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Clinical Efficacy of Modified Shashen Maidong Decoction as Adjuvant for Acupoint Application in the Treatment of Patients with Non-small Cell Lung Cancer and its Effect on T Lymphocyte Subsets

Wujie Zhai#1, Wenjie Zhai#2, Yanhui Zhang*3

[1]The Hospital of Sinochem Second Constructing Group co, LTD, 030000, Taiyuan, Shanxi, China

[2]Xi County Longquan Town Health Centre, 041300, Linfen, Shanxi, China

[3]The 8th Hospital of PLA, 100091, Beijing, China

#These authors contributed equally to this work.

Keywords

Modified Shashen Maidong Decoction, Acupoint application, Non-small cell lung cancer, T lymphocyte subset

Correspondence

Yanhui Zhang, The 8th Hospital of PLA, No.A17, Hei Shan Hu Road, 100091, Haidian District, Beijing, China

Email: 15210468343@163.com.

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Abstract

Background This study aims to investigate the clinical efficacy of modified Shashen Maidong Decoction as adjuvant for acupoint application in the treatment of patients with non-small cell lung cancer (NSCLC) and its effect on T lymphocyte subsets. **Methods** 108 elderly NSCLC patients received chemotherapy in our hospital from February 2020 to February 2022 were randomly divided into control group and observation group, with 54 cases in each group. Patients in both groups received conventional chemotherapy and acupoint application while patients in the observation group were additionally given modified Shashen Maidong Decoction. Traditional Chinese medicine (TCM) syndrome scores, immune function, Karlsruhe functional status (KPS) scores and European Research Group on Cancer Therapy Oncology Quality of Life Questionnaire (EORTC QLQ-C30) scores were compared between two groups. **Results** After treatment, the scores of six TCM symptoms, including cough, sputum and blood, fatigue, upset and sleeplessness, low-fever night sweats and dry and hard stool were significantly declined, and those in the observation group were lower than those in the control group. After treatment, CD_3^+, CD_4^+ and CD_4^+/CD_8^+ levels, KPS abd EORTC QLQ-C30 scores were all largely increased, and increases were more significant in the observation group than in the control group. Besides, incidence of adverse reactions in the observation group was lower than that in the control group. **Conclusion** Modified Shashen Maidong Decoction as adjuvant of acupoint application therapy can effectively alleviate clinical symptoms of elderly patients with

NSCLC, enhance immune system function, improve life qualify of patients, and reduce the incidence of adverse chemotherapy reactions.

1. Introduction

Non-small cell lung cancer (NSCLC) accounts for 80% of pulmonary cancers and surgery is the definitive treatment for early NSCLC (1). However, as the pre-symptoms of NSCLC are not obvious, most patients are diagnosed at intermediate or advanced stages, missing the optimal timing of surgery, and thus need comprehensive treatments such as chemotherapy and targeted therapy (2). Patients with intermediate or advanced NSCLC are usually treated with chemotherapy which effectively improves the 5-year survival rate of NSLCL patients (3). Nevertheless, chemotherapy damages not only tumour tissues but also normal surrounding tissues, triggering adverse effects such as bone marrow suppression and liver and kidney dysfunction.

Weakened immune function is a key factor in the development of NSCLC, and abnormal whole blood T-cell subsets have been reported as important risk factors for the progression of cancer (4). $CD3^+$ and $CD4^+$ T cells are helper T cells, which can secrete various cellular mediators, regulate the immune response and exert anti-tumour effects. Higher $CD3^+$ and $CD4^+$ levels represent stronger immune function; $CD8^+$ T cells are activated as cytotoxic T cells, which can specifically kill tumour cells. Immune dysfunction in NSCLC patients will lead to imbalanced proportion of $CD4^+$ T cells and $CD8^+$ T cells and an abnormal decrease in $CD4^+/CD8^+$ levels.

Traditional Chinese medicine (TCM) has has been widely used to treat many diseases, such as lung cancer, allergic diseases and dementia (5-7). Shashen Maidong Decoction (*Wenzhi Zhuanfang* -Volume 1), is a famous prescription for generating body fluid with drugs of sweet flavour and cold nature and nourishing lung and stomach. It has been reported that Shashen Maidong Decoction improved chronic intermittent hypoxia-induced cognitive impairment through regulating NR2B-ERK signaling pathway (8). Shashen Maidong Decoction has a significant improvement in the levels of relevant indexes in pediatric mycoplasma pneumonia (9). A previous study has proven the effects of Shashen Maidong Decoction on the syndrome of yin deficiency of lung and stomach in patients with early-stage lung cancer who received chemotherapy (10). Acupoint application as one of the characteristic treatments of TCM can stimulate acupoints, promote drug penetration and avoid the first-in reaction. Acupoint application combined with Chinese medicinal formulae has been implicated in reducing adverse gastrointestinal reactions in lung cancer patients with chemotherapy (11). The present study aims to find out the clinical efficacy of modified Shashen Maidong Decoction as adjuvant for acupoint application in the treatment of patients with NSCLC and its effect on T lymphocyte subsets, so as to provide an insight for clinical treatment.

2. Data and Methods

2.1 General data

From February 2020 to February 2022, 108 elderly NSCLC patients admitted to our hospital were selected for this study and randomly divided into the observation group (n=54) and the control group (n=54). There were no significant differences in gender, age, average course of disease (COD) and tumour stage between the two groups (Table 1, $P>0.05$). The study was approved by the Medical Ethics Committee and the patients were informed and consented.

Table 1 Comparisons of general data between two groups

Group	Case	Gender (case)		Age (years old)	COD (year)	Tumour stage (case)	
		male	female			Ⅲ stage	Ⅳ stage
Observation	54	29	25	69.19±5.71	1.52±0.54	28	26

group							
Control group	54	31	23	69.06±6.66	1.48±0.50	27	27
χ^2/t		0.150		0.109	0.399	0.037	
P		0.699		0.919	0.690	0.847	

2.2 Inclusion criteria

(1) Patients diagnosed with NSCLC by X-ray chest radiograph, magnetic resonance imaging, ultrasonography and other imaging examinations and pathological biopsy (12); (2) Patients meet the criteria for primary bronchogenic carcinoma in *the guidance principle of clinical study on traditional Chinese medicine* (13) and *the Internal Chinese Medicine*, and have the syndrome of yin deficiency and internal heat, coughing without sputum or with little sputum, bloodly sputum, hemoptysis, chest pain, dysphoria and poor sleep, low-fever and night sweating, high or long-term fever, thirst, dry and hard stool, red tongue with yellow coating, thready and rapid pulse; (3) tumour stage: Patients in stage III~IV, Karlsruhe functional status (KPS) ≥70 points; (4) Patients with complete clinical data, good compliance, no history of relevant drug allergy; (5) Patients meet the indications for chemotherapy and have not recently undergone radiotherapy or targeted therapy and cannot be radically cured by surgery.

2.3 Exclusion criteria

(1) Patients with malignant tumours in other areas; (2) patients with serious organ diseases and neurological, haematological and immune dysfunction; (3) those with other lung diseases such as tuberculosis and pulmonary fibrosis.

2.4 Treatments

Patients in both groups were given conventional chemotherapy and symptomatic support treatment for NSCLC according to their conditions. Patients in the control group were given an acupoint application on this basis. White mustard seeds, wild ginger, kansui root, corydalis tuber and prepared pinellia were finely ground together, and fresh ginger juice was added. Acupuncture was applied on Dazhui (DU14) and Tiantu (RN22) and covered with fever paste for 6 hours (h) each time, once a day (d). Treatment was performed for 8 courses with 7 d for each course. Patents in observation group were given 200 mL modified Shashen Maidong Decoction (ingredients: glehnia root 12 g, ophiopogonis radix 12 g, fragrant solomonseal rhizome 10 g, folium mori 10 g, lablab 10 g, radix trichosanthis 10 g and licorice root 3 g, with dosage adjusted according to the severity of syndromes; additional 10 g bletilla tuber for patients coughing with sputum or blood, additional 10g curcuma root for patients with chest pain, and additional 6 g amygdala, 6 g rhubarb and 10 g hemp seed for vomiters) on the basis of the control group, 1 dose/d, orally taken in the morning and evening for 8 consecutive weeks.

2.5 Detective indexes

(1) TCM syndrome scores (14): 6 TCM syndromes, including cough, phlegm and blood, fatigue, upset and sleeplessness, low-fever night sweats, and dry and hard stool, were recorded before and after 8 weeks of treatment in both groups and scored according to the severity of syndromes (0: no syndrome; 1: mild syndrome; 2: moderate syndrome; 3: severe syndrome), with higher scores representing more severe symptoms. (2) Immune function: Before treatment and after 8 weeks of treatment, the whole blood T-lymphocyte subsets, including $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$, were measured using a fully automated biochemical analyzer (BS-850, Shenzhen Myriad, Shenzhen, China) in both groups. (3) KPS score (15) and European Research Group on Cancer Therapy Oncology Quality of Life Questionnaire (EORTC QLQ-C30) score (16): before treatment and after 8 weeks of treatment, the KPS (100 in total) and EORTC QLQ-C30 were used to assess the life quality of patients in both groups. A higher KPS score refers

to better health status and self-care ability; EORTC QLQ-C3 covers 30 areas and its score is in direct proportion to the life quality of patients. (4) Adverse reactions: adverse reactions such as gastrointestinal reactions, bone marrow suppression, and liver and kidney dysfunction during treatment in two groups were recorded.

2.6 Statistical analysis

Statistical analysis was performed using SPSS 20.0. Counting data were compared using the χ^2 test, and measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$). Comparisons between two groups were assessed with unpaired t-tests, while those in the same group at different time points were evaluated using paired sample t-tests. Statistical significance was established at $P<0.05$.

3. Results

3.1 Modified Shashen Maidong Decoction as adjuvant of acupoint application therapy improved the TCM syndrome of NSCLC patients

Before treatment, there was no statistical significance in the comparison of the scores of six TCM symptoms, including cough, sputum and blood, fatigue, upset and sleeplessness, low-fever night sweats and dry and hard stool between the two groups (Table 2, $P>0.05$); after treatment, the scores of six TCM symptoms were significantly lower than those before treatment ($P<0.05$), and those in the observation group were significantly lower than those in the control group ($P<0.05$).

3.2 Modified Shashen Maidong Decoction as adjuvant of acupoint application therapy improved immune function of NSCLC patients

Before treatment, no significant differences in CD_3^+, $CD_4^+$and CD_4^+/CD_8^+ levels between the observation group and the control group were observed (Table 3, $P>0.05$). However, after treatment, CD_3^+, $CD_4^+$and CD_4^+/CD_8^+ levels in both groups were largely increased ($P<0.05$), and those in the observation group were notably higher than those in the control group ($P<0.05$).

Table 2 Comparisons of TCM syndrome score between two groups ($\bar{x} \pm s$, score)

Observation indexes		Observation group (n=54)	Control group (n=54)	*t*	*P*
cough	Pre-treatment	1.76±0.35	1.75±0.33	0.153	0.879
	Post-treatment	0.86±0.17*	1.28±0.25*	-10.209	0.000
sputum/blood	Pre-treatment	2.02±0.46	2.06±0.40	-0.482	0.631
	Post-treatment	0.98±0.28*	1.32±0.40*	-5.117	0.000
fatigue	Pre-treatment	1.58±0.54	1.62±0.53	-0.388	0.698
	Post-treatment	0.81±0.18*	1.05±0.31*	-4.920	0.000
upset/sleeplessness	Pre-treatment	2.11±0.42	2.12±0.31	-0.142	0.888
	Post-treatment	1.02±0.33*	1.53±0.51*	-6.170	0.000
low-fever night sweats	Pre-treatment	1.37±0.37	1.38±0.42	-0.131	0.896
	Post-treatment	0.76±0.17*	0.99±0.19*	-6.629	0.000
dry and hard stool	Pre-treatment	1.77±0.64	1.75±0.53	0.177	0.860
	Post-treatment	0.90±0.30*	1.28±0.42*	-5.410	0.000

* vs. pre-treatment, *$P<0.05$

Table 3 Comparison of immune function between both groups before/post-treatment ($\bar{x} \pm s$)

Group	Case	CD_3^+（%）		CD_4^+（%）		CD_4^+/CD_8^+	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment

Observation group	54	67.48±3.94	76.96±5.03*	37.78±6.69	49.07±5.81*	1.14±0.12	1.33±0.17*
Control group	54	67.10±3.67	71.80±5.30*	37.41±6.24	43.90±5.73*	1.12±0.13	1.23±0.14*
t		0.519	5.189	0.297	4.656	0.831	3.337
P		0.605	0.000	0.767	0.000	0.410	0.001

* vs. pre-treatment,*$P<0.05$

3.3 Modified Shashen Maidong Decoction as adjuvant of acupoint application therapy increased the KPS and EORTC QLQ-C30 scores of NSCLC patients

Before treatment, the comparisons of KPS and EORTC QLQ-C30 scores between two groups showed no significant differences (Table 4, $P>0.05$); after treatment, KPS and EORTC QLQ-C30 scores were largely upregulated in both groups than those before treatment ($P<0.05$); compared with those in the control group, KPS and EORTC QLQ-C30 scores in the observation group were significantly higher ($P<0.05$).

3.4 Modified Shashen Maidong Decoction as adjuvant of acupoint application therapy reduced the adverse reactions of NSCLC patients

Compared with that in the control group, the incidence of adverse reactions was lower in the observation group (Table 5, $P<0.05$).

Table 4 Comparisons of KPS and EORTC QLQ-C30 scores between both groups before/post-treatment ($\bar{x} \pm s$, score)

Group	Case	KPS Score		EORTC QLQ-C30 Score	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Observation group	54	69.59±4.25	82.50±5.34*	49.50±9.55	73.85±12.32*
Control group	54	69.56±4.40	78.11±4.34*	49.39±10.57	64.58±11.13*
t		0.036	4.688	0.057	3.983
P		0.971	0.000	0.955	0.000

* vs. pre-treatment,*$P<0.05$

Table 5 Comparison of adverse reactions between two groups [case(%)]

Group	Case	Gastrointestinal reactions	Bone marrow suppression	Liver dysfunction	Kidney dysfunction	Total incidence rate
Observation group	54	2 (3.70)	0 (0.00)	1 (1.86)	0 (0.00)	3 (5.56)
Control group	54	4 (7.41)	2 (3.70)	3 (5.56)	2 (3.70)	11 (20.37)
χ^2						5.252
P						0.022

4. Discussion

In TCM, lung cancer is defined as "pulmonary

retention" and "abdominal distention and hypochondrium mass", which is caused by the weakness of the body, toxins, a disorder of Qi movement, and turbid phlegm and blood stasis in the lung, resulting in accumulation of lung masses. In TCM, " pulmonary retention " is classified into four syndromes: Qi stagnation and blood stasis, phlegm-dampness and aggregating lung, Yin deficiency and toxic heat, and deficiency of both Qi and Yin. Among these, early-stage lung cancer presents syndromes of internal deficiency of positive Qi and external invasion of toxins along with phlegm-dampness in the lung. Patients with advanced lung cancer present syndromes of Yin deficiency and toxic heat, and deficiency of both Qi and Yi. Therefore, the treatment of advanced lung cancer should focus on reinforcing healthy Qi to eliminate pathogenic factors as well as treating both manifestation and the root cause of the disease. Reinforcing healthy Qi relies on invigorating the spleen, tonifying and replenishing the kidney and lung while eliminating the pathogenic needs to dissipate phlegm and blood stasis and detoxicating (17). The present study adopted modified Shashen Maidong Decoction as adjuvant for acupoint application in the treatment of elderly patients with intermediate or advanced NSCLC during chemotherapy and investigated its combined effects on the clinical efficacy, immune function, life quality and incidence of adverse reactions incidence.

The results demonstrated that the scores of six TCM symptoms, including cough, sputum and blood, fatigue, upset and sleeplessness, low-fever night sweats and dry and hard stool all dropped due to treatment, and those in the observation group were significantly lower than those in the control group. After treatment, the KPS scores and EORTC QLQ-C30 scores were largely upregulated in both groups, with more significant decreases found in the observation group than those in the control group. Moreover, a significantly lower incidence of adverse reactions was observed in the observation group, as compared with that in the control group. These findings indicated that modified Shashen Maidong Decoction as adjuvant for acupoint application can effectively alleviate TCM syndromes of elderly patients with NSCLC in chemotherapy, improve the life quality of patients, and reduce the incidence of adverse chemotherapy reactions. He et al. reported that Shashen Maidong Decoction treatment increased the KPS scores and TCM syndrome score of patients with lung cancer cachexia (18), which is similar to the results of this study. Acupoint application refers to the application of Chinese herbs pastes on acupuncture points. The paste is further absorbed by the skin and transmitted through the meridians. Acupoint application functions by regulating Qi and blood, reinforcing and tonifying healthy Qi. Among herbs used in this study, white mustard seeds can disinhibit Qi and resolve dry phlegm; wild ginger dispels wind and dissipates cold, as well as promotes urination and relieves stuffy nose; and kansui root disperses swelling and dissipates bind; the acupuncture points of Dazhui and Tiantou were chosen as Dazhui located in the conjunction of three yang meridians in hand and foot and governor meridian, the application to which benefits Qi and strengthen Yang. In addition, Tiantou belongs to the conception channel, which contributes to chest relaxation, Qi regulation, phlegm reduction and lung-Qi dispersion (19). In the modified Shashen Maidong Decoction, glehnia root and ophiopogonis radix eliminate heat by nourishing Yin; fragrant solomonseal rhizome and radix trichosanthis generate liquid and detoxify; lablab and licorice root reinforce Qi and improve physical quality; folium mori clears and diffuses heat to moisten dryness, with dosage adjusted according to the syndromes. Patients coughing with sputum or blood were given bletilla tuber to treat cutaneous infection with hemostasis, patients with chest pain were treated with curcuma root to regulate Qi and cool the blood for dispelling melancholy; vomiters received amygdala, rhubarb and hemp seed to respectively moisten lung to arrest cough, purge toxins and moisten the intestines as well as alleviate constipation. Together, the receipt functions by clearing the lung and nourishing the stomach as well as promoting body fluid and moistening dryness. Modern pharmacological studies

have shown that ingredients in modified Shashen Maidong Decoction exhibit vital functions on several targets of lung cancer, participate in the synthesis of proteoglycan and protein and the regulation of glucose metabolism in tumour cells, and induce tumour cell apoptosis by interfering with the cell cycle, thereby attenuating cancer progression (10).

Shashen Maidong Decoction has the effects of anti-inflammatory reaction and enhancing immune system (9, 18, 20), and it inhibited cancer growth under intermittent hypoxia conditions by suppressing oxidative stress and inflammation (21). In addition, Shashen Maidong Decoction improved the level of peripheral blood lymphocytes and regulate immune function in rats (22). The results of this study revealed that $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ levels in both groups were boosted after treatment, and the levels in the observation group were lower than those in the control group. In this case, it is suggested that modified Shashen Maidong Decoction as adjuvant for acupoint application can regulate the number of T cell subpopulations and improve the immune function in elderly patients with advanced NSCLC in chemotherapy (23). According to modern pharmacological study, glehnia root and fragrant solomonseal rhizome have presented immunomodulatory and anti-tumour effects; the active components of saponins and polysaccharides in ophiopogonis radix could improve the immune function and promote the production of antibody and complement (24). Xu Nuo et al. (25) found that Shashen Maidong Decoction combined with chemotherapy in the treatment of NSCLC patients could effectively lift $CD3^+$ and $CD4^+$ levels and improve the immune function of patients, which echoes the results of this study.

5. Conclusion

The modified Shashen Maidong Decoction as adjuvant for acupoint application can effectively relieve the clinical symptoms of elderly NSCLC patients, enhance immune system function, improve the life quality of patients and reduce the incidence of adverse reactions to chemotherapy.

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Not applicable.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Conceptualization, W. J. Z. and W. J. Z.; Data curation, Y. H. Z.; Formal analysis, W. J. Z. and W. J. Z.; Methodology, Y. H. Z.; Writing-original draft, W. J. Z. and W. J. Z.; Writing-review and editing, W. J. Z., W. J. Z. and Y. H. Z.; All authors have read and agreed to the published version of the manuscript.

Ethical Approval and Consent to Participate

The experiments were conducted in accordance with the principles approved by the Medical Ethics Committee and the patients were informed and consented.

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Availability of Data and Materials

The data presented in this study are availability on request from the corresponding author.

Supplementary material

Not applicable.

Reference

[1] Mao Y, Yang D, He J, et al. Epidemiology of Lung Cancer. Surg Oncol Clin N Am. 2016;25(3):439-45.

[2] Alexander M, Kim SY, Cheng H. Update 2020: Management of Non-Small Cell Lung Cancer. Lung. 2020;198(6):897-907.

[3] Hirsch FR, Scagliotti GV, Mulshine JL, et al. Lung cancer: current therapies and new targeted treatments. Lancet. 2017;389(10066):299-311.

[4] Zhao X, Ding L, Lu Z, et al. Diminished CD68+ cancer-associated fibroblast subset induces regulatory T-cell (Treg) infiltration and predicts poor prognosis

of oral squamous cell carcinoma patients. 2020;190(4):886-99.

[5] Zhang XW, Liu W, Jiang HL, et al. Chinese Herbal Medicine for Advanced Non-Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis. Am J Chin Med. 2018;46(5):923-52.

[6] Chan HHL, Ng T. Traditional Chinese Medicine (TCM) and Allergic Diseases. Curr Allergy Asthma Rep. 2020;20(11):67.

[7] Li S, Wu Z, Le W. Traditional Chinese medicine for dementia. Alzheimers Dement. 2021;17(6):1066-71.

[8] Zhao Y, Yang S, Guo Q, et al. Shashen-Maidong Decoction improved chronic intermittent hypoxia-induced cognitive impairment through regulating glutamatergic signaling pathway. J Ethnopharmacol. 2021;274:114040.

[9] Wang J, Ma X, Wei S, et al. Clinical Efficacy and Safety of Shashen Maidong Decoction in the Treatment of Pediatric Mycoplasma Pneumonia: A Systematic Review and Meta-Analysis. Front Pharmacol. 2021;12:765656.

[10] Wu W LJ, Yin X, et al. Mechanism of Shashen Maidong Decoction in Treatment of Lung Cancer Based on Network Pharmacology. Chinese Journal of Library and Information Science for Traditional Chinese Medicine 2021;45(2):6-10.

[11] Cheng Q GL, Yan S, et al. Impact Observation of Traditional Chinese Medicine Special Nursing Intervention on Toxic and Side Effects for NSCLC Chemotherapy. Journal of Sichuan of Traditional Chinese Medicine. 2020;38(7):208-11.

[12] Y Z. Chinese lung cancer treatment guideline (2015 edition). Chinese Journal of Oncology. 2015;37(1):67-78.

[13] Chen E, Li Q, Wang H, et al. MiR-32 promotes tumorigenesis of colorectal cancer by targeting BMP5. Biomed Pharmacother. 2018;106:1046-51.

[14] Zheng H HM, Pu T, et al. Effects of adjuvant treatment of modified Shashen Maidong decoction on immune function and adverse reactions in patients with lung cancer Medical Journal of West China. 2020;32(6):896-9+ 903.

[15] Frappaz D, Bonneville-Levard A, Ricard D, et al. Assessment of Karnofsky (KPS) and WHO (WHO-PS) performance scores in brain tumour patients: the role of clinician bias. 2021;29:1883-91.

[16] Wang R CH. Effect of Yiqi Yangyin Tang Combined with Chemotherapy on Quality of Life in Patients with Advanced Non-Small Cell Lung Cancer. 2021;53(03):121-4.

[17] Zhang T CW, Zhang R, et al. Clinical significance of phlegm detoxification on survival with tumor in advanced NSCLC patients based on the phlegm-poison theory. Chinese Journal of General Practice. 2019;17(12):2042-5, 150.

[18] He M, Luo Y, Chen L, et al. Shashen maidong decoction: the effect of TNF-α and IL-6 on lung cancer cachexia based on cancer toxicity theory. Am J Transl Res. 2021;13(6):6752-8.

[19] Liu Y WK, Yang Z, et al. Clinical observation of oral administration of traditional Chinese medicine combined with acupoint application in the treatment of postoperative cough of phlegm-dampness accumulation of lung in patients with lung cancer World Clinical Drugs. 2021;42(09):798-804.

[20] Zeng P, Li J, Chen Y, et al. The structures and biological functions of polysaccharides from traditional Chinese herbs. Prog Mol Biol Transl Sci. 2019;163:423-44.

[21] Zheng Y, Yang S, Si J, et al. Shashen-Maidong Decoction inhibited cancer growth under intermittent hypoxia conditions by suppressing oxidative stress and inflammation. J Ethnopharmacol. 2022;299:115654.

[22] Yang Y, Zhou Y. Shashen-Maidong Decoction-Mediated IFN-γ and IL-4 on the Regulation of Th1/Th2 Imbalance in RP Rats. Biomed Res Int. 2019;2019:6012473.

[23] Li Y YT, Liao X, et al. Literature Research of Origin and Application of Shashen Maidong Decoction. Acta Chinese Medicine and Pharmacology. 2021;49(11):51-7.

[24] Gao S LJ, Huang F, et al. Pharmacological and Clinical Research Progress of Shashen Maidong Decoction. Guiding Journal of Traditional Chinese Medicine and Pharmacy. 2020;26(2):115-8, 23.

[25] Xu N ZQ, Feng Z. Effect of Modified Shashen

Maidong Decoction Combined with Chemotherapy on Non-small Cell Lung Cancer Patients with Yin Deficiency and Toxic Heat Syndrome. Journal of Guangzhou University of Traditional Chinese Medicine. 2021;38(1):21-6.