Original Article

Study on Medication Rules of Modern Chinese Herbal Medicine in the Treatment of Non-small Cell Lung Cancer Based on Data Mining

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Abstract

Objective: Based on data mining technology, we attempted to explore the medication rules of modern traditional Chinese medicine (TCM) compounds in non-small cell lung cancer (NSCLC) treatment, to provide a reference for clinical drug use. **Methods:** From 2010 to 2017, TCM compounds used for NSCLC treatment were collected from the Beijing 301 Hospital. The modern TCM compounds utilized in the treatment of NSCLC were established in the prescription database. Excel, SPSS 22, and SPSS Modeler14.2 software were utilized for the frequency analysis, factor analysis, cluster analysis, and association analysis. Then, the quantitative and qualitative analyses of the regularity of TCM compound medications were performed, and the possible mechanism was discussed. **Results:** The treatment of NSCLC using Chinese herbal compounds involved 231 prescriptions, 389 types of Chinese herbs, and 135 types of high-frequency Chinese herbs. Of these, *Fritillaria cirrhosa*, stir-baked fried *Scutellariae*, raw Os Draconis, *Poria cocos* (Schw.) Wolf, and *Scutellaria barbata* were the top five frequently prescribed Chinese herbs. Among the 39 types of drugs, heat-clearing and detoxifying drugs and qi-tonifying drugs were the leading. Cold, warm, flat, slightly cold, sweet, bitter, and pungent of four properties and five tastes and the meridians of lung, spleen, and stomach were most commonly selected. Factor analysis extracted 12 common factors, and the cumulative contribution rate was 65.595%, which mainly contained tonifying qi and blood; tonifying yin, clearing away heat, and eliminating stagnation; tonifying the spleen, regulating qi, and eliminating phlegm. Forty drug groups were obtained by cluster analysis; a total of 63 association rules were obtained by association analysis. The pairs of *Poria cocos* → dried tangerine peel and fried *Atractylodes macrocephala* → dried tangerine peel were commonly used in NSCLC, while the three most frequent herb groups were raw *Astragalus* → fried *A. macrocephala* and *Poria cocos*; raw-medicated leaven → fried *A. macrocephala* and *Poria cocos*; and dried tangerine peel → fried *A. macrocephala* and *Poria cocos*. **Conclusion:** Lung cancer is mainly caused by qi stagnation, phlegm obstruction, phlegm, and blood stasis. Based on the principle of strengthening the body and dispelling pathogens, clinical treatment of NSCLC involves clearing heat and detoxifying, tonifying the spleen, regulating qi, eliminating phlegm to dispel pathogens, and tonifying qi and blood to strengthen the body.

Keywords: Data mining, modern Chinese medicine compounds, non-small cell lung cancer

Introduction

Lung cancer is a malignant tumor that occurs in the bronchial mucosa, glands, and alveolar epithelium. Studies have demonstrated that[1,2] lung cancer has the highest incidence and mortality rate in China. Furthermore, non-small cell lung cancer (NSCLC) accounts for 75%–80% of all lung cancers, which is a serious threat to human health. Early symptoms of lung cancer are mainly cough or dry cough, which are extremely common for patients to notice. Hence, lung cancer is usually discovered in the middle and later stages when the possibility of surgery, radiotherapy, or chemotherapy is no longer available. A large number of clinical studies[3-5] have shown that Chinese

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medicine has unique advantages in inhibiting malignant tumor growth, regulating immunity, increasing the efficiency, and reducing side effects of radiotherapy or chemotherapy.

In ancient books of traditional Chinese medicine (TCM), there is no mention of "lung cancer," but similar records of lung cancer symptoms have been documented. For example, "Suwen Qibinglun" (one ancient book of Chinese medicine) said, "the disease is called Xiji, which has the symptoms of fullness under the ribs and adverse rising of qi, etc." "Shengji Zonglu" (another ancient book) recorded, "pulmonary retention, also called Xiben, expresses cough and hemoptysis." The pathogenesis of lung cancer[6,7] is extremely complicated, in which the deficiency of healthy qi is considered primary while the spread of pathogen toxins to the whole body is considered secondary.

In this article, we attempted to analyze the data of Chinese medicine compounds utilized for NSCLC treatment (in the chemotherapy stage) from the Beijing 301 Hospital, during 2010–2017. We performed frequency analysis,[8] cluster analysis,[9] association rule analysis,[10] and factor analysis, to calculate the frequency of TCM and its four natures, five flavors, meridian tropism, and efficacy variables. We assessed drug groups for treating lung cancer, analyzed the combination rules of various Chinese medicines in compounds quantitatively and qualitatively, analyzed the law of drug utilization, and discussed various consensus and rules for the use of TCM in NSCLC treatment.

All these outcomes could provide objective data for the clinical treatment of NSCLC, improving the efficacy of TCM in the treatment of lung cancer and providing reference for future clinical treatment and novel drug research and development.

Search methods

Prescription source

From 2010 to 2017, TCM compounds used for NSCLC treatment (with chemotherapy treatment) were collected from the Beijing 301 Hospital, obtained from the National Scientific Data Sharing Platform for Population and Health.

Chinese Medicine Compound Screening and Entry

Inclusion criteria

All TCM compounds for NSCLC treatment were included.

Data specification

We referred to the "Twelfth Five-Year Plan" textbook of "Chinese Pharmacy" and the 2015 edition of the "Chinese Pharmacopoeia" of the National Higher Hospital of TCM and regulated the names of TCMs, such as Epimedium and Xianlingpi, termed Epimedium in this research. Furthermore, efficacy was classified. For example, *Codonopsis pilosula*, processed licorice, and fried *Atractylodes macrocephala* were classified as qi-tonifying drugs. Cooked rehmannia, peony, and *Angelica* were classified as blood-tonifying drugs.

Data processing and analysis

The TCM compounds utilized for the treatment of NSCLC were established in the prescription database using the Excel software. Excel (Microsoft Corporation, Redmond, Washington, USA) was used for frequency analysis, SPSS 22.0 (SPSS 21 Inc., Chicago, IL, USA) was used for factor and cluster analysis, and the SPSS Modeler14.2 (Inc., Chicago, IL, USA) software for employed for association rule analysis.

Results and Analysis

Based on the search and screening, 231 Chinese medicinal compounds were finally determined, and the Chinese herbal compounds were sorted to establish a database of Chinese herbal medicines for treating NSCLC as shown in Table 1.

Analysis of absolute frequency and percentage frequency

Analysis of absolute frequency and percentage frequency of high-frequency traditional Chinese medicine

The database listed a total of 389 types of Chinese herbal medicines. The Chinese herbal medicines whose frequency was below the average absolute frequency were excluded. A total of 135 types of Chinese herbal medicines remained, and the absolute frequency and percentage frequency analysis results are shown in Table 2, with the arrangement of the Chinese herbal medicines in order of absolute frequency from high to low.

Efficacy analysis of high-frequency traditional Chinese medicine

Table 3 and Figure 1 present the heat-clearing and toxin-resolving drugs, especially *Hedyotis diffusa* and *Cremastra appendiculata* (D.Don) Makino, which are most commonly used in modern Chinese medicine for NSCLC treatment, with a percentage frequency of 7.98%. The second was the qi-tonifying drugs (7.75%), demonstrating no significant difference compared to the first. The percentage frequency of each of the top five categories of TCM was over 5.5%. Furthermore, the heat-clearing, toxin-resolving, and qi-tonifying drugs were at the forefront of these data mining results, indicating the importance to strengthen the body and dispel pathogens during NSCLC treatment.

Analysis of meridian tropism of high-frequency traditional Chinese medicine

The meridian tropism of high-frequency Chinese medicine was 12. Arranged in the order of frequency from high to low, the frequency analysis results are shown in Table 4 and Figure 2. The top six meridian tropisms were as follows: lung meridian (39.36%), spleen meridian (59.48%), liver meridian (55.80%), stomach meridian (34.46%), heart meridian (34.15%), and kidney meridian (29.35%), while each absolute frequency was over 1200. Furthermore, in lung cancer treatment, replenishing the spleen and stomach and regulating the heart, liver, and kidney were crucial.

Analysis of the four natures of high-frequency traditional Chinese medicine

Based on the analysis results in Table 5 and Figure 3, the first

Table 1: Treatment of non-small cell lung cancer prescription database with the Chinese herbal compounds

Chinese medicines	Lithospermum	Bamboo shavings	Polyporus umbellatus	Processed radix asteris	Processed *Polygala tenuifolia*	Processed *cyperus rotundus* L	Processed radix polygoni multiflori	Processed cortex Mori	Processed loquat leaves	Processed ephedra
I71503837659	0	0	0	0	0	0	0	0	1	1
I71544607659	0	1	1	0	0	0	0	0	1	0
I71582777659	0	0	0	1	0	0	0	1	1	0
I71600677659	0	0	0	0	0	0	0	1	1	0
I74072897659	0	1	0	0	1	1	1	0	0	0
I60419096548	0	0	0	0	0	0	0	0	1	0
I60540406548	0	0	0	1	0	0	0	0	1	0
I65015576548	0	0	0	0	0	0	0	0	1	0
I26040052104	0	0	0	0	0	0	0	0	0	0
I48253384326	0	0	0	1	0	0	0	0	0	0

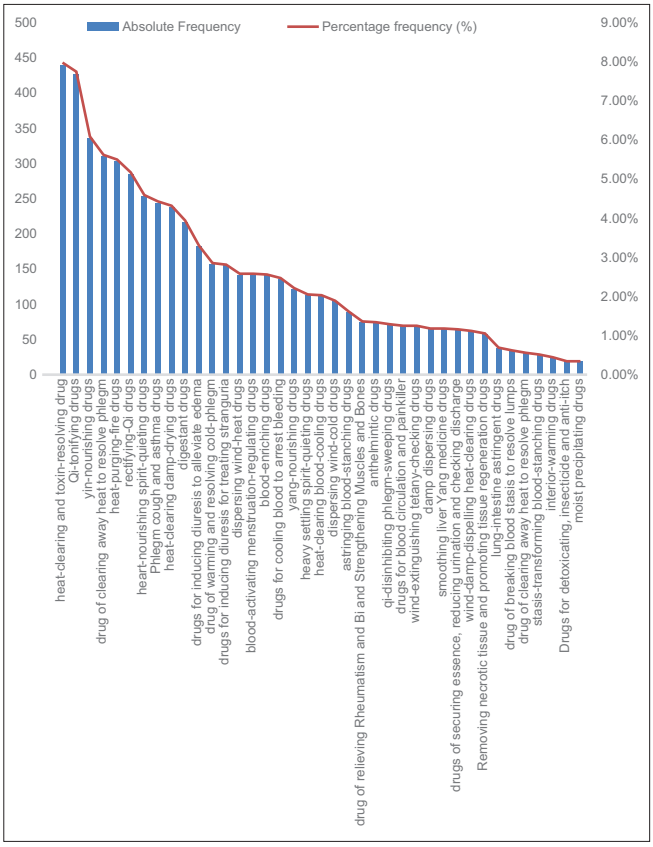

Figure 1: Efficacy analysis of high-frequency traditional Chinese medicine

four were cold (22.35%), warm (21.51%), gentle (21.51%), and slight cold (18.43%), and the absolute frequency of each of the top four natures of TCM was over 1000. Hence, our results demonstrated that Chinese medicines, with the four natures, i.e. cold, warm, gentle, and slight cold, were more commonly used for the treatment of NSCLC.

Analysis of the five flavors of high-frequency traditional Chinese medicine

In Table 6 and Figure 4, in high-frequency Chinese medicines, the top three of the five flavors presented were sweet (66.26%), bitter (48.88%), and pungent (42.06%), with each absolute

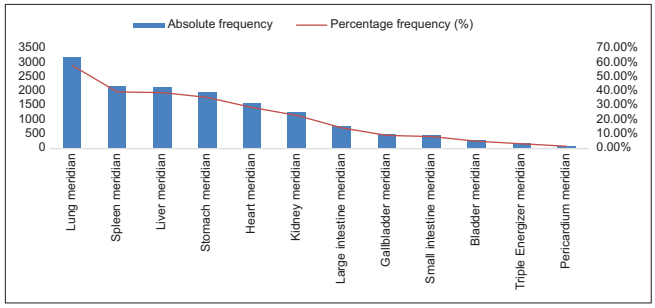

Figure 2: Analysis of meridian tropism of high-frequency traditional Chinese medicine

frequency exceeding 2400. Chinese medicines with the three flavors, i.e., sweet, bitter, and pungent were more commonly used for the treatment of NSCLC.

Factor analysis

In Table 7, factor analysis was performed on every single Chinese medicine with an absolute frequency of over 41, and the results are presented in Table 7 and Figure 5. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was 0.850, which was over 0.5 ($P < 0.05$). Hence, factor analysis could be applied. In Table 8, twelve common factors were finally extracted based on a featured root greater than one, and the cumulative contribution rate was 65.595%. In Table 9, according to the principle that the load factor was greater than 0.5, ten groups of several drug-combination factors affecting NSCLC treatment were finally extracted. The extraction results and the specific treatment methods reflected by each group of drugs are shown in Table 10.

Cluster analysis

The cluster analysis was performed on Chinese medicines with a frequency of 20 times or greater. The results of the analysis and the results of the combined extraction are shown in Table 11 and Figure 6.

Analysis results of association rules

According to the association rules, the parameter support degree was over ten, and the confidence level was over 50 (the support degree reflected the frequency of the drug groups; the confidence level reflected the reliability degree and

Table 2: Frequency analysis of high-frequency traditional Chinese medicine

Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)	Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)	Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)
1	*Fritillaria cirrhosa*	126	54.55	46	Raw glycyrrhizae	42	18.18	91	Dendrobium	25	10.82
2	Fried *Scutellariae*	115	49.78	47	Processed spinosae Ziziphi semen	42	18.18	92	Pinelliae rhizoma	25	10.82
3	*Raw* Os Draconis	113	48.92	48	*Codonopsis pilosula*	40	17.32	93	Root of balloon flower	25	10.82
4	*Poria cocos* (Schw.) wolf	109	47.19	49	Pinelliae rhizome	40	17.32	94	Golden lotus flower	25	10.82
5	*Hedyotis diffusa*	107	46.32	50	Rhizoma imperatae	39	16.88	95	Scorched areca seed	25	10.82
6	Raw *Scutellariae*	96	41.56	51	Pearl powder	38	16.45	96	Herba patriniae	25	10.82
7	Processed *Astragalus memeranaceus*	95	41.13	52	Schisandra	38	16.45	97	*Bolbostemma paniculatum*	24	10.39
8	Raw *Cyperus rotundus* L	93	40.26	53	Raw farfarae flos	38	16.45	98	*Ligustrum lucidum*	24	10.39
9	Raw gypsum	93	40.26	54	*Cistanche deserticola*	37	16.02	99	*Oroxylum indicum*	24	10.39
10	*Cremastra appendiculata* (D.Don) Makino	91	39.39	55	Nelumbinis plumula	37	16.02	100	Dried ginger	24	10.39
11	Raw lotus roots	89	38.53	56	Arisaema cum Bile	37	16.02	101	Wax gourd peel	24	10.39
12	Processed *Atractylodes macrocephala*	81	35.06	57	Rhizoma dioscorea septemloba	37	16.02	102	Processed coicis semen	24	10.39
13	*Glehnia littoralis*	78	33.77	58	Rhizoma phragmitis	36	15.58	103	Spinosae Ziziphi semen	23	9.96
14	Raw malt	75	32.47	59	*Concha margaritifera*	35	15.15	104	Polygoni orientalis fructus	23	9.96
15	*Juncus effusus*	73	31.6	60	*Lophatherum gracile*	35	15.15	105	Raw crataegus pinnatifida bunge	23	9.96
16	Raw *Gardenia jasminoides*	72	31.17	61	Mulberry leaves	34	14.72	106	Ligusticum chuanxiong hort	23	9.96
17	Raw *Sanguisorba officinalis* L	71	30.74	62	Sputum	34	14.72	107	Lithospermum	22	9.52
18	Mustard seed	71	30.74	63	Toosendan fructus	34	14.72	108	Processed trionycis carapax	22	9.52
19	Asari radix et rhizoma	65	28.14	64	Endothelium corneum gigeriage galli	33	14.29	109	Raw Loquat leaves	22	9.52
20	*Inula japonica* Thunb.	62	26.84	65	Bupleuri radix	33	14.29	110	Orange	22	9.52
21	*Stephaniae tetrandrae* radix	62	26.84	66	Aurantii fructus	32	13.85	111	Angelica	22	9.52
22	Asparagus	60	25.97	67	Angelica	32	13.85	112	*Cibotium barometz*	22	9.52
23	Processed radix polygoni multiflori	59	25.54	68	Armeniacae semen	31	13.42	113	Radix paconiac rubra	22	9.52
24	*Fritillaria thunbergii* miq	59	25.54	69	Gastrodiae rhizome	31	13.42	114	Lily	22	9.52
25	Processed loquat leaves	58	25.11	70	Coked crataegi fructus	31	13.42	115	*Polygala tenuifolia*	21	9.09
26	Raw *Scutellariae*	58	25.11	71	*Trichosanthes pericarpium*	31	13.42	116	Rehmanniae radix	21	9.09
27	Borax	58	25.11	72	Raw oyster	30	12.99	117	Polygonum bistorta L	21	9.09
28	Processed licorice	56	24.24	73	Pinelliae Rhizoma	30	12.99	118	Seman Platycladi	21	9.09
29	Poria cocos	56	24.24	74	Paris polyphylla smith	30	12.99	119	Radix stemonae	21	9.09
30	Epimedium	55	23.81	75	Raw *Atractylodes*	29	12.55	120	*Houttuynia cordata* thunb	20	8.66
31	*Taxillus chinensis* (DC.) danser	53	22.94	76	Poria cutis	29	12.55	121	Peach kernel	20	8.66
32	Tangerine peel	53	22.94	77	Raw medicated leaven	28	12.12	122	Radix adenophorae	20	8.66
33	*Crocus sativus* L	52	22.51	78	Raw peony	28	12.12	123	Windproof	20	8.66

Contd...

Table 2: Contd...

Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)	Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)	Serial number	Chinese medicine	Absolute frequency	Percentage frequency (%)
34	*Solanum nigrum*	52	22.51	79	Radix notoginseng	28	12.12	124	Semen benincasae	20	8.66
35	Processed radix *stemonae*	49	21.21	80	Hypericum erectum thumb	28	12.12	125	Arcae concha	19	8.23
36	Raw coicis semen	49	21.21	81	Salvia miltiorrhiza bge	28	12.12	126	Salvia chinensis herba	19	8.23
37	Raw *areca catechu* L.	49	21.21	82	Bupleuri radix	28	12.12	127	*Cnidium monnieri* (L.) cuss	19	8.23
38	*Prunella vulgaris* L	48	20.78	83	Coptidis rhizome	27	11.69	128	*Amomum villosum* Lour	19	8.23
39	*Scrophularia ningpoensis* hemsl	47	20.35	84	Magnolia officinalis	27	11.69	129	Fried cassia tora	19	8.23
40	*Ophiopogon japonicus*	47	20.35	85	Processed crataegus pinnatifida bunge	27	11.69	130	Rosae laevigatae fructus	19	8.23
41	*Chrysanthemum*	47	20.35	86	Processed *cyperus rotundus* L	26	11.26	131	*Cannabis fructus*	19	8.23
42	Scutellaria rarbata	47	20.35	87	*Pseudostellaria heterophylla*	26	11.26	132	Polygonati rhizoma	19	8.23
43	Turmeric	46	19.91	88	Raw *platycladus orientalise* leaf	26	11.26	133	Cinnamomi Ramulus	19	8.23
44	*Fructus corni*	46	19.91	89	*Fructus aurantii* immaturus	25	10.82	134	*Lycium barbarum*	19	8.23
45	Talc	45	19.48	90	*Perilla frutescens* seed	25	10.82	135	*Alpinia katsumadai* Hayata	19	8.23

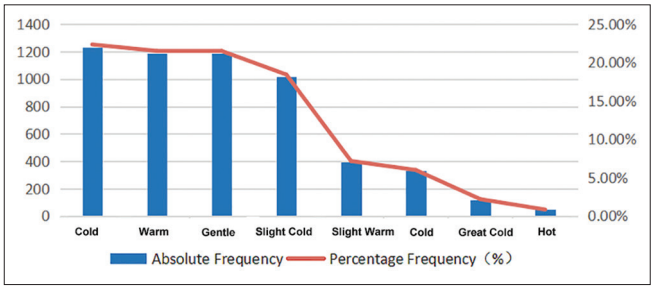

Figure 3: Analysis of the four natures of high-frequency traditional Chinese medicine

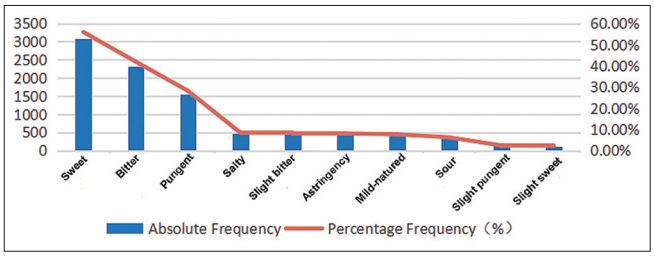

Figure 4: Analysis of five tastes of high-frequency traditional Chinese medicine

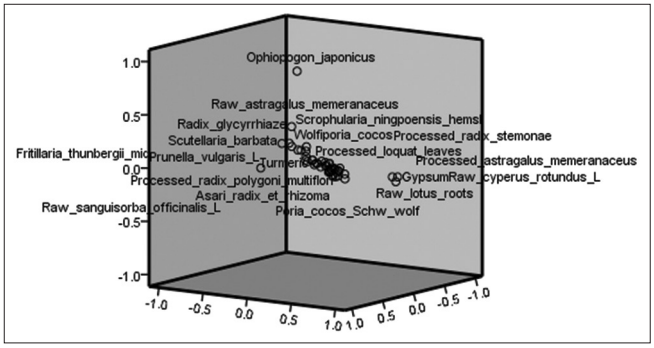

Figure 5: Component plot in rotated space

the prediction intensity of the association rule of the drug groups). Using *a priori* for correlation analysis, the degree of association among TCM compounds was evaluated in the sNSCLC treatment, and the results are presented in Table 12. There were 63 association rules for the drug groups. Among these, there were 36 association rules for the 36 drug pairs and 27 association rules for the 27 drug groups of the three Chinese medicines. As shown in Table 12, the two TCM association rules, two drug pairs, *Poria cocos* (Schw.) Wolf → tangerine peel and processed *Atractylodes* → tangerine peel, ranked first with 73.20% support. In addition, in the three TCM association rules, the three-drug groups, which were raw *Scutellariae* → processed *Atractylodes* and *Poria cocos*, raw-medicated leaven → processed *Atractylodes* and *Poria cocos*, tangerine peel → processed *Atractylodes* and *Poria cocos*, ranked first with 58.82% support.

Discussion

Lung cancer is a common malignant tumor that has a high disease incidence in clinics. In TCM, it is termed "Fei Ji" and "Xi Ben."

Table 3: Efficacy analysis of high-frequency traditional Chinese medicine

Efficacy	Absolute frequency (%)	Chinese medicine
Heat-clearing and toxin-resolving drugs	440 (7.98)	*Hedyotis diffusa*, *Cremastra appendiculata* (D.Don) Makino, *Solanum nigrum*, *Scutellaria barbata*, *Hypericum erectum* thunb, Golden lotus flower, *Herba patriniae*, *Oroxylum indicum*, *Polygonum bistorta* L, *Houttuynia cordata* thunb
Qi-tonifying drugs	427 (7.75)	Processed *Astragalus memeranaceus*, Fried *Atractylodes*, Raw *Scutellariae*, Processed licorice, Raw licorice, *Codonopsis pilosula*, Raw *Atractylodes*, *Pseudostellaria heterophylla*
Yin-nourishing drugs	336 (6.09)	*Glehnia littoralis*, *Asparagus*, *Ophiopogon japonicas*, *Dendrobium*, *Ligustrum iucidum*, processed *Trionycis carapax*, Lily, Radix adenophorae, Polygonati rhizome
Drugs of clearing away heat to resolve phlegm	310 (5.62)	*Fritillaria cirrhosa*, *Fritillaria thunbergii* miq, the Root of balloon flower, Bolbostemma panicul, atum, Semen benincasae, Arcae concha
Heat-purging-fire drugs	303 (5.5)	Raw gypsum; Raw *gardenia jasminoides*, *Prunella vulgaris* L, Rhizoma phragmitis, *Lophatherum gracile*, Fried cassia tora
Rectifying-Qi drugs	285 (5.17)	Raw *Cyperus rotundus* L, Tangerine peel, Toosendan fructus, Aurantii fructus, Processed *Cyperus rotundus* L, *Fructus aurantii* immaturus
Heart-nourishing, spirit-quieting drugs	253 (4.59)	Processed spinosae Ziziphi semen, Spinosae Ziziphi semen, *Polygala tenuifolia*, Seman platycladi, *Poria cocos* (Schw.) wolf, Nelumbinis plumula
Phlegm cough and asthma drugs	244 (4.43)	Processed loquat leaves, Processed radix stemonae, Raw farfarae flos, Armeniacae semen, *Perilla frutescens* seed, Raw loquat leaves radix stemonae
Heat-clearing, damp-drying drugs	238 (4.32)	Fried *Scutellariae*, Coptidis rhizome
Digestant drugs	217 (3.94)	Raw malt, endothelium corneum gigeriage galli, Coked crataegi fructus, Raw massa medica, Fermentata, Processed crataegus pinnatifida Bunge, Raw crataegus pinnatifida bunge
Drugs for inducing diuresis to alleviate edema	182 (3.3)	Poria cocos, Raw coicis semen, Poria cocos, Waxgourd peel, Processed coicis semen
Drugs of warming and resolving cold-phlegm	157 (2.85)	Inula japonica thumb, Pinelliae rhizome
Drugs for inducing diuresis for treating stranguria	155 (2.81)	Juncus effuses, Talc, Rhizoma dioscoreae septemlobae
Dispersing wind-heat drugs	142 (2.58)	*Chrysanthemum*, Mulberry leaves, Bupleuri radix, Vinegar-processed bupleuri radix
Blood-activating menstruation-regulating drugs	142 (2.58)	Salvia miltiorrhiza Bge, Polygoni orientalis fructus, Peach kernel, Salvia chinensis herba, *Crocus sativus* L
Blood-enriching drugs	141 (2.56)	Processed radix polygoni multiflora, Raw angelica, Raw peony, Angelica
Drugs for cooling blood to arrest bleeding	136 (2.47)	Raw *sanguisorba officinalis* L, Rhizoma imperatae, *Platycladus orientalise* leaf
Yang-nourishing drugs	122 (2.21)	Epimedium, *Cistanche deserticola*, Paris polyphylla smith
Heavy settling spirit-quieting drugs	113 (2.05)	*Raw* Os Draconis
Heat-clearing blood-cooling drugs	112 (2.03)	Scrophularia ningpoensis hemsl, Lithospermum, Radix paconiac rubra, Rehmanniae radix
Dispersing wind-cold drugs	104 (1.89)	Asari radix et rhizome, Windproof, Cinnamomi ramulus
Astringing blood-stanching drugs	89 (1.61)	Raw lotus roots
Drugs of relieving rheumatism and qi and strengthening muscles and bones	75 (1.36)	*Taxillus chinensis* (DC.) danser, *Cibotium barometz*
Anthelmintic drugs	74 (1.34)	Raw *areca catechu* L, Scorched areca seed
Qi-disinhibiting phlegm-sweeping drugs	71 (1.29)	Mustard seed
Drugs for blood circulation and painkiller	69 (1.25)	Turmeric, Ligusticum, Chuanxiong Hort
Wind-extinguishing tetany-checking drugs	69 (1.25)	Pearl powder, Gastrodiae rhizome
Damp dispersing drugs	65 (1.18)	Magnolia officinalis, *Amomum villosum* Lour, *Alpinia katsumadai* Hayata
Smoothing liver yang medicine drugs	65 (1.18)	Concha margaritifera, Raw oyster
Drugs of securing essence, reducing urination and checking discharge	64 (1.16)	*Fructus corni*, Rosae laevigatae fructus
Wind-damp-dispelling heat-clearing drugs	62 (1.12)	Stephaniae tetrandrae radix
Removing necrotic tissue and promoting tissue regeneration drugs	58 (1.05)	Borax
Lung-intestine astringent drugs	38 (0.69)	*Schisandra*
Drugs of breaking blood stasis to resolve lumps	34 (0.62)	Sputum
Drugs of clearing away heat to resolve phlegm	31 (0.56)	*Trichosanthes pericarpium*
Stasis-transforming blood-stanching drugs	28 (0.51)	Radix notoginseng
Interior-warming drugs	24 (0.44)	Dried ginger
Drugs for detoxicating insecticide and anti-itch	19 (0.34)	*Cnidium monnieri* (L.) cuss
Moist precipitating drugs	19 (0.34)	*Cannabis fructus*

Table 4: Analysis of meridian tropism of high-frequency traditional Chinese medicine

Meridian tropism	Absolute frequency (%)
Lung meridian	3216 (58.33)
Spleen meridian	2189 (39.71)
Liver meridian	2170 (39.36)
Stomach meridian	1982 (35.95)
Heart meridian	1593 (28.9)
Kidney meridian	1282 (23.25)
Large intestine meridian	808 (14.66)
Gallbladder meridian	511 (9.27)
Small intestine meridian	471 (8.54)
Bladder meridian	289 (5.24)
Triple Energizer meridian	191 (3.46)
Pericardium meridian	94 (1.71)

Table 5: Frequency analysis of the four natures of high-frequency traditional Chinese medicine

Four natures	Absolute frequency (%)
Cold	1232 (22.35)
Warm	1186 (21.51)
Gentle	1186 (21.51)
Slight cold	1016 (18.43)
Slight warm	395 (7.16)
Cool	330 (5.99)
Great cold	120 (2.18)
Hot	46 (0.83)

Table 6: Analysis of five flavors of high frequency traditional Chinese medicine

Five flavors	Absolute frequency (%)
Sweet	3085 (55.95864)
Bitter	2314 (41.97352)
Pungent	1552 (28.15164)
Salty	464 (8.416470)
Slight bitter	443 (8.035552)
Astringency	443 (8.035552)
Mild-natured	420 (7.618357)
Sour	341 (6.18538)
Slight pungent	128 (2.321785)
Slight sweet	119 (2.158534)

Table 7: Kaiser-Meyer-Olkin and Bartlett's test

Statistical terms	Value
KMO measure of sampling adequacy	0.850
Bartlett's test of sphericity	
Approximately χ^2	5473.291
df	1081
Significant	0.000

Significant is the *P* value of Bartlett's spherical test ($P<0.05$ has statistical significance). KMO: Kaiser-Meyer-Olkin

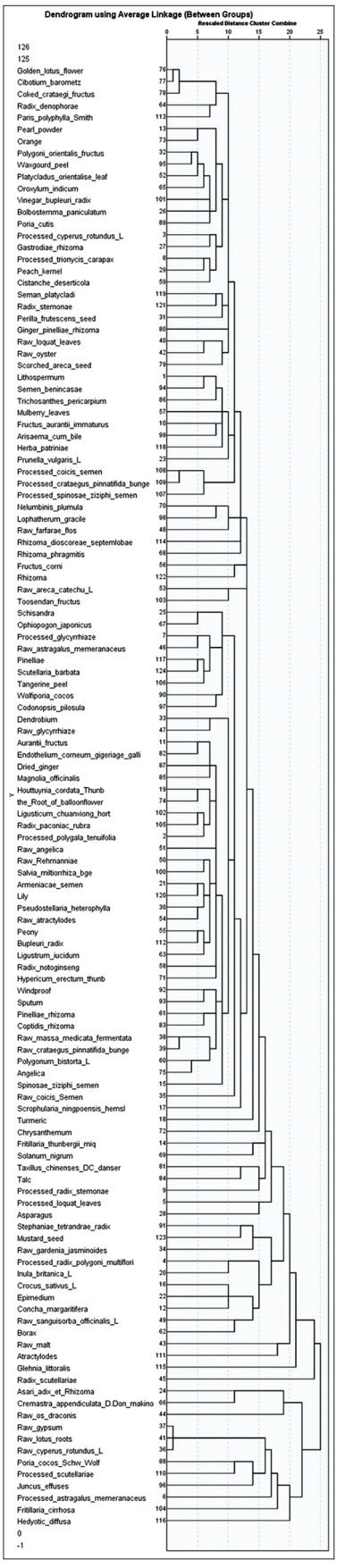

Figure 6: Dendrogram using average linkage (between groups)

Table 8: Total variance explained

Component	Initial eigenvalues			Extraction sums of squared loadings			Rotation sums of squared loadings		
	Total	Percentage of variance	Cumulative (%)	Total	Percentage of variance	Cumulative (%)	Total	Percentage of variance	Cumulative (%)
1	10.407	22.142	22.142	10.407	22.142	22.142	6.324	13.455	13.455
2	5.207	11.078	33.220	5.207	11.078	33.220	3.663	7.794	21.249
3	2.485	5.287	38.507	2.485	5.287	38.507	3.582	7.622	28.872
4	1.929	4.105	42.612	1.929	4.105	42.612	2.738	5.825	34.696
5	1.697	3.611	46.223	1.697	3.611	46.223	2.632	5.600	40.296
6	1.572	3.345	49.568	1.572	3.345	49.568	2.139	4.551	44.847
7	1.466	3.119	52.687	1.466	3.119	52.687	2.048	4.358	49.205
8	1.381	2.937	55.625	1.381	2.937	55.625	1.765	3.756	52.961
9	1.338	2.846	58.471	1.338	2.846	58.471	1.563	3.325	56.285
10	1.266	2.694	61.165	1.266	2.694	61.165	1.520	3.234	59.519
11	1.080	2.297	63.462	1.080	2.297	63.462	1.487	3.164	62.683
12	1.003	2.133	65.595	1.003	2.133	65.595	1.369	2.912	65.595
13	0.918	1.954	67.549						
14	0.887	1.888	69.437						
15	0.870	1.851	71.289						
16	0.823	1.752	73.040						
17	0.800	1.702	74.743						
18	0.707	1.505	76.248						
19	0.700	1.490	77.738						
20	0.671	1.428	79.166						
21	0.630	1.341	80.507						
22	0.624	1.328	81.835						
23	0.610	1.298	83.133						
24	0.593	1.262	84.396						
25	0.556	1.183	85.578						
26	0.524	1.115	86.693						
27	0.516	1.097	87.790						
28	0.488	1.038	88.827						
29	0.463	0.985	89.812						
30	0.444	0.945	90.757						
31	0.437	0.931	91.688						
32	0.387	0.823	92.511						
33	0.371	0.790	93.301						
34	0.364	0.774	94.075						
35	0.343	0.731	94.805						
36	0.330	0.702	95.507						
37	0.286	0.609	96.116						
38	0.266	0.567	96.683						
39	0.240	0.511	97.194						
40	0.236	0.501	97.695						
41	0.225	0.478	98.173						
42	0.218	0.463	98.636						
43	0.211	0.450	99.086						
44	0.158	0.336	99.422						
45	0.154	0.329	99.751						
46	0.078	0.166	99.917						
47	0.039	0.083	100.000						

According to Za Bing Yuan Liu Xi Zhu (an ancient book of TCM), "pathogen was accumulated in the chest, and the airway was blocked, so the qi was not allowed to pass." The pathogen could include phlegm, blood stasis, or indigestion induced by overeating, all of which could fight with the healthy qi. After the pathogen is successful, it accumulates and palpable blockages are formed. Strong evil qi will damage healthy qi, and finally cause organ dysfunction, poor qi-bood circulation and even tangible

Table 9: Component score coefficient matrix

	Component											
	1	2	3	4	5	6	7	8	9	10	11	12
Processed radix polygoni multiflori	−0.180	0.147	0.315	0.324	0.069	0.248	0.077	0.405	0.074	0.029	0.093	0.239
Processed loquat leaves	0.114	0.130	0.231	0.701	−0.009	−0.114	0.154	−0.081	0.052	0.052	−0.197	0.027
Processed astragalus memeranaceus	−0.018	0.584	0.310	−0.214	0.095	0.115	0.244	0.050	0.255	−0.192	0.135	−0.096
Processed licorice	0.768	−0.138	−0.222	−0.057	−0.050	−0.053	0.045	−0.084	0.084	0.090	−0.147	0.124
Processed radix stemonae	0.020	0.063	0.209	0.193	−0.046	0.203	0.140	0.062	0.086	0.698	0.040	0.044
Fritillaria thunbergii miq	0.603	0.023	0.070	0.110	−0.104	0.140	0.211	−0.101	0.034	0.144	0.065	−0.159
Crocus sativus L	−0.139	0.053	0.152	0.079	0.691	0.217	0.074	−0.008	−0.018	−0.145	0.029	0.080
Scrophularia ningpoensis hemsl	0.558	0.086	0.020	−0.111	−0.030	−0.143	0.175	0.303	−0.316	0.226	0.099	−0.117
Turmeric	0.282	0.040	0.054	0.074	−0.154	0.396	0.057	−0.002	0.109	−0.293	0.335	0.325
Inula britanica L	−0.218	0.230	0.139	0.163	0.147	0.144	0.169	0.683	−0.054	−0.095	−0.013	0.238
Epimedium	−0.095	0.001	0.142	0.056	0.765	0.048	0.219	0.082	0.078	0.042	0.052	0.052
Prunella vulgaris L	0.149	0.054	−0.011	0.646	0.035	0.208	0.107	−0.102	0.077	0.031	0.247	0.056
Asari radix et rhizoma	−0.057	0.086	0.051	0.080	0.175	0.776	−0.010	0.118	0.022	0.213	0.077	−0.130
Asparagus	−0.041	0.170	0.287	0.278	−0.154	0.363	0.231	0.136	0.127	0.020	−0.208	−0.419
Raw *gardenia jasminoides*	−0.158	0.137	0.185	0.022	0.117	0.063	0.171	−0.014	0.105	0.036	0.686	0.017
Raw coicis semen	0.635	−0.106	−0.077	0.158	0.079	0.108	−0.202	−0.012	0.049	−0.236	0.160	−0.050
Raw *Cyperus rotundus* L	−0.131	0.253	0.848	0.049	0.171	0.077	0.026	0.075	0.176	0.087	0.089	0.005
Gypsum	−0.146	0.224	0.861	0.121	0.147	0.097	0.009	0.030	0.116	0.070	0.107	−0.015
Raw lotus roots	−0.224	0.232	0.860	0.052	0.187	0.091	0.018	0.039	0.114	0.098	0.074	0.011
Raw malt	0.145	0.194	−0.020	0.194	0.214	0.100	0.062	0.192	0.089	0.089	0.016	0.638
Raw Os Draconis	−0.300	0.333	0.110	−0.174	0.425	0.324	0.124	0.202	−0.099	0.009	0.218	−0.047
Fried *Scutellariae*	0.189	0.169	−0.010	0.660	0.123	−0.016	−0.113	0.167	−0.044	0.111	0.051	0.057
Raw *Scutellariae*	0.804	−0.195	−0.171	−0.012	−0.114	−0.106	−0.021	−0.064	−0.027	−0.041	−0.124	0.076
Radix glycyrrhizae	0.464	−0.218	−0.008	0.238	−0.127	−0.029	−0.043	0.132	0.050	−0.291	0.251	−0.065
Raw *sanguisorba officinalis* L	−0.233	0.230	0.413	0.278	0.388	0.038	0.007	0.149	−0.006	0.189	−0.057	0.005
Raw *areca catechu* L.	−0.134	0.396	0.156	0.391	0.291	0.059	−0.131	−0.015	0.105	0.319	0.000	−0.004
Fructus corni	0.142	0.383	0.233	0.137	0.097	0.048	0.183	0.033	0.507	−0.183	−0.273	−0.039
borax	−0.263	0.201	0.262	0.401	0.460	0.156	0.045	0.097	−0.088	−0.021	−0.166	−0.004
Cremastra appendiculata (D.Don) makino	−0.114	0.093	0.130	0.005	0.204	0.796	0.024	0.018	−0.057	0.024	−0.011	0.164
Ophiopogon japonicus	0.658	−0.189	−0.060	0.043	−0.185	−0.111	0.011	0.054	−0.093	−0.106	−0.035	−0.050
Solanum nigrum	0.211	0.036	−0.022	0.432	0.068	0.113	0.559	−0.040	−0.013	−0.044	−0.160	−0.048
Chrysanthemum	0.081	−0.053	0.006	−0.100	0.040	0.028	0.017	0.800	0.167	0.079	−0.019	−0.069
Taxillus chinensis (DC.) danser	−0.155	0.171	0.257	−0.092	0.025	−0.093	−0.011	0.182	0.640	0.088	0.148	0.012
Talc	−0.132	0.167	0.206	0.286	−0.180	0.067	−0.091	0.042	0.516	0.350	0.181	0.074
Poria cocos (Schw.) wolf	−0.348	0.624	0.244	0.167	0.014	0.132	0.087	−0.062	0.117	0.229	0.087	−0.018
Poria cocos	0.688	−0.099	−0.152	−0.011	−0.059	−0.025	0.232	0.030	−0.033	−0.024	−0.127	0.180
Stephaniae tetrandrae radix	−0.148	0.328	0.164	−0.022	0.455	0.029	0.317	0.014	−0.058	0.232	0.335	0.058
Juncus effuses	−0.249	0.598	0.162	0.042	0.174	0.168	−0.096	0.071	0.140	0.157	−0.100	0.146
Fritillaria cirrhosa	−0.231	0.692	0.104	0.162	0.014	0.017	0.052	0.139	0.134	−0.010	−0.003	0.023
Tangerine peel	0.771	−0.091	−0.031	0.057	−0.028	−0.066	−0.041	−0.053	−0.053	−0.025	−0.060	−0.039
Processed spinosae Ziziphi semen	0.284	0.172	−0.339	0.070	0.274	0.055	−0.158	0.159	0.294	0.050	0.077	−0.456
Fried *Scutellariae*	−0.275	0.578	0.215	0.115	0.139	0.056	0.144	−0.158	0.137	0.143	0.002	−0.059
Atractylodes	0.602	0.116	−0.054	0.171	0.061	0.094	−0.172	−0.002	0.195	0.255	0.044	0.339
Glehnia littoralis	0.188	0.086	0.001	−0.004	0.167	−0.070	0.752	0.123	0.017	0.095	0.119	0.037
Hedyotis *diffusa*	0.104	0.664	0.130	0.265	−0.025	−0.025	−0.001	0.101	−0.162	−0.065	0.236	0.131
Mustard seed	−0.278	0.097	0.098	−0.004	0.316	0.126	0.645	0.084	−0.023	0.041	0.302	0.066
Scutellaria barbata	0.798	−0.082	−0.133	0.082	−0.142	−0.063	0.012	−0.025	−0.124	−0.083	−0.041	−0.023

block. When the physical blocks appear in the lungs, lung cancer is present. The program formulated by the National Administration of TCM[11] in 2011 classified lung cancer into five types, including qi-stagnation and blood-stasis syndrome, phlegm-heat obstruction of the lung syndrome, lung-spleen qi deficiency syndrome, lung yin deficiency syndrome, and qi-yin deficiency syndrome. Currently, the treatment principle is generally based on replenishing the deficiency of the healthy qi and clearing of the residual pathogen

Table 10: Drug combination factor extraction results

Drugs combination factor	Treatment
Licorice, *Fritillaria thunbergii* miq, Scrophularia ningpoensis hemsl, Raw coicis semen, Raw *Scutellariae,* Ophiopogon japonicas, Poria cocos, Tangerine peel, *Atractylodes*, *Scutellaria barbata*	Tonifying the spleen, regulating qi, and eliminating phlegm
Processed astragalus memeranaceus, *Poria cocos* (Schw.) wolf, Juncus effuses, *Fritillaria cirrhosa*, fried *Scutellariae, Hedyotis* diffusa	Rectifying qi, quieting the spirit, transforming phlegm, and dissipating binds
Cyperus rotundus L, Gypsum, Rawlotus roots	Clearing heat, transforming phlegm, and dissipating binds
Processed loquat leaves, *Prunella vulgaris* L, Raw fried *Scutellariae*	Downbearing qi, transforming phlegm, and dissipating binds
Crocus sativus L, Epimedium	Warming yang and quickening the blood
Cremastra appendiculata (D.Don) makino, Asari radix et rhizoma	Transforming phlegm and dissipating binds
Solanum nigrum, *Glehnia littoralis*, Mustard seed	Nourishing yin, warming the lung, freeing the network vessels, and transforming phlegm
Chrysanthemum, Inula japonica thunb	Coursing wind and dissipating heat
Fructus corni, *Taxillus chinensis* (DC.) danser, Talc	Nourishing yin, clearing heat, and boosting the kidney
Processed radix stemonae	Moistening the lung and suppressing cough
Raw *gardenia jasminoides*	Clearing heat and draining fire
Raw malt	Moving qi and fortifying the spleen

Table 11: Cluster analysis of drug combination extraction results

Serial number	Medicine pairs	Serial number	Medicine groups
1	Pearl powder, Orange	23	Golden lotus flower, *Cibotium barometz*, Coked crataegi fructus, Radix adenophorae, Paris polyphylla smith
2	Processed *cyperus rotundus* L, Gastrodiae rhizoma	24	Polygoni orientalis fructus, Wax gourd peel, *Platycladus orientalise* leaf, Oroxylum indicum
			Vinegar-processed bupleuri radix, *Bolbostemma paniculatum*, Poria cocos
3	*Fructus aurantii* immaturus, Arisaema cum Bile	25	Processed trionycis carapax, Peach kernel, *Cistanche deserticola*
4	*Fructus corni*, Rhizoma imperatae	26	Seman platycladi, Radix stemonae, *Perilla frutescens* seed
5	Raw *areca catechu* L, Toosendan fructus	27	Raw loquat leaves, Raw oyster, Scorched areca seed
6	*Schisandra, Ophiopogon japonicus*	28	Lithospermum, Semen benincasae, *Trichosanthes pericarpium*
7	Licorice, Raw *Scutellariae*	29	Processed coicis semen, Processed crataegus pinnatifida bunge, Processed spinosae Ziziphi semen
8	Poria cocos, *Codonopsis pilosula*	30	Nelumbinis plumula, *Lophatherum gracile*, Raw farfarae flos
9	Dendrobium, Radix glycyrrhizae	31	Pinelliae rhizome, *Scutellaria barbata*, Tangerine peel
10	*Houttuynia cordata* thumb, Root of balloon flower	32	Aurantii fructus, Endothelium corneum gigeriage galli, Dried ginger, Magnolia officinalis
11	Rehmanniae radix, Salvia miltiorrhiza Bge	33	Ligusticum chuanxiong hort, Radix paconiac rubra, *Polygala tenuifolia*
12	Armeniacae semen, Lily	34	Raw peony, Bupleuri radix, *Ligustrum lucidum*
13	*Pseudostellaria heterophylla*, Raw *Atractylodes*	35	*Taxillus chinensis* (DC.) danser, Talc, Processed radix stemonae
14	Windproof, Sputum	36	Stephaniae tetrandrae radix, Mustard seed, Raw *gardenia jasminoides*
15	Rhizome pinelliae rhizome, Coptidis rhizoma	37	*Crocus sativus* L, Epimedium, Concha margaritifera
16	Raw medicated leaven, raw crataegus pinnatifida bunge	38	Asari radix et rhizome, Cremastra appendiculata (D.Don) Makino, *Raw* Os Draconis
17	Polygonum bistorta L, Winy angelica	39	Gypsum, Raw lotus roots, Raw *Cyperus rotundus* L
18	*Fritillaria thunbergii* miq, *Solanum nigrum*	40	*Poria cocos* (Schw.) wolf, fried *Scutellariae*, *Juncus effusus*, Processed astragalus memeranaceus, *Fritillaria cirrhosa*, *Hedyotis* diffusa
19	Processed loquat leaves, Asparagus		
20	Processed radix polygoni Multiflori, Inula japonica thunb		
21	Raw *sanguisorba officinalis* L, Borax		
22	Raw malt, processed *Atractylodes*		

and poison. In other words, this implies strengthening the healthy qi, dispelling the pathogen, consolidating the body resistance, and cleaning the source of disease.

We retrieved 231 formulas of Chinese medicine in the database and combined the results of the above data analysis to present the following outcomes:

Table 12: Analysis results of association rules

Serial number	Drug pair	Support (%)	Confidence (%)	Serial number	Drug pair	Support (%)	Confidence (%)
1	Poria cocos→Tangerine peel	73.20	78.57	33	Processed *Atractylodes*→pinelliae rhizoma	53.59	84.15
2	Processed *Atractylodes*→Tangerine peel	73.20	75.00	34	Tangerine peel→*ophiopogon japonicus*	51.63	72.15
3	Tangerine peel→Raw *Scutellariae*	69.28	72.64	35	Poria cocos→ophiopogon japonicus	51.63	70.89
4	Processed *Atractylodes*→Raw *Scutellariae*	69.28	71.70	36	Raw Scutellariae→*ophiopogon japonicus*	51.63	82.28
5	Poria cocos→Raw *Scutellariae*	69.28	70.75	37	Raw *Scutellariae*→processed *Atractylodes*, poria cocos	58.82	71.11
6	Raw *Scutellariae*→Poria cocos	69.28	70.75	38	Raw medicated leaven→processed Atractylodes, poria cocos	58.82	70.00
7	Processed *Atractylodes*→Poria cocos	69.28	84.91	39	Tangerine peel→processed *Atractylodes,* poria cocos	58.82	84.44
8	Tangerine peel→Poria cocos	69.28	83.02	40	Raw crataegus pinnatifida bunge→raw malt, raw mssa medicata fermentata	57.52	98.88
9	Poria cocos→Processed *Atractylodes*	68.63	85.71	41	Processed *Atractylodes*→poria cocos, tangerine peel	57.52	86.36
10	Tangerine peel→Processed *Atractylodes*	68.63	80.00	42	Poria cocos→raw malt, raw medicated leaven	57.52	79.55
11	Raw *Scutellariae*→Processed *Atractylodes*	68.63	72.38	43	Processed *Atractylodes*→raw malt, raw medicated leaven	57.52	77.27
12	Raw massa medicata Fermentata→Raw malt	58.17	98.88	44	Tangerine peel→raw malt, raw medicated leaven	57.52	77.27
13	RawMalt→Raw medicated leaven	58.17	98.88	45	Pinelliae rhizoma→poria cocos, tangerine peel	57.52	76.14
14	Raw crataegus pinnatifida bunge→Raw malt	58.17	97.75	46	Raw *Scutellariae*→raw malt, raw massa medicata fermentata	57.52	72.73
15	Raw crataegus pinnatifida bunge→Raw medicated leaven	58.17	97.75	47	Raw crataegus pinnatifida bunge→poria cocos tangerine peel	57.52	71.59
16	Poria cocos→Raw medicated leaven	58.17	79.78	48	Raw medicated leaven→poria cocos, tangerine peel	57.52	71.59
17	Poria cocos→raw malt	58.17	78.65	49	Raw malt→poria cocos, tangerine peel	57.52	70.45
18	Tangerine peel→raw malt	58.17	77.53	50	Poria cocos→raw crataegus pinnatifida bunge, raw malt	56.86	80.46
19	Processed *Atractylodes*→raw medicated leaven	58.17	77.53	51	Poria cocos→raw crataegus pinnatifida bunge, raw medicated leaven	56.86	80.46
20	Tangerine peel→raw medicated leaven	58.17	77.53	52	Processed *Atractylodes*→rawcrataegus pinnatifida bunge, raw malt	56.86	78.16
21	Processed *Atractylodes*→raw malt	58.17	76.40	53	Tangerine peel→raw crataegus pinnatifida bunge, raw malt	56.86	78.16
22	Raw *Scutellariae*→raw malt	58.17	73.03	54	Processed *Atractylodes*→Raw crataegus pinnatifida bunge, Raw medicated leaven	56.86	78.16
23	Raw *Scutellariae*→raw medicated leaven	58.17	73.03	55	Tangerine peel→raw crataegus pinnatifida bunge, raw medicated leaven	56.86	78.16
24	Raw malt→raw crataegus pinnatifida bunge	57.52	98.88	56	Raw *Scutellariae*→raw crataegus pinnatifida bunge, raw malt	56.86	72.41
25	Raw massa medicata Fermentata→raw crataegus pinnatifida bunge	57.52	98.88	57	Raw *Scutellariae*→raw crataegus pinnatifida bunge, raw medicated leaven	56.86	72.41
26	Tangerine peel→raw crataegus pinnatifida bunge	57.52	78.41	58	Raw massa medicata fermentata→raw crataegus pinnatifida bunge, raw malt	56.86	100.00
27	Processed *Atractylodes*→raw crataegus pinnatifida bunge	57.52	77.27	59	Raw malt→raw crataegus pinnatifida bunge, raw medicated leaven	56.86	100.00
28	Raw *Scutellariae*→raw crataegus pinnatifida bunge	57.52	71.59	60	Pinelliae rhizoma→processed *Atractylodes*, tangerine peel	54.90	75.00
29	Poria cocos→raw crataegus pinnatifida bunge	57.51	80.68	61	Poria cocos→processed Atractylodes, tangerine peel	54.90	90.48
30	Raw *Scutellariae*→pinelliae rhizoma	53.59	71.95	62	Poria cocos→raw *Scutellariae*, tangerine peel	50.33	77.92
31	Tangerine peel→pinelliae rhizoma	53.59	91.46	63	Processed *Atractylodes*→Raw *Scutellariae*, Tangerine peel	50.33	74.03
32	Poria cocos→pinelliae rhizoma	53.59	86.59				

Treatment

Yizhong Bidu (another ancient book of Chinese medicine), written by Zhongzi Li, has presented that "at the beginning of the disease, the healthy qi is still strong, while the evil qi is still shallow. As the disease progresses, the evil qi is stronger, while the healthy qi is weaker. When the disease is long lasting, the evil qi invades, while the healthy qi disappears." Influenced by these thoughts, modern doctors[12-15] believe "the theory of pathogenic toxin invading the lung," "the theory of phlegm-damp gathering inside," and "the theory of healthy qi deficiency." Hence, we believe that in the early stage of NSCLC treatment, the treatment mainly focuses on attacking the pathogenic factors, strengthening and attacking equally in the mid-term, and mainly strengthening the healthy qi in the later-term. Lung cancer[16,17] is a kind of disease, which is deficiency in nature and excess in superficiality. Deficiency of healthy qi and serious cancer toxin will further damage the healthy qi. Hence, it is difficult to inhibit the progress of lung cancer by strengthening the healthy qi only.

Simultaneously, along with modern means of treatment (such as radiotherapy and chemotherapy), pathogen-attacking TCM can be used to enhance the efficacy and eliminate residual cancer cells. Zhongying Zhou,[18] a TCM master, put forward the "cancer toxin" theory, which indicated that "eliminating the pathogen precedes the strengthening the healthy qi." Furthermore, he proposed that in the late stage of lung cancer, the deep spreading of the toxin, such as lung cancer–brain metastasis and lung cancer–liver metastasis, occurred due to the exuberant phlegm-heat and toxin. Cancer toxins such as heat-toxin and phlegm-toxin[19] are the direct causes of lung cancer, so eliminating the pathogen mainly relied on heat-clearing and toxin-resolving.

In NSCLC treatment, the Beijing 301 Hospital has used a higher proportion of pathogen-attacking drugs, including heat-clearing and toxin-resolving drugs, and drugs clearing away heat and resolving phlegm, with heat-clearing and toxin-resolving drugs (7.98%) ranking first. In addition, the frequency of use of health-supporting drugs, such as qi-tonifying drugs and yin-nourishing drugs, was also high, with qi-tonifying drugs (7.75%) ranking second. The treatment method for NSCLC was based on clearing heat and relieving toxicity, tonifying qi, nourishing yin, clearing heat and removing phlegm, and clearing heat and purging fire. Based on research and analysis, it was observed that the NSCLC patients undergoing chemotherapy were prescribed the TCM treatment of clearing heat and relieving toxicity to eliminate the pathogen, tonifying qi and yin to strengthen healthy qi, and reflecting the principle of pathogen-eliminating and healthy qi-strengthening in a balanced manner. Ancient and modern doctors have had similar opinions: In lung cancer, due to qi stagnation, phlegm gathering and blood stasis are bound to each other to form the tumor block. The cancer toxin is the key to the disease progression; when blocked, the disease is developing abnormally, and pathological products, such as phlegm and heat toxin, consume qi and yin. Therefore, treatment is based on resisting cancer and relieving toxicity. Concurrently, supporting health is crucial to treat the primary disease, thus supporting and strengthening health throughout treatment. An NSCLC patient in the chemotherapy stage is still considered the early stage when the healthy qi is not deficient, and the evil qi is just beginning to take over. In addition, the cancer toxin is an important factor in the occurrence and development of lung cancer. Therefore, the main treatment is heat clearing and toxin resolving to attack the pathogen, due to healthy qi deficiency. Furthermore, it is also vital to tonify qi and yin to strengthen health. However, as the data were derived from NSCLC patients undergoing chemotherapy, bias of data results cannot be ruled out.

High-frequency Chinese medicines

The results demonstrated that five kinds of Chinese medicine, including *Fritillaria cirrhosa* (54.55%), processed-fried *Scutellariae* (49.78%), raw Os Draconis (48.92%), *Poria cocos* (Schw.) Wolf (47.19%), and *H. diffusa* (46.32%), were the commonly used compounds in the treatment of NSCLC. Combined with the cluster analysis results on drug combination extraction, *F. cirrhosa*, processed fried *Scutellariae*, and *H. diffusa* often appeared in combination. As mentioned above, the main pathogenic factors of lung cancer were heat toxin and phlegm toxin. Chinese medicine of heat-clearing and toxin-resolving drugs, such as *H. diffusa* (46.32%), *C. appendiculata* (D.Don) Makino (39.39%); qi-tonifying drugs, such as processed *Astragalus memeranaceus* (41.13%) and processed *Atractylodes* (35.06%); and yin-tonifying drugs, such as *Glehnia littoralis* (33.77%) and *Asparagus* (25.97%), were most commonly used.

Modern clinical studies have indicated that the antitumor mechanisms of *H. diffusa*[20] included immune regulation, inhibition of tumor cell proliferation, inhibition of telomerase activity. *C. appendiculata* (D.Don) Makino has been commonly used as an anticancer agent in TCM,[21] containing a variety of alkaloids, that could inhibit the mitosis and proliferation of cancer cells and exhibit nonselective medium-intensity cytotoxic activity against cells, such as lung cancer cells and liver cancer cells. *Astragali radix*[22,23] promotes tumor cell apoptosis, inhibits tumor proliferation, migration, and enhances immune functions. Atractylenolide[24] down-regulates the levels of factors associated with cancer-related cell differentiation. *G. littoralis*[25,26] inhibits tumor cell migration and invasion and enhances T-cells, B-cells, white blood cells, lymphocytes, etc., thereby promoting immune function. Drugs clearing away heat to resolve phlegm, such as *F. cirrhosa* D.Don,[27,28] can inhibit the efflux activity of P-gp, thereby reversing the multidrug resistance observed in tumor cells.

Combined with modern research on high-frequency Chinese medicine, the antitumor effect of TCM is mainly mediated through the following mechanisms:[29] (1) Activation of an immune response. For example, regulating receptor signals such as lymphocytes to improve immunity, such as *H. diffusa*, *A. radix,* and *G. littoralis*; (2) Regulation of inflammatory

factors and other mechanisms to improve the tumor microenvironment, such as *H. diffusa*, *A. radix*, *F. cirrhosa* D.Don, and fried *Scutellariae*; (3) Regulation of tumor cell proliferation, migration, differentiation, and apoptosis by regulating metabolic pathways such as tumor-suppressor factors, including *H. diffusa*, dogtooth violet, and *A. radix*.

Drug pairs and drug groups

Forty common drug groups were extracted using cluster analysis. Association analysis demonstrated that the drug pairs, *Poria cocos* → tangerine peel and processed *Atractylodes* → tangerine peel, were most commonly used. In addition, the drug groups, raw *Scutellariae* → processed *Atractylodes* and *Poria cocos*, raw Massa Medicata Fermentata → processed *Atractylodes* and *Poria cocos*, tangerine peel → processed *Atractylodes* and *Poria cocos*, were most commonly used. Data analysis suggested that the four herbs, *Poria cocos*, *Atractylodes*, *A. radix*, and tangerine peel, often appeared in pairs or in groups of three, and each of the four herbs could strengthen the spleen.

The spleen is the foundation of acquired constitution, the source of qi and blood production. Furthermore, the spleen earth promotes the lung gold; hence, whether the lung qi is complete or not depends on whether the spleen function of transportation and transformation of water, grain, and refined essence are normal. As stated by Shiduo Chen in "Shishi Milu Zhengyifa" (another book of Chinese medicine), "it was very difficult to treat the lung by the routine treatment. It should be transferred to treat the spleen, replenishing the spleen qi, then the earth promotes the gold." Therefore, in the case of lung disease, it is especially necessary to invigorate the spleen and stomach.

Poria cocos promotes urination and invigorates the spleen, also calming the mind; *A. radix* replenishes the lung qi and spleen qi and promotes urination; *Atractylodes* invigorates the spleen and tonifies qi, dries dampness, and promotes urination; tangerine peel replenishes qi, invigorates the spleen, dries dampness, and resolves phlegm. The combination is selected based on the clinical type of the patient syndrome, invigorating the spleen and tonifying qi, to ensure that the spleen qi is smooth and the water, grain, and refined essence can be normally transported to the whole body.

Meridian tropism

The meridian tropism of TCM was mainly based on the lung, spleen, stomach, heart, liver, and kidney meridians. Danxi Zhu believed that "the qi and blood were uncoordinated, and diseases did not occur. Once stagnation occurred, various diseases generated; hence, the illness was mostly induced by stagnation." Clearly, qi and blood stagnation are keys to all diseases.

Based on the occurrence and development of lung cancer, the disease pathogenesis[30] is mostly based on the disorder of Zang-Fu qi and stagnation. Then, qi which cannot disperse the body fluid causes phlegm condensation, and qi stagnation and blood stasis lead to cancer. Lungs govern qi and control the dispersing and sending downward of qi. When healthy qi is deficient, the lungs are dysfunctional. Spleens and stomachs digest the food. Furthermore, they can also transport and transform water, grain, and refined essence. However, transportation relies on the lungs dispersing and sending downward to spread to the whole body. When the lung function is lost, the transportation of body fluid is abnormal, and the retention of water damp produces phlegm. The spleen is a source of phlegm, while the lung is a phlegm vessel. With phlegm in the lungs and disordered function, lung qi is obstructed and stagnated. Spleen insufficiency is primary, nature is deficient and the superficiality is excessive.

Therefore, in the clinic, *H. diffusa* and *C. appendiculata* (D.Don) Makino are used to clear heat, relieve toxicity, and attack pathogens, combined with *Astragali radix*, *Atractylodes*, and other qi-supplementing and spleen-strengthening drugs. If the spleen qi can be transported and can transform normally, there is no phlegm produced. Furthermore, when it takes a prolonged long time, it damages the collaterals, leading to collateral stasis, when the phlegm and blood stasis bind together called "Feiji.". Livers smoothen the qi. Emotional disorders can cause liver qi stagnation and loss of function, inducing abnormal body fluid transportation. Furthermore, the body fluid can condense into phlegm. Stagnation of liver qi can change into fire, and stagnated fire consuming the body fluid can refine fluid into phlegm. Liver wood can restrain spleen earth, causing spleen dysfunction in transportation and transformation, which permits the development of turbid phlegm, which may condense into the tumor mass.

Four natures and five flavors

The statistics demonstrated that cold, warm, flat, and slight cold were the main four natures, while sweet, bitter, and pungent were the main five flavors. TCM treatment is regulating the function of the entrails[31] and qimovement (upward, downward, inward, and outward movement). The lungs govern qi and breathing. Furthermore, it has functions of dispersing and sending downward qi, which are interdependent and mutually constrained to maintain the physiological functions of the lungs. Pungency medicines can be used to disperse dysfunctions of lung qi, and bitterness can be used to lower adverse rising. The spleen and stomach remain in the middle energizer, demonstrating the energy of upward and downward qi movement. In addition, the spleen sends the clear upward and the stomach sends digested foods downward. Treatment of spleen deficiency is mainly based on sweet and warm drugs, and treatment of stomach fire uses bitterness to adapt to stomach descent. The liver and kidney are in the lower energizer, and the liver blood, kidney essence, and the ministerial fire are contained within. Liver and kidney diseases are mainly caused by the deficiency of yin blood and kidney essence, which can be combined with liver yang or ministerial rising fire. Sweet medicines tonify the liver blood or kidney essence, salty medicines tonify the kidney, acid medicines tonify the liver, and bitter medicines purge fire. Wu[32] observed that Chinese medicines of the lung meridian are mainly cold and have clinical effects such

as relieving asthma, dispelling phlegm, and relieving cough. Moreover, the pharmacological effects also include dispelling phlegm, relieving asthma, and antitumor effects.

This study demonstrated that in the treatment of lung cancer, doctors commonly prescribed bitter and cold medicines. Furthermore, doctors used their efficacy of clearing heat and dampness and resolving phlegm for anticancer, antipyretic, and antiviral applications in the clinic. While bitter and cold medicines are mainly heat clearing and toxin resolving, clearing away heat could resolve phlegm. Chinese medicines of sweet flavor and cold nature can tonify yin and clear heat, which were mainly tonifying-yin medicines. Chinese medicines of sweet in flavor and warm in nature, can tonify yang qi, and relieve spasm.This kind of medicines is mainly tonifying qi medicines. Pungency medicine herbs can disperse and move, which move qi and activate blood. This kind of medicines is mainly qi-regulating medicines.

Conclusion

This study refined the academic opinions of the 301 hospitals in Beijing for the treatment of NSCLC through data analysis, and it was in line with the ancient and modern doctor's cognition and clinical application of the etiology, pathogenesis, treatment, and medication of the disease, so it can provide clinical reference for clinical treatment of NSCLC. However, because of the restrained data sources from only one hospital, the study lacked the generalization. Furthermore, as the data were derived from NSCLC patients during chemotherapy, data bias cannot be ruled out. Further research needs to sum up the regular pattern of the TCM treatment by utilizing multicenter and large samples.

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Conflicts of interest

There are no conflicts of interest.

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