and fluid.At this stage, "attacking evil" is also "strengthening the body", which means "removing evil leads to good health, but when most of it declines", it is often given drugs such as Angelica, Sparganium, zedoary, frankincense, myrrh, laminaria, seaweed, rhubarb, areca, etc; With the progress of the disease, the macroscopic "cancer toxin" gradually appears.When the toxin is in love with the deficiency of vital energy, damaging the viscosa, and causing damage due to disease, the main method is to strengthen vital energy, such as using Sijunzi decoction or Liujiunzi Decoction to form the basic prescription, and further using drugs according to syndrome differentiation.In the later stage of the disease, "cancer toxin" penetrates into the whole body. Phlegm, blood stasis, depression and toxin are combined to form a visible lump. It is deep-rooted and difficult to resolve,and the body 's deficiency is obvious. When unable to remove 'cancer toxin', it is often need to balance attack and supplement, and a large number of supplements to protect and alleviate pain as a right and appropriate strategy, and it is necessary to 'remove evils and attack toxins' on the basis of caring for healthy Qi to cause serious diseases. Therefore, the weight medication in each stage of the development of macroscopic "cancer toxin" disease should adhere to the core dialectical thinking of traditional Chinese medicine, prescription medication, and make the body reach the physiological state of reconciliation and balance.

Principles of analysis, rules of summary

In the clinical treatment of macroscopic "cancer toxin" related diseases, it is necessary to comprehensively grasp the treatment principle of "cancer toxin" pathogenesis. The principle of strengthening healthy Qi is to supplement Qi, blood, Yin and Yang in combination with the specific clinical situation. According to the stage of the disease, strengthening the right and eliminating pathogenic factors should be of primary and secondary importance, and the fundamental treatment should be attributed to strengthening the spleen and Qi to support the acquired foundation; The leading treatment can be summarized as regulating Qi movement and dredging down. The core of treatment is anti-cancer and detoxification. Based on the above analysis, the medication rules of the included prescriptions and the results of the new prescription analysis, it is speculated that the basic point of TCM treatment for the macroscopic "cancer toxin" related diseases is "strengthening the body",that is, to improve the symptoms of deficiency of vital energy in the pathogenesis, so that the body can actively fight against 'cancer toxin'. The treatment focuses on resolving phlegm, removing blood stasis and detoxification to resolve and eliminate the basic pathogenesis of 'cancer toxin'. Therefore, strengthening spleen and replenishing Qi, strengthening healthy Qi and tonifying deficiency are used to achieve smooth Qi movement of the whole body.
body, paving the way for the addition and subtraction of "attacking toxin" drugs on the basis of strengthening healthy Qi, and ultimately achieving the purpose of seeking both temporary and permanent solutions. The above results and analysis provide the basis and ideas for the treatment of macroscopic "cancer toxin" related diseases under the guidance of "eliminating pathogenic factors and attacking toxin" theory.

References