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Research on the medication rules of the famous Chinese medicine professor Ma Zhanping in the treatment of COPD by data mining

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Abstract: *Objective: To collect and organize the clinical TCM prescriptions of Professor Ma Zhanping in the diagnosis and treatment of chronic obstructive pulmonary disease (COPD), to clarify and analyze the commonly used TCM compatibility of Professor Ma Zhanping in the treatment of COPD, and to summarize his clinical experience in the treatment of COPD. In order to provide some reference for clinical treatment of COPD. Methods: The Chinese medicine prescriptions for COPD treated by Professor Ma Zhanping in the outpatient department of Shaanxi Provincial Hospital of Traditional Chinese Medicine from January 2019 to March 2021 were collected. After screening, data mining techniques such as statistical frequency, association rule analysis, drug network link relationship analysis, and cluster analysis were used, analyze the drug compatibility relationship, summarize the medication rules, and visualize the results. Results: A total of 271 first-diagnostic prescriptions were screened, involving 160 flavors of drugs, and the frequency of use reached 4012 times. Among them, commonly used drugs include bitter almond, ephedra, coix seed, pinellia chinensis and perilla seed. Coix seed, at the same time cluster analysis obtained 4 groups of clusters. Conclusion: Professor Ma Zhanping believes that the treatment of COPD should firstly identify the external and internal injuries, differentiate the syndrome by stages, and choose the prescription flexibly, so as to promote the normalization of qi in the body, and then the qi will be smooth and smooth.*

Keywords: *Data mining; COPD; Ma Zhanping; Medication rule*

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a clinically common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow restriction [1-3]. Its multiple organ complications and high fatality rate still make it one of the refractory respiratory diseases in clinic [1]. Its main symptoms are repeated shortness of breath, wheezing and cough, which can be classified as "lung distension and asthmatic syndrome" in Chinese medicine. Recent studies have shown that TCM has a series of in-depth studies on the etiology, pathogenesis, syndrome differentiation and treatment of COPD, and the integrated treatment of traditional Chinese and western medicine has achieved a good effect on improving patients' clinical symptoms and quality of life [4-6]. TCM has gradually become one of the important means for the treatment and prevention of COPD.

Professor Ma Zhanping is a first-class chief physician, master tutor, a famous Chinese medicine in Shaanxi Province, under the guidance of Professor Liu Huawei, a national famous Chinese medicine, and heir to the academic theory of Five Elements Qi machine gasification. Professor Ma Zhanping has been in medicine for more than 30 years, and has unique insights on TCM treatment of COPD, with good clinical efficacy. Therefore, this study used data mining technology, combined with the author's perception of following diagnosis and the interview with Professor Ma Zhanping, to summarize the medication rules and dispensing characteristics of Professor Ma Zhanping in the treatment of COPD, to provide reference for further inheritance of TCM experience, and to provide theoretical support for later clinical and experimental research.

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2. Materials and Methods

2.1. Cases of source

The cases of COPD treated by Professor Ma Zhanping in the outpatient department of Shaanxi Provincial Hospital of Traditional Chinese Medicine from January 2019 to March 2021 were collected, and the patient's medical records were screened. When there were prescriptions for return visit in the patient's medical records, only the first TCM prescription was taken, and a total of 271 TCM prescriptions were collected.

2.2. Selection criteria

2.2.1. Diagnostic criteria

The main reference is Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease 2021 report [2] and Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2013 Revision) [3].

2.2.2. Included in the standard

FEV1/FVC<0.7 after the application of bronchodilation agent in pulmonary function examination, the patient was diagnosed as an outpatient with COPD, and the outpatient medical record was written with standard and complete prescriptions.

2.2.3. Exclusion criteria

Those who do not meet the diagnostic criteria; Patients with severe heart disease or severe mental illness; The outpatient medical record writing is not standard, prescription is incomplete.

2.3. Data specification

With reference to the national industry of higher education of Chinese medicine "much starker choices-and graver consequences-in planning teaching material" science "[7] and the China pharmacopoeia (2020 edition) [8] on the classification into the name of the prescription of traditional Chinese medicine, efficacy and flavour to the normalization processing, such as wax gourd" benevolence "corrections for" winter melon seeds ", "pearl barley" corrections for coix seed, etc.

2.4. Data entry

The standardized outpatient prescriptions were input into Excel to establish a database, and classified according to the basic information of patients, TCM syndromes, prescription names and TCM single drugs. In order to prevent data entry errors, two personnel will review the data after completion to ensure the accuracy of the data.

2.5. The data analysis

After data entry and review were completed, Excel was used to make statistics on the frequency and meridian of drugs in the database, calculate their frequency, and classify the efficacy of high-frequency drugs. Data were imported into IBM SPSS Modeler 18.0 software. Drug association rules and network link analysis were carried out on high-frequency drugs based on Apriori algorithm. After the analysis, network link results were imported into Cytoscape software for drug network link network diagram. Then IBM SPSS Statistics 25 software was used for system cluster analysis and tree graph was drawn.

3. Result

3.1. Frequency and frequency of commonly used drugs

In this study, 271 outpatient TCM prescriptions for COPD treated by Professor Ma Zhanping were collected, involving 160 TCM prescriptions, and the total frequency of use was 4012 times. In addition to licorice, the high frequency were almond (79.7%), ephedra (73.8%), Coix seed (64.6%), pinellia pinellia (63.8%) and Perilla seed (52.8%), etc., as shown in Table 1.

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Table 1: Frequency and frequency of TCM used by Professor Ma Zhanping in the treatment of COPD (frequency ≥25%, except licorice).

sort	Traditional Chinese medicine name	Frequency/time	Frequency / %		sort	Traditional Chinese medicine name	Frequency/time	Frequency / %
1	Bitter apricot kernels	216	79.7%		11	agilawood	100	36.9%
2	ephedra	200	73.8%		12	Magnolia bark	100	36.9%
3	Semen coicis	175	64.6%		13	cinnamon	98	36.2
4	Qing pinellia	173	63.8%		14	peucedanum root	90	33.2%
5	Perilla	143	52.8%		15	lily	79	29.2%
6	angelica	135	49.8%		16	Semen raphani	72	26.6%
7	Winter melon seeds	131	48.3%		17	Purple Perilla leaf	72	26.6%
8	Phragmites communis	126	46.5%		18	dangshen	71	26.2%
9	Peach kernel	123	45.4%		19	Large-headed atractylodes	69	25.5%
10	Poria cocos	108	39.9%		20	Dried tangerine or orange peel	69	25.5%

3.2. Efficacy classification

49 traditional Chinese medicines with frequency ≥20 times (4012 times in total, 84.2% of the total frequency) were classified into efficacy categories, and the frequency and frequency of each category were calculated. A total of 12 kinds of TCM were classified, among which the ones with high frequency were phlegm-reducing, cough relieving and asthma relieving drugs (953 times), tonifying deficiency drugs (557 times), moistening water and dampening dampness drugs (436 times), surface relieving drugs (381 times) and qi regulating drugs (327 times), as shown in Table 2.

Table 2: Drug efficacy classification analysis (frequency ≥ 20 times, except licorice).

sort	Drug category	Number/flavor of Chinese medicine	Frequency/time	Frequency / %	Common drugs/frequency
1	Phlegm relieving cough relieving asthma	14	953	23.8%	Bitter apricot kernels(216), Qing pinellia(173), Perilla(141), peucedanum root(90), Loquat leaf(45), Mustard seed(44), Zhejiang fritillary(42), Golden buckwheat(41), White mulberry(33), clamshell(30), Coltsfoot flower(30), Platycodon grandiflorum(24), ginkgo(22), Bamboo shavings(20)
2	Tonify deficiency medicine	9	557	13.9%	angelica(135), lily(79), dangshen(71), Large-headed atractylodes(69), Dwarf lilyturf(67), Caulis dendrobii(46), The root of remembranous milk vetch(40), yam(26), Radix paeoniae alba(24)
3	Moistening agent for water	4	436	10.9%	Semen coicis(175), Winter melon seeds(131), Poria cocos(108), alisma(22)
4	Nourish the medicine	5	381	9.5%	ephedra(200), Purple Perilla leaf(72), Cassia twig(43), cohosh(37), Radix bupleuri(29)
5	Spleen medicine	4	327	8.2%	agilawood(100), Magnolia bark(100), Dried tangerine or orange peel(69), Pummelo peel(58)
6	Heat medicine	4	223	5.6%	Phragmites communis(126), Rhizoma anemarrhenae(37), Scutellaria baicalensis georgi(36), Rhizoma coptidis(24)
7	Xiaoshi drugs	2	137	3.4%	Semen raphani(72), Millet sprout(65)
8	Promoting blood circulation and removing blood stasis	1	123	3.1%	Peach kernel(123)
9	Temperature in medicine	1	98	2.4%	cinnamon(98)
10	Astringent medicine	2	55	1.4%	Fruit of Chinese magnoliavine(67), cuttlebone(23)
11	Antiseptic for liver and wind	2	46	1.1%	earthworm(33), Batryticated silkworm(21)

3.3. Statistical analysis of drug flavor

From the point of view of the four drugs, the most used drugs are warm drugs, followed by mild cold, flat drugs; There are many kinds of drug-induced flavor classification, but there are primary and

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secondary ones. Therefore, this study only included the first attribute into the statistics. From the perspective of five tastes, sweet, bitter and sweet drugs were the most used. From the point of view of the meridian, the lung meridian is the most, followed by the spleen; See Figure 1 for details.

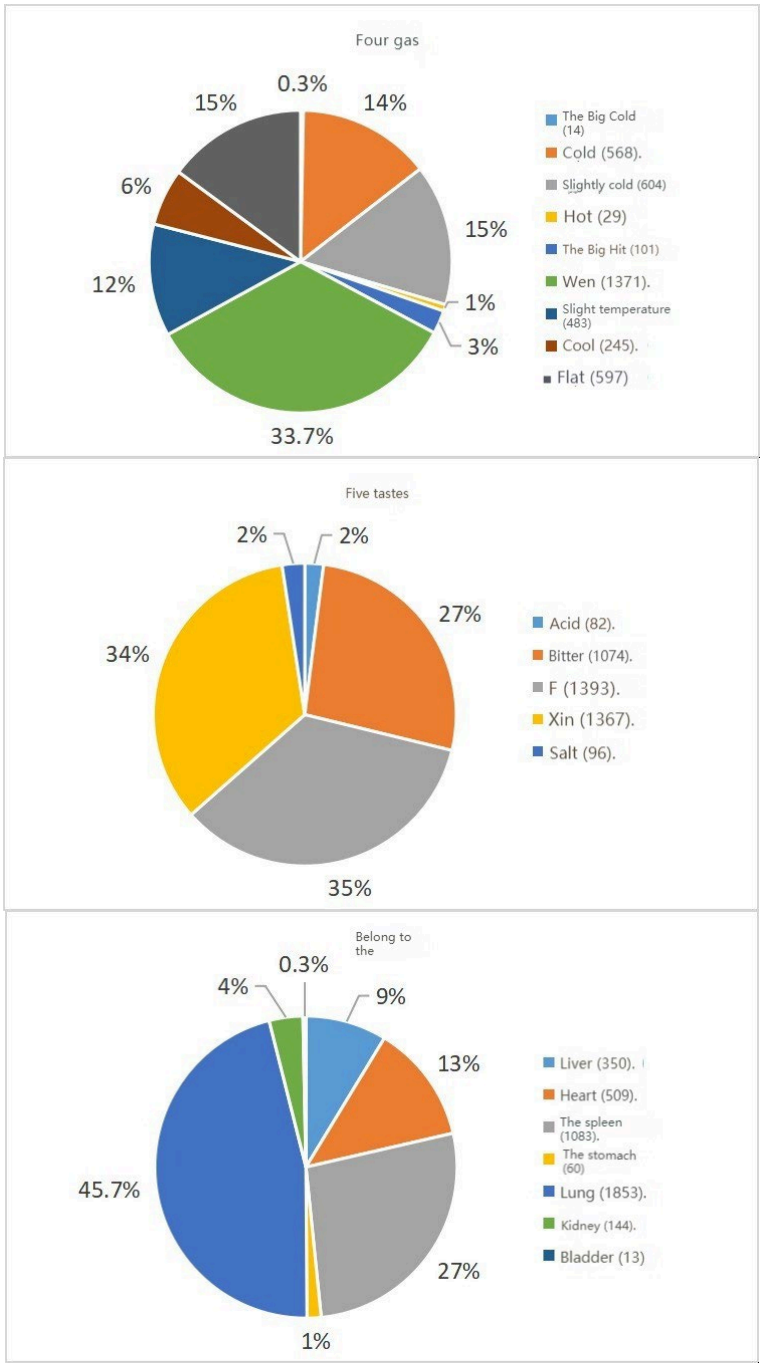

Figure 1: Drug-induced taste meridians.

3.4. Correlation degree analysis

Apriori algorithm was used to conduct correlation analysis for high-frequency drugs. According to the data analysis rule [9], the minimum support degree was set as ≥30%, the minimum confidence degree as ≥80%, and the maximum number of the first item as 1. The two TCM combinations commonly used by Professor Ma Zhanping in the treatment of COPD were obtained. The top 10 TCM combinations were selected in order of support, as shown in Table 3.

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Table 3: Analysis of association rules of drugs for treating COPD by Professor Ma Zhanping (ranking of support drgree).

sort	Traditional Chinese medicine combination	Frequency/time	Support / %	Confidence / %
1	ephedra- Bitter apricot kernels	216	79.7	83.8
2	ephedra-Semen coicis	175	64.6	81.7
3	Bitter apricot kernels-Semen coicis	175	64.6	85.7
4	Perilla-Qing pinellia	173	63.8	80.9
5	ephedra-Qing pinellia	173	63.8	83.2
6	Bitter apricot kernels-Qing pinellia	173	63.8	86.1
7	Qing pinellia-Perilla	143	52.8	97.9
8	ephedra-Perilla	143	52.8	81.8
9	Bitter apricot kernels-Perilla	143	52.8	86.0
10	Peach kernel-Winter melon seeds	131	48.3	93.1

Association rule analysis was conducted for drugs again, and the maximum number of previous items was set as 4, the minimum support degree was ≥30%, the minimum confidence degree was ≥80%, and the minimum enhancement degree was > 1. Relevant promotion rules are obtained, and the first 10 groups are sorted according to the degree of promotion. See Table 4 for details.

Table 4: Analysis of association rules of multi-drug combinations in the treatment of COPD by Professor Ma Zhanping (ranking of promotion degree).

sort	Traditional Chinese medicine combination	Ascension degree	Support / %	Confidence / %
1	cinnamon-Magnolia bark→peucedanum root	2.82	35.4	93.75
2	cinnamon-Perilla→peucedanum root	2.82	35.4	93.75
3	cinnamon-Qing pinellia→peucedanum root	2.82	35.4	93.75
4	Magnolia bark-Perilla→peucedanum root	2.82	35.4	93.75
5	angelica-Perilla→peucedanum root	2.82	35.4	93.75
6	angelica-Qing pinellia→peucedanum root	2.82	35.4	93.75
7	cinnamon-Magnolia bark-angelica→peucedanum root	2.82	35.4	93.75
8	cinnamon-Magnolia bark-Perilla→peucedanum root	2.82	35.4	93.75
9	cinnamon-Magnolia bark-Qing pinellia→peucedanum root	2.82	35.4	93.75
10	cinnamon-angelica-Perilla→peucedanum root	2.82	35.4	93.75

3.5. Analysis of drug network link relationship

IBM SPSS Modeler 18.0 software was used to analyze the network link relationship of commonly used drugs, setting strong link > 45, weak link < 25, and the rest as medium link. After analysis, the values were processed and imported into Cytoscape software for topological analysis. The top 26 Chinese medicines were sorted according to the Degree value to draw a network diagram. The size and color of the top 26 Chinese medicines were set according to the Degree value. The width and color of the set edge vary with the number of links. The larger the width and the darker the color, the more links it has. The figure shows the strongest correlation between bitter almond, ephedra and Coix seed, as shown in Figure 2.

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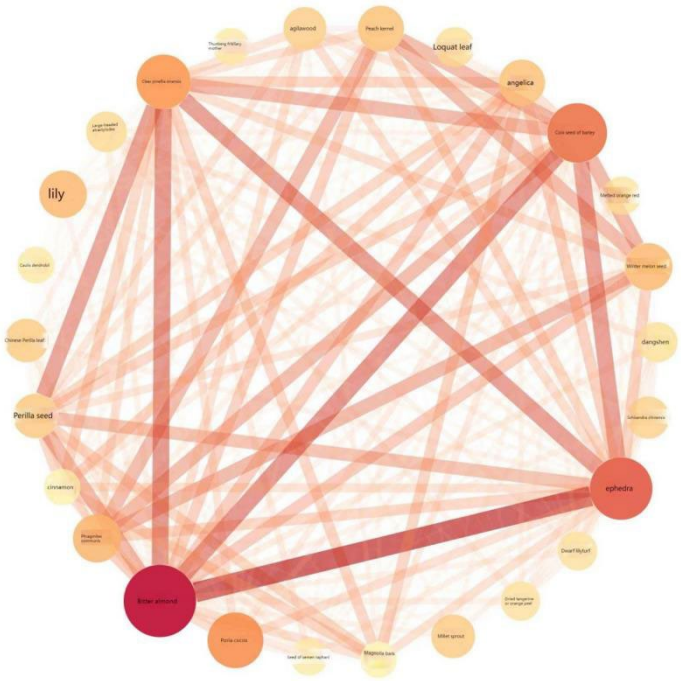

Figure 2: High-frequency drug network link diagram

3.6. Clustering analysis

The top 20 drugs with the highest frequency were imported into IBM SPSS Statistics 25 software for cluster analysis. The inter-group linking method was adopted, the square Euclidean distance was selected for distance measurement, and the tree graph format was output. When the distance =25, and output the tree. According to the clinical follow-up practice of the author, four cluster groups were obtained: Group C1: reed root, peach kernel, coix seed and winter melon seed; Group C2: ephedra, bitter almond; C3 group: Pinellia sinensis, Perilla seeds, magnolia officinalis, cinnamon, Fore-hu, angelica sinensis, aloes; C4 group: Poria cocos, Semen raphani, Perilla leaf, Codonopsis codonopsis, Atractylodes atractylodes, orange peel, lily. See Figure 3 for details.

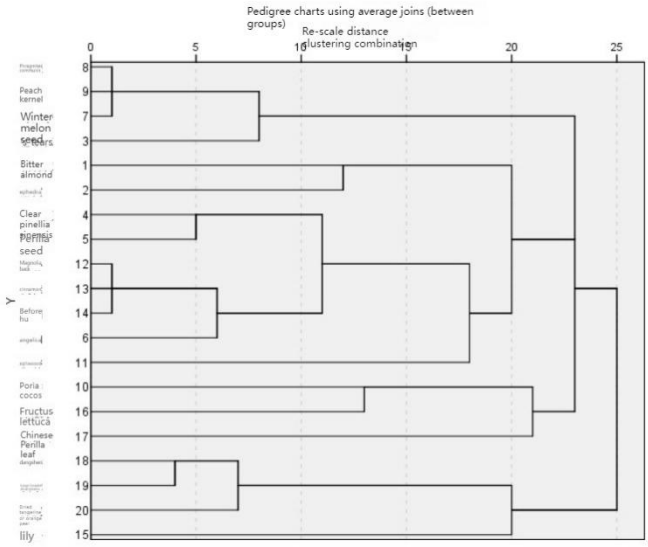

Figure 3: Tree of clustering analysis of high-frequency drugs

4. Discuss

Professor Ma Zhanping believes that COPD can be classified as "lung distension, cough and

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asthma", and its disease location is mainly in the lung, which is closely related to the spleen and kidney, and its main pathogenesis is "deficiency of lung and kidney Qi, interjunction of phlegm and blood stasis". As the Danxi Mind Law says: "Lung distension and cough, or left or right cannot sleep, this phlegm stasis obstructs gas and disease". Professor Ma believes that at the beginning of the onset of lung distention, most of the lung qi is not concentrated down, the lung qi does not fall, its publicity and release of the Gong lost department, external drink to stay in the phlegm, then the son disease and mother, temper will be weak; The goldwater is not born, the spleen is not transported, the kidney is taken, and the wheezing is getting worse. Phlegm drink due to the loss of the three viscera shall not be gasified out, block the Qi machine, blood stasis also follows, the two together block the airway, more hinder the gasification of the viscera, the disease is also intensified. Therefore, in the treatment should be to restore the normal Qi machine gasification between the zang Fu organs as the purpose, and to dispel evil, and according to the different periods of the disease, the first differentiation of external sensation, internal injury, external evil not solved, when to dispel the wind and cold, Qi and asthma; Internal injury should be tonifying lung and kidney, promoting blood and phlegm, qi and asthma as the purpose, according to its condition, with the syndrome, flexible medication.

4.1. The characteristics of drug use were analyzed from sex and taste meridian classification, efficacy classification and drug frequency

According to the result of drug flavor normalization, the drugs used by Professor Ma to treat lung distension are mainly warm, slightly cold and flat, and sweet, sweet and bitter. Lung distension is usually caused by the combination of deficiency, phlegm and blood stasis [10], so it is usually mild, flat, cold and clear, and light infiltration. From the perspective of medicinal taste, Xin can disperse wind, Gan can replenish deficiency, bitter can dry phlegm and remove blood stasis; Professor Ma believes that lung distension is usually caused by external evil. Therefore, it is necessary to remove external wind by cooling, promote lung Qi, and reduce phlegm and blood stasis by bitter warmth. When there is no Qi deficiency, it is mainly caused by internal injury, and Ganping is used to replenish deficiency and promote gasification, followed by bitter and warm ones to eliminate phlegm and blood stasis and promote the circulation of Qi machine. It is recommended to use a warm medicine and medicine to decant the diseased phlegm and to use a cold drink to harm the lung, and to use the Cough and Cure the Disease in the Jinjue Section. Two in accordance with the "plain question · to really big theory" "the wind is in the inside, to treat with xin cool, with bitter, with gentle, with xin dispersing... Wet in the body, with bitter heat, with acid light, with bitter dryness, with light release of the "purpose, together and promote the normal function of gas machine gasification in the body. From the point of view of drug meridian classification and efficacy classification, the drugs used were mainly phlegm-relieving, cough relieving and asthma relieving drugs, tonifying deficiency drugs, moistening and dampening drugs and relieving surface drugs. The lung was the most important drug for meridian classification, followed by the spleen. The drug characteristics were consistent with the disease location, pathogenesis and treatment proposed by Ma Shi.

From the perspective of drug frequency, the first six flavors are bitter almond, ephedra, Coix seed, pinellia, Perilla seed and angelica, among which ephedra and bitter almond are common drug pairs, both of which promote and reduce the meaning of promoting lung and reducing Qi and smoothing Qi. Ephedra xin, slightly bitter, warm, return to the lung, bladder meridian, function of sweating and cold, Xuan lung asthma, Li water detumescence; Modern pharmacological studies have shown that ephedra has good antipyretic and perspiratory effects, antitussive and antiasthmatic effects, and diuretic anti-inflammatory effects [11], but the medicinal properties of ephedra are too severe. In clinical practice, Professor Ma used honey ephedra to obtain the effects of ephedra and antiasthmatic effects. Bitter almond taste bitter, mild sex, return to the lung, large intestine meridian, function to reduce gas, relieve cough, relieve asthma, moisten bowel; Modern studies have shown that bitter almonds have good antitussive, antiasthmatic, immunomodulatory, anti-inflammatory and antioxidant effects [12]. At the same time, pharmacological studies have also reported that the combination of ephedra and bitter almond has a better synergistic effect on relieving asthma and cough [13], which coincides with the theory of TCM phase and need. Perilli seed, coix seed, Qingpinellia can reduce qi, relieve phlegm and relieve asthma, or can permeate dampness and remove phlegm, or dry dampness and relieve phlegm, which can be increased or decreased with the syndrome. Angelica is sweet, sweet, warm, and can return to the liver, heart and spleen. It functions to replenish blood and promote blood circulation, regulate the circulation and relieve pain, moisten intestines and relieve constipation. Modern studies have shown that Angelica has a protective effect on ischemia reperfusion injury and antiasthma effect [14-15]. The use of Perilla seed, Coix seed, Pinellia sinensis and Angelica sinensis was consistent with the pathogenesis of phlegm-stasis interknot proposed by Professor Ma.

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4.2. The characteristics of drug use were analyzed by association rules and systematic clustering

Based on association rules, the first three pairs of two drugs were ephedra - bitter almond, ephedra - Coix seed and bitter almond - Coix seed, which were the main components of Maxing Coix Decoction. Hemp apricot job sweet soup comes from the golden chamber, spasm, wet Ye disease pulse card cure ", originally "wet on the table, whole body all pain" set, based on many years clinical experience of professor ma, hemp apricot job in gansu following the ephedra, almond, for lifting, xuan to drop, with semen coicis can strengthen its phlegm moisture penetration, with lung expansion mechanism, can be used in the phlegm wet aggregates junction lung distension. The first three multi-flavor medicine pairs were: cinnamon-magnolia officinalis→Qianhu, cinnamon-perilla seed→Qianhu and cinnamon-pinellia chinensis → Qianhu, which were the main components of Suzi Qi lowering soup. Suzi Qi decoction comes from the "Taiping Huimin and agent prescription", clinical mostly used in the upper sheng under the deficiency, kidney deficiency cannot receive lung distention, the prescription for the treatment of the upper Gu, the specimen is taken into account, to reduce the qi and relieve asthma, the best formula for the return of Qi to Yuan. Modern studies have shown that Suzi Qi lowering decoction can significantly improve the lung function of patients and effectively relieve their clinical symptoms when applied to lung distension [16]. Above all, professor ma in clinical use antiasthmatic soup, hemp apricot job sweet soup with proposed the "lung kidney deficiency, phlegm and blood stasis knot" pathogenesis is consistent, suggests that the professor attaches great importance to the lung, spleen and kidney in the treatment of COPD and phlegm retention, blood stasis, and thinks that lung and spleen kidney deficiency, gasification division, liquid water from the Yin to phlegm and blood stasis, block jet, jet inverse chaos, the inverse for asthma, Therefore, it is necessary to tonify lung and kidney, promote blood and eliminate phlegm, and relieve qi and asthma as the fundamental treatment of lung distension.

Through systematic clustering, four traditional Chinese medicine clustering groups were obtained: Group C1: reed root, peach kernel, Coix seed and winter melon seed, which is Qianjin Weijing Decoction, which comes from Ancient and Modern Record Prescription and later in Sun Simiao's Bei Jian Qianjin Yaofang, and is mainly used in clinical treatment of phlegm and blood stasis interknot syndrome. For example, Liu Huawei et al.[17] used Qianjin Weijing decoction to treat phlegm-heat and blood-stasis type lung distension, which promoted the removal of phlegm and blood stasis, clear internal heat and smooth qi flow, and had a good effect. Moreover, experiments have proved that Jiawei Qianjin Weijing Decoction can alleviate lung tissue damage in COPD model rats, and has a protective effect on lung tissue of COPD model rats [18]. Group C2: Ephedra and bitter almond are important drug pairs for the clinical treatment of COPD by Professor Ma Zhanping. They promote health and health, cooperate and interact with each other, and play the function of promoting lung, reducing qi and relieving asthma together. They are clinically applicable to various syndrome types, and can be added or subtraction as appropriate. C3 group: Qing pinellia, Perilla, magnolia bark, cinnamon, radix peucedani, angelica, aloes, and this is mainly composed of antiasthmatic soup, clinical professor of aloes, often on the basis of the party used to enhance the party's gas and asthma, aloes, bitter, lukewarm, spleen, stomach and kidney meridian, qi analgesic function, stop ou, and gas and asthma, modern research has shown that Aloes has good anti-asthmatism, anti-inflammation and anti-oxidation effects [19-20], which is clinically suitable for lung distension with deficiency of upper and lower levels. C4 group: Poria, Semen raphani, Perilla leaf, codonopsis codonopsis, atractyloides, Tangerine peel and lily are actually two Chen soup, three sons nourishing kin soup and four junzi soup. This three-party combination has the effect of invigorating spleen and qi, eliminating phlegm and dampness. Professor Ma Zhanping often uses this three-party combination in clinical treatment of lung distention (deficiency of lung temper, phlegm dampness), and the effect is better. As Professor Ma Zhanping's commonly used additive and subduction drugs, Lily is characterized by sweetness, cold, Guishin and lung meridian, which function to nourish Yin and moisten lung, clear heart and soothe the mind. Clinical use of lily is mainly based on its sweetness, cold and moistening properties, one is to warm dryness of medicine, the other is to regulate lung dryness.

This paper analyzed and summarized the medication rules of the famous TCM professor Ma Zhanping in the treatment of COPD, expounded the idea that Professor Ma Zhanping attaches importance to the three viscera of lung, spleen and kidney, phlegm and blood stasis, and believed that they play an important role in the pathogenesis of lung distension, and proposed that the diagnosis and treatment of lung distension should first distinguish external and internal injuries. Active use of cold dispelling evil, tonifying lung and kidney, promoting blood and phlegm, qi and asthma to promote the normal gasification of the body as the treatment concept, and summed up the core prescription used in the treatment of lung distension. But in view of the disadvantages of data mining itself, some special cases, rare data are difficult to be excavated, such as horse draw with professor commonly used small

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qinglong decoction treatment of cold drink type lung distension, anti-asthma soup or big tsing lung tonga subtraction treatment outside the cold internal heating type lung distension, use "gecko, earthworm, batryticated silkworm," such as insect drugs and so on, also have a significant effect.

To sum up, this study combined the author's perception with the teachers, the interview content of famous traditional Chinese medicine professor Ma Zhanping and the data mining technology to comprehensively summarize the drug use experience of Professor Ma Zhanping in the treatment of COPD, hoping to provide some reference for clinical treatment and theoretical support for later theoretical and basic research.

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