Data Mining-Based Research on the Prescriptions of Ancient Chinese Medicine Prescription Book Type Documents for Mouth Sores

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Abstract: Objective: To explore the prescription patterns of ancient Chinese medical literature on mouth sores and provide references and ideas for the treatment of mouth sores in Chinese medicine. METHODS: We searched the section of "Chinese Medical Canon" - "Formula Books" - "Comprehensive formula books", counted the prescriptions that met the inclusion criteria, and used the TCM transmission aid platform (V2.5) The Chinese herbal medicines were analyzed in terms of taste, meridian, frequency and clustering rules. RESULTS: 134 prescriptions were collected, involving 199 herbal medicines, and the drugs appearing ≥23 times in the order of licorice, scutellaria, asclepias, Huanglian, gardenia, rhubarb, maitong, and ginseng; there were 11 groups of drug combinations with frequencies ≥12 times; most of the bitter, sweet, and pungent herbs were used; the drug ascriptions were mainly in the stomach, spleen, and lung meridians; two groups of core combinations and one new prescription were deduced. CONCLUSION: This paper focuses on clearing heat and detoxifying toxins, tonifying the spleen and benefiting Qi, while protecting the spleen and stomach at the same time.

1. Introduction

Mouth sores are superficial, single or multiple yellowish-white ulcers of varying sizes on the oral mucosa and tongue, characterized by burning and painful recurrent episodes. Mouth sores are also known as mouth ulcers and mouth chancre. The name of the disease is first found in Suwen - Qi Jiaoyu Dazhan (The Great Treatise on Qi Crossing), "The year-old gold is not enough, and the fire is active. ...... people are sick with mouth sores". This disease is usually found on the lips, tongue, cheeks, gums, hard palate and other parts of the body, and can occur singly or repeatedly, with intense localized burning-like pain, and generally heals in about 10 days. It can occur at any age, and it attacks every time when eating carelessly, malnutrition, overexertion, sleep deprivation, etc. It is mostly seen in young adults, with slightly more women than men. Clinically, it can be divided into two categories: actual and deficient. The deficient evidence is often prone to recurrence, and some have a history of more than a decade or even decades. The recurrent mouth sores, idiopathic aphthous stomatitis, or recurrent oral ulcers, as they are called in Western medicine, are similar to this disease, so we can refer to this disease to identify and treat it. In the Su Wen, it is said that "all

painful and itchy sores belong to the heart." The spleen is the orifice of the mouth and the heart is the orifice of the tongue, and mouth sores occur on the tongue and lip and cheek mucosa of the mouth. Most medical practitioners believe that the occurrence of mouth sores is a mixture of deficiency and reality, with the origin being yin deficiency and fire and the symptoms being heat accumulation in the heart and spleen [1], and Chinese medicine has a long history of treating this disease. The book "Chinese Medical Dictionary" contains prescriptions of famous Chinese medical practitioners from various periods for the treatment of mouth sores, and we now use data mining techniques to summarize the medication combinations used in this book for the treatment of mouth sores.

2. Materials and methods

2.1. Data sources

The fifth edition of the Chinese Medical Canon is a large electronic series of books made by the Chinese Academy of Traditional Chinese Medicine, Hunan Electronic Audio and Video Publishing House, and Jiahong Technology Development Co. The latest version of the Chinese Medical Canon contains 1156 ancient Chinese medical books, with tens of thousands of volumes, bringing together the major Chinese medical works of all generations before the founding of New China, including many rare copies and isolated books, covering roughly the main achievements of Chinese medical culture up to the Republic of China, and is the most ambitious electronic series of Chinese medicine to date. In this study, we mainly searched the section of "Chinese Medical Dictionary" - prescription books - comprehensive prescription books.

2.2. Inclusion criteria

1) Formulas described in the original text of the literature for the treatment of "mouth sores", "sores in the mouth", "sores on the tongue", etc. 2) Formulas described in other parts of the original text, including (2) Formulas that include "mouth sores", "sores in the mouth", "sores on the tongue", etc. in other parts of the original formulas, and that mean "mouth sores" as the main treatment of the formula. (3) The prescriptions of soup, pill, powder, and elixir.

2.3. Exclusion criteria

1) duplicate prescriptions; 2) prescriptions in other dosage forms than soup, pill, powder, and dan; 3) folk food therapy prescriptions or prescriptions; 4) prescription names without prescriptions.

2.4. Data processing

2.4.1. Standardized processing of Chinese medicine

Referring to the 2020 edition of the Pharmacopoeia of the People's Republic of China [2] and the 13th Five-Year Plan Textbook of Higher Education in Traditional Chinese Medicine, Traditional Chinese Medicine [3], the names of Chinese medicines with different names and the same medicine were standardized and unified, e.g., peony was unified as white peony, licorice root was unified as licorice, and Chuan mannitifolia was unified as mannitifolia.

2.4.2. Establishment of database

A total of 134 prescriptions meeting the criteria were screened according to the inclusion and

exclusion criteria, involving 199 Chinese herbal medicines, and the prescriptions were independently entered into the TCM transmission aid platform system (V2.5) by two investigators and cross-checked, and if the disagreement was too great, they were entered after consulting third-party opinions to ensure the true reliability of the results.

2.4.3. Statistical methods

Statistical analysis of the established database was performed using data mining, including statistics on the frequency of drugs, attribution, four qi, and five flavors, as well as analysis of prescription patterns and new prescriptions, to derive the common drugs as well as prescription patterns, new drug combinations, and prescriptions for the treatment of mouth sores in the ancient Chinese medicine literature of prescription books.

3. Results

3.1. Statistics on the frequency of medication use

From Table 1, we can find that the top 6 drugs with the highest frequency in the treatment of mouth sores in ancient Chinese medical literature are Glycyrrhiza glabra, Scutellaria baicalensis, Shengma, Huanglian, Gardenia jasminoides, and Rhubarb, in addition to Mai Dong, Ginseng, Xuan Shen, and Fang Feng, which are also commonly used.

3.2. Distribution of drug attribution

From Figure 1, it can be seen that the drug meridians used in ancient TCM prescriptions for the treatment of mouth sores were mainly the stomach, spleen, and lung meridians, supplemented by the selection of drugs from the heart, large intestine, and liver meridians.

Table 1: Single drug frequency ≥ 13 times

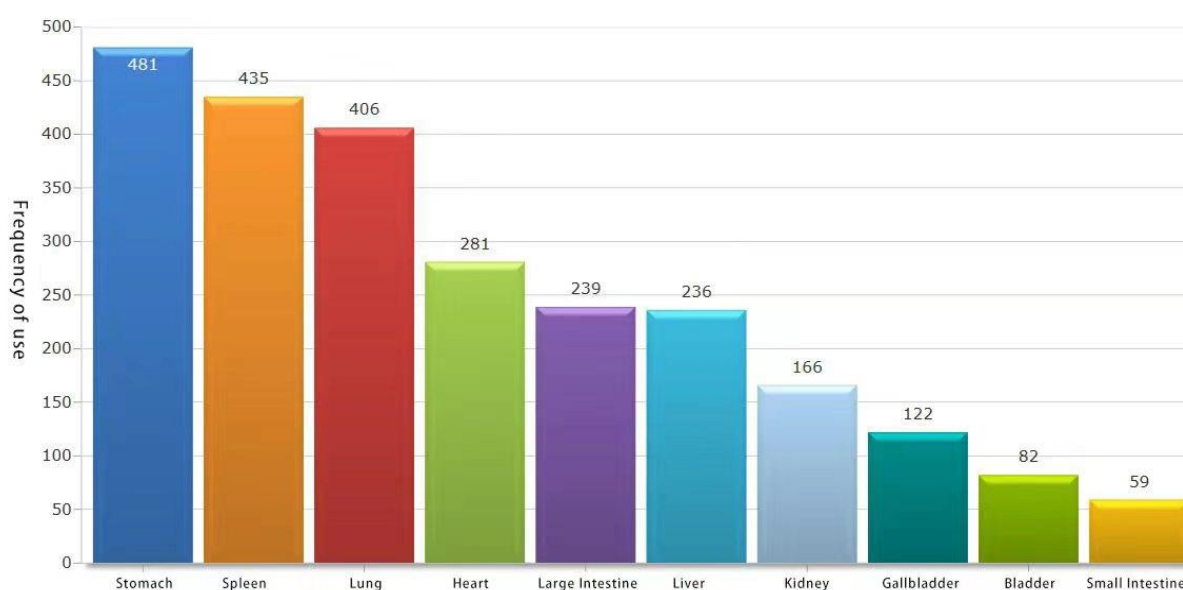| No.	Drug	Frequency	No.	Drug	Frequency
1	Glycyrrhiza glabra	59	11	Radix Bupleurum	19
2	Baicalin	39	12	Radix Rehmanniae	17
3	Radix Rehmanniae	33	13	Radix Glycyrrhiza glabra	17
4	Huang Lian	29	14	Atractylodes Macrocephala	16
5	Gardenia jasminoides	28	15	Mangosteen	16
6	Da Huang	27	16	Bai Shao	16
7	Mai Dong	24	17	Huang Bai	15
8	Ginseng	23	18	Radix Platycodon	15
9	Radix et Rhizoma Ginseng	20	19	Antelope's horn	14
10	Fangfeng	20	20	Rhinoceros horn	13

Figure 1: Distribution of drugs by meridian

3.3. Analysis of the five flavors of drugs

In ancient Chinese medical literature, the use of bitter, sweet, and pungent tastes in the treatment of mouth sores was dominant, while salty, sour, and astringent tastes were relatively rare, as shown in Figure 2.
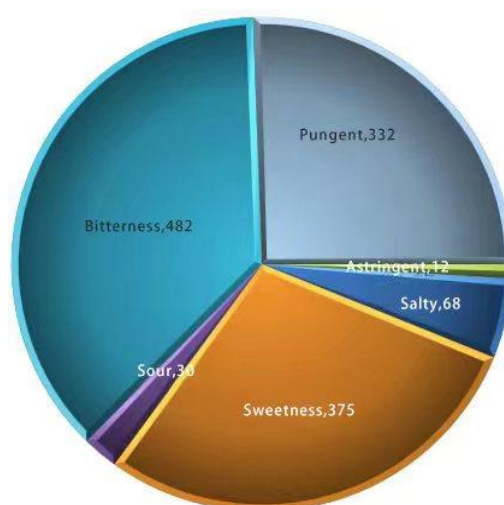

Figure 2: Distribution of the five flavors of drugs

3.4. Combination statistics based on association rules

With the help of the "Formulation rules" section of the TCM heritage support platform system (V2.5), the "number of support" was set to 12 and the "confidence" was set to 0.6, and the core The drug combinations were sorted from highest to lowest frequency, and the combinations with higher frequency were "Scutellaria baicalensis - Glycyrrhiza glabra", "Glycyrrhiza glabra - Rhubarb", "Mai Dong - Glycyrrhiza glabra ", "Glycyrrhiza glabra - Shengma", "Huanglian - Glycyrrhiza glabra", see Table 2; and the association rules of drug combinations with higher frequencies were reflected in network diagrams, see Figure 3.

Table 2: Drug combinations with support ≥12

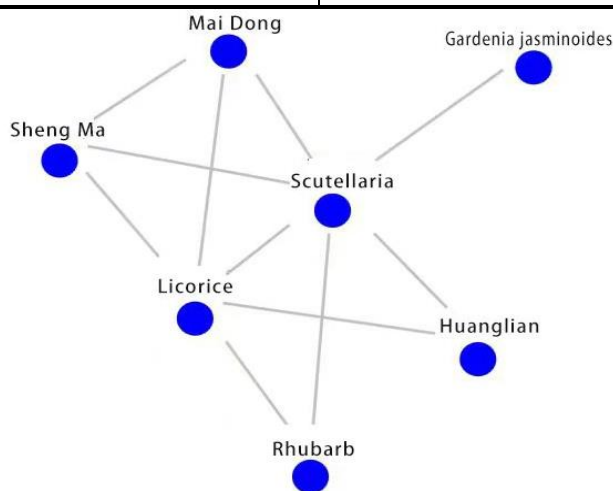| No.	Drug combination	Support degree	No.	Drug combination	Support degree
1	Scutellaria baicalensis, Glycyrrhiza glabra	20	7	Mai Dong, Glycyrrhiza glabra	14
2	Scutellaria baicalensis, Asclepias	18	8	Huanglian, Glycyrrhiza glabra	14
3	Glycyrrhiza glabra, Asclepias	16	9	Mai Dong, Scutellaria	13
4	Glycyrrhiza glabra, Rhubarb	15	10	Scutellaria baicalensis, Rhizoma scutellaria	12
5	Scutellaria, Rheum	15	11	Mai Dong, Sheng Ma	12
6	Scutellaria baicalensis, Gardenia jasminoides	15			

Figure 3: Association rule network display diagram

3.5. Clustering analysis based on entropy clustering rules

Applying the "New prescription analysis" function panel of the TCM inheritance support platform (V2.5), setting the "correlation degree" to 5 and the "penalty degree" to 3, the selected prescriptions were subjected to Based on the cluster analysis, a core combination of Radix et Rhizoma Ginseng, Radix et Rhizoma Fenugreek and Radix et Rhizoma Ginseng was obtained. As shown in figure 4.
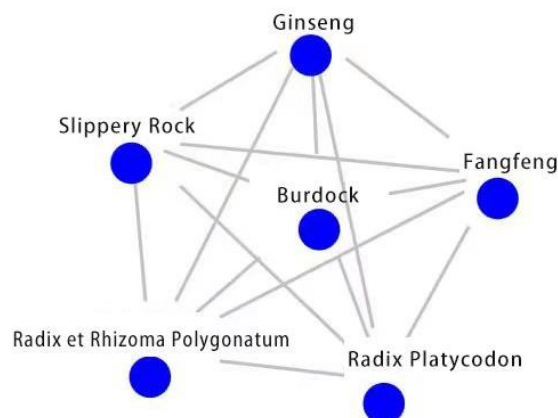

Figure 4: New prescription drug network display chart

4. Discussion

4.1. Etiology and pathogenesis

In the Shengji General Record-Men of the Mouth and Teeth, it is recorded that "the theory says that mouth sores are caused by heat in the heart and spleen, and the gas rushes to the upper jiao and fumigates the mouth and tongue, thus making sores." In the Ming Dynasty, the "Standard Rules for the Treatment of Disease - Miscellaneous Diseases" also pointed out that "the middle qi is injured and the lip and mouth are created ......" and the "Xue's Medical Case Selection - Mouth and Teeth Category" said, "Mouth sores are caused by real heat in the upper jiao, deficiency cold in the middle jiao, and yin fire in the lower jiao, each of which is transmitted and changed, and should be treated separately. The treatment should be separate. This is summarized clinically as follows: Heat accumulation in the heart and spleen: the accumulation of heat in the heart and spleen due to excessive consumption of spicy and thick flavors or alcoholic and sweet drinks, which causes heat to become fire and attack the oral cavity through the meridians; or due to uncleanliness of the oral cavity or damage to the mucous membrane, which causes the invasion of poisonous evil and the decay of the muscle membrane. Yin deficiency fire: Yin deficiency in the body, coupled with the disease or excessive labor, Yin loss, false fire on the inflammation of the oral cavity can also develop. Spleen and kidney yang deficiency: because of the endowment of yang deficiency, yin and cold within the Sheng, false yang upward, burning the oral cavity, or because of the Yang deficiency of warming and dysregulation, cold and dampness trapped in the oral cavity and the onset.

4.2. Frequency of medication and high frequency drug combinations

From the frequency of medication use in Table 1, it can be found that the medications used in this study for the treatment of mouth sores in ancient TCM prescriptions were mainly for clearing heat and fire and detoxifying the toxins, and the first six medications used most frequently were licorice, scutellaria, asclepias, Huanglian, gardenia, and rhubarb, and the more frequent drug combinations were "scutellaria-glycyrrhiza", "Glycyrrhiza", "glabra-rhubarb", "Medicago", "sativa-glycyrrhizae", "Glycyrrhiza glabra-ascending marijuana", "Huanglian-glycyrrhizae" and so on.

Baicalin is bitter and cold in nature and belongs to the lung, gall bladder, spleen, large intestine and small intestine meridians. It is used raw to clear heat and fire and detoxify the toxins. Shengma is pungent, slightly sweet and slightly cold. It belongs to the lung, spleen, stomach and large intestine meridians. Clearing heat and detoxifying, toothache, mouth sores, sore throat, Yang poisonous hair spots. Huang Lian is bitter, cold. Enters the heart, stomach and large intestine meridians. Clearing heat and drying dampness, removing fire and detoxifying. Gardenia is bitter and cold in nature. Enters the heart, liver, lung and stomach meridians. Clearing heat, relieving dampness, cooling the blood and detoxifying the toxin. Rhubarb is bitter and cold in nature. Involves the spleen, stomach, large intestine, liver and pericardium meridians. Clearing heat and intestines, cooling the blood and detoxifying the toxin. All the above drugs are combined with licorice, which is flat in nature. It belongs to the heart, lung, spleen and stomach meridians. It clears heat and detoxifies the body, tonifies the spleen and benefits the qi, and harmonizes all the medicines. It can reconcile the coldness of the above medicines, and at the same time protects the spleen and stomach.

4.3. Five flavors of drugs

From the distribution of the five tastes in Figure 2, we can find that the drugs used are mainly

bitter, sweet and pungent, while salty, sour and astringent drugs are used relatively less. The bitter taste is diarrheic and dry, the sweet taste is tonic and slow, and the pungent taste is dispersing and active. In this study, most of the drugs used are cold in nature, considering that the etiology of this disease is mostly due to deficiency of fire and yin and fluid, while bitter drugs can drain and dry, and sweet drugs can tonify, harmonize and slow down, which can supplement the qi, blood, yin and yang of the body and relieve the deficiency of qi, blood, yin and yang of the body, while pungent drugs can move and disperse, which can disperse the surface evil and move qi and blood to regulate qi and blood.

4.4. Drug meridian

From Figure 1, it can be seen that the main drug channels are the stomach, spleen and lung channels, supplemented by the heart, large intestine and liver channels. The lung is a delicate organ that is susceptible to the six evil spirits; the stomach is prone to heat, the spleen is prone to dampness, and the heart and spleen are prone to heat accumulation; therefore, most drugs used to treat mouth sores are classified as lung, stomach, heart, and spleen.

4.5. Analysis of the new formula based on entropy clustering

The new formula is composed of ginseng, slippery stone, bifeng, burdock, orris, and thornberry spike. It enters the stomach and bladder meridians. It can clear heat and detoxify the toxin; Fangfeng and Thornbush can relieve the symptoms and eliminate sores and toxins, both of them are used together to clear the surface evil; Radix et Rhizoma oryzaeum and Arctium lappa are bitter and pungent and enter the lung meridian, both of them can benefit the throat and eliminate swelling.

The two are used together to eliminate carbuncles, sores and toxins. The whole new prescription is based on relieving symptoms and dispelling wind, promoting the pharynx and subduing swelling, and helping to dispel evil.

References

[1] Lin Minfeng. An overview of the etiology of recurrent mouth sores and the effect of Chinese medicine treatment [J]. Electronic Journal of General Practice Dentistry, 2017.
[2] National Pharmacopoeia Committee. Pharmacopoeia of the People's Republic of China [M]. Beijing: China Medical Science and Technology Press, 2020.
[3] Zhou Zhenxiang, Tang Dcai. Traditional Chinese medicine [M]. Beijing: China Chinese Medicine Publishing House, 2016.