

Research Progress in the Adjuvant Treatment of non-small Cell Lung Cancer with Chinese Medicine Injections

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Abstract: *Non-small cell lung cancer (NSCLC) is a common type of lung cancer. Patients with advanced NSCLC often lose the chance of surgery. Integrated traditional Chinese and western medicine therapy, especially traditional Chinese medicine injection, has shown its advantages in the treatment of non-small cell lung cancer. It plays an anti-cancer role by inhibiting cell proliferation, promoting apoptosis, inhibiting tumor invasion and metastasis, and improving anti-tumor drug resistance. It has shown advantages in reducing adverse reactions, improving efficacy and quality of life of patients.*

Keywords: Traditional Chinese medicine injection, Non-small cell lung cancer, Combination of traditional Chinese medicine and western medicine, review.

1. Introduction

Lung cancer is the malignant tumour with the highest incidence rate and the heaviest cancer burden in China [1], and one of the malignant tumours with a high incidence rate in countries around the world. Non-small cell lung cancer (NSCLC) is the most common pathological type of lung cancer, accounting for approximately 85% of all lung cancers [2]. More than half of NSCLC patients have developed distant metastases at the time of first diagnosis, are inoperable with late staging, have an overall 5-year survival rate of less than 25%, and most have a poor prognosis [3-4]. Chinese medicine injections have become an important method for TCM to participate in the treatment of NSCLC patients due to its dosage advantage of avoiding digestive reactions and entering the blood circulation directly. A large number of published studies have shown that the role of TCM injections in the adjuvant treatment of malignant tumours is mainly manifested in increasing clinical efficacy, reducing toxic side effects, and improving the quality of life of patients. Studies have shown that a variety of Chinese medicine injections play an important role in the treatment of NSCLC by combining with radiotherapy and chemotherapy. Now, we would like to review the studies on Chinese herbal injections commonly used in clinical practice for the adjuvant treatment of NSCLC.

2. TCM Etiology and Pathogenesis of NSCLC

Although there is no record of 'lung cancer' in ancient Chinese medicine books, according to its clinical characteristics, it can be classified into the categories of 'lung stagnation', 'haemoptysis', 'chest pain', 'xiben' and 'lung congestion'. However, according to its clinical characteristics, it can be classified as 'lung accumulation', 'haemoptysis', 'chest pain', 'resting cardia', 'lung congestion' and so on. According to traditional Chinese medicine, the main cause of lung cancer is the depletion of positive qi in the organism, which is commonly seen in yin deficiency and qi and yin deficiency, leading to dysfunction of internal organs, invasion of evil and poison, stagnation of evil qi, unsmooth qi,

stagnation of blood, uncomfortable fluids, accumulation of fluids into phlegm, phlegm and stagnation of blood, stasis of blood, stagnation of blood, phlegm and stagnation of toxicity, and formation of lumps [5]. On the whole, lung cancer is a kind of disease with deficiency as the root and evil as the symptom, which is caused by deficiency and mixed with deficiency and reality, and its disease is located in the lungs, with emphasis on the spleen and kidneys. The pathogenic factors of lung cancer development are mainly deficiency, toxicity, stasis and phlegm, while phlegm, deficiency and stasis run through the whole pathogenesis [6]. Clinically, in the early stage of NSCLC, deficiency of qi and yin and deficiency of lung, spleen and qi are common, and in the late stage, deficiency of yin and internal heat or deficiency of yin and yang are common [7]. The treatment of NSCLC is mostly based on the principle of 'supporting the positive and dispelling the evil'.

3. Mechanisms of Chinese Medicine Injection in the Adjuvant Treatment of NSCLC

Chinese medicine injection is an injectable dosage form made of effective substances extracted from traditional Chinese medicine or compound traditional Chinese medicine by using modern science and technology and methods under the guidance of Chinese medicine theory. It has the advantages of rapid onset of action, high bioavailability, and localised or targeted administration, and is suitable for drugs that are not suitable to be made into oral dosage forms, or for patients who cannot receive oral administration. The emergence of anti-tumour herbal injections can be used to directly treat or indirectly assist in the treatment of cancer. Because lung cancer cells have the biological characteristics of unlimited proliferation and resistance to apoptosis [8], it is easy to obtain a survival advantage. Basic research has shown that Chinese medicine injection can inhibit NSCLC cell proliferation, block the cell cycle, induce apoptosis and autophagy of tumour cells, affect tumour cell invasion and metastasis, inhibit tumour angiogenesis, and improve body immunity, improve tumour drug resistance, and increase the

effectiveness and reduce the toxicity of radiotherapy and other interventions, so as to exert the effect of adjuvant treatment of NSCLC.

3.1 Inhibition of NSCLC Cell Proliferation and Promotion of Apoptosis

Apoptosis is a genetically controlled and active cell death process in the body to maintain the stability of the internal environment, and the occurrence of lung cancer is related to the blockage of the normal apoptosis process, malignant transformation of cells and unlimited proliferation of tumour cells. Studies have shown that traditional Chinese medicine injections can effectively inhibit tumour cells from dividing and proliferating too quickly, and regulate protein expression to induce tumour cell apoptosis, and improve the sensitivity of NSCLC cells to targeted drugs and other drugs. Xiao Zhenzhen et al [9] suggested that Reduning injection could regulate the metabolism of tumour cells, thus enhancing the proliferation inhibition and pro-apoptotic effect of gefitinib on NSCLC cells; Wei Xueqin [10] explored that Aidi injection combined with anlotinib hydrochloride could inhibit the proliferation of NSCLC cells. Aidi injection combined with anlotinib hydrochloride can inhibit the proliferation and induce apoptosis of lung cancer cell line A549 and its mechanism of action.

3.2 Inhibition of NSCLC Cell Invasion and Metastasis

Prevention and treatment of tumor metastasis is one of the important ways to reduce mortality. Studies have shown that both the growth and metastasis of primary tumors depend on neovascularization from existing blood vessels and the establishment of their own blood supply system from the host matrix, and the enhanced intensity of angiogenesis is positively correlated with the metastasis ability of tumors. Tumor cells can also secrete a variety of pro-endothelial growth factors to promote endothelial cell proliferation and migration, thus promoting neovascularization. Studies have shown that composite Kushen injection (CKI) can exert its anticancer effect through neovascugensis. Studies have shown that matrine can significantly inhibit the expression of HIF-1 α and VEGF, and reduce the release of angiogenic factors. Inhibition of endothelial cell production [11]. In addition, matrine can significantly down-regulate the expression of migration-related gene PAX2, increase the expression of E-cadherin, and decrease the expression of N-cadherin, thereby inhibiting the activity of the epithelial-mesenchymal transformation signaling pathway, and ultimately inhibit migration and invasion [12]. Fang Chuanci et al. [13] pointed out that disodium cantharidinate injection can inhibit angiogenesis by activating PI3K/PKB/mTOR pathway, and significantly inhibit the proliferation and migration of lung cancer A549 cells.

3.3 Synergistic and Toxic Effects of Radiotherapy and Chemotherapy

The synergistic effect is reflected in the ability to increase the sensitivity of tumor cells to radiotherapy and chemotherapy, which can cooperate with radiotherapy and chemotherapy to inhibit tumor growth, thereby reducing the amount of radiotherapy and chemotherapy. Attenuated toxin refers to the

relief of toxicity and side effects caused by radiotherapy and chemotherapy, such as bone marrow suppression, tissue and organ function impairment, pain, vomiting, fever, hair loss, etc. In terms of improving clinical efficacy, the study of Liu Qiaozhen et al. [14] showed that Aidi injection combined with TP regimen in the treatment of non-small cell lung cancer could increase FVC and FEV1 / FVC compared with chemotherapy with TP regimen, and significantly improve the therapeutic efficiency. Zhou Juan et al. [15] conducted a study on Conlite combined with docetaxel + cisplatin. Compared with the control group that only used Docetaxel + cisplatin, the observation group was superior to the control group in terms of 1-second rate (FVC/FEV1) cue, visual pain analogue score (VAS) decrease, and NSE, CA125 and CEA levels decrease. In terms of alleviating toxic and side effects, Tang Zhongming [16] found that Aidi injection combined with TP regimen in the treatment of non-small cell lung cancer could reduce the possibility of leukopenia and hemoglobin decline caused by chemotherapy under TP regimen, improve clinical symptoms, and reduce TCM symptom score. According to Guo Chunhui et al. [17], in addition to the effective rate of Aidi injection combined with oxaliplatin in the treatment of elderly NSCLC patients, the levels of IgG, IgA and IgM after chemotherapy were higher than those in the conventional paclitaxel + oxaliplatin group, and the incidence of adverse symptoms was lower than that in the conventional group, which had little impact on the immune function of patients.

3.4 Improving Drug Resistance Against NSCLC

Anti-tumor drug resistance can be divided into resistance to a certain drug or resistance to a class of drugs with similar structure and function, which has become a major challenge in cancer treatment. Many studies have shown that Chinese medicine injection can improve the resistance of chemotherapy drugs against NSCLC and play a sensitizing role for chemotherapy. Yi Fei et al. [18] found that Yadanzi Youru injection could regulate the expression of B-cell lymphomato-2 and its related X protein to enhance the sensitivity of A549 cells to cisplatin (DDP) chemotherapy. Pan Pengyu et al. [19] pointed out that Kang'ai injection may induce autophagy and apoptosis of A549/DDP cells by regulating Beclin1 protein expression, thereby effectively improving DDP resistance. Zhou Huan et al. [20] found that Kangai injection combined with DDP could inhibit the glycolysis of tumor cells through up-regulation of FOXO3a expression, and then improve the DDP resistance of A549/DDP cells.

4. Clinical Study of Traditional Chinese Medicine Injection in the Treatment of NSCLC

Compared with traditional Chinese medicine dosage forms, Chinese medicine injection has the advantages of high concentration of active ingredients, convenient use, rapid onset of effect and good patient tolerance, providing a new choice for the treatment of cancer, and its clinical application is increasingly widespread. It can be roughly divided into exorcism type, Fuzheng type and Fuzheng and exorcism type. The exorcism type was mainly to attack pathogen and suppress tumor, and the common ones were Chinbufosin injection, brucea javanica oil milk injection, compound

matrine injection, etc. Fuzheng type is mainly to improve immunity, the common varieties are Shenqi Fuzheng injection, Kangai injection, Shenmai injection, etc. The common varieties of both strengthening and expelling evil include Aidi injection and Kanglaite injection [21].

4.1 Attacking Pathogenic Chinese Medicine Injection

4.1.1 Cinobufacini injection

Cinobufacini injection is a kind of injection which is mainly extracted from the dried whole skin of *bufo chinensis* by strict process. It has the functions of clearing heat and detoxifying, reducing swelling and relieving pain, promoting blood circulation and removing blood stasis, softening and dispersing. Cinobufacini contains three natural active ingredients, namely cardiac aglycans, indole alkaloids and pteridine, which have exceptionally strong anti-tumor effects and stimulate the function of the immune system. The anti-tumor mechanism of cinobufacini is to inhibit the synthesis of DNA and RNA of cancer cells, hinder the division and reproduction of cancer cells, inhibit their growth, and induce apoptosis of cancer cells. In addition, cinobufacini can prevent and cure the decrease of white blood cell count in lung cancer patients, promote cellular immunity and body immune function, improve the anticancer effect of chemotherapy drugs and reduce their toxicity [22]. Clinical studies have shown that Cinobufacini injection combined with chemoradiotherapy in the treatment of NSCLC can not only alleviate adverse reactions, but also improve malignant pleural effusion and reduce the expression level of vascular endothelial growth factor, with significant effects on survival and quality of life [23-24].

4.1.2 Brucea javanica oil emulsion injection

Brucea javanica oil emulsion injection is a new anticancer drug made from the active components extracted from Brucea javanica, a mature fruit of the quassaceae plant. It has certain killing or inhibiting effects on G1, S and G2 phases of cancer cells, thus inhibiting DNA synthesis and blocking the growth process of cancer cells. It is a non-specific anticancer drug of cell cycle. Modern pharmacological studies have shown that the main active components of Brucea javanica have extensive anti-tumor effects [25]. It can protect and promote bone marrow hematopoietic stem cells, enhance immunity, help reduce the adverse reactions of radiotherapy and chemotherapy, and has significant adjuvant therapeutic effect on a variety of tumors, especially in the treatment of Qi-Yin deficiency, stasis and internal junction syndrome and lung Qi qi deficiency syndrome of NSCLC [26]. Brucea javanica oil emulsion injection can inhibit DNA synthesis of tumor cells and induce apoptosis and differentiation of tumor cells. Combined with chemotherapy and targeted treatments, it can effectively improve the immunity of patients with NSCLC, enhance clinical efficacy, reduce the incidence of adverse reactions [27], and reduce the levels of inflammatory factors and tumor markers [28].

4.1.3 Compound kushen injection (CKI)

Compound kushen injection (CKI) is a traditional Chinese medicine injection extracted and processed with bitter and

white Tuling at a ratio of 7:3, with the effects of clearing heat and dampness, cooling blood and detoxifying, and clearing and relieving pain [29]. It mainly contains matrine, oxymatrine, sophorine, oxysophorine and other active substances. Pharmacological studies have shown that compound kushen injection can reshape the immune microenvironment, enhance the efficacy of chemotherapy drugs, inhibit angiogenesis, regulate tumor metabolic signaling pathways, regulate cell cycle, energy metabolism, DNA repair pathways, and inhibit tumor cell proliferation [30-31]. In addition, CKI can inhibit the expression of inflammatory factors, tumor markers and factors related to tumor growth, thereby alleviating adverse reactions such as radiotherapy and chemotherapy and targeted drugs, improving patients' immunity, relieving tumor pain, and controlling malignant pleural effusion [32]. When lung cancer metastases, tumor cells initiate associated inflammatory responses, leading to the secretion of more nerve growth factor by the body's immune system and stromal cells. After conventional chemotherapy combined with CKI, the levels of inflammatory factors IL-6, IL-10 and tumor necrosis factor- α in serum were significantly reduced, indicating that the adjuvant treatment of CKI can better alleviate the inflammation that may occur in patients during the course of disease or treatment [33]. Some scholars have also pointed out that CKI has significant curative effect on phlegm-dampness-toxic NSCLC [34].

4.2 Tonic Chinese Medicine Injection

4.2.1 Shenqi Fuzheng injection

Shenqi Fuzheng injection is an important anti-tumor Chinese patent medicine composed of Codonopsis and Astragalus. It has the effects of tonifying middle qi, promoting blood circulation and removing blood stasis as well as reducing swelling and clearing up, and is often used in lung cancer patients with lung qi deficiency and qi blood deficiency [35]. Modern studies have shown that Shenqi Fuzheng injection has anti-tumor properties, including inhibiting tumor growth, promoting cell apoptosis, enhancing chemotherapy sensitivity and improving immune function [36]. Clinically, Shenqi Fuzheng injection is often combined with NSCLC, which has obvious effects on improving patients' immune function and quality of life, reducing adverse reactions, and reducing tumor marker levels and related tumor factors, especially in improving cancer-related fatigue [37-38].

4.2.2 Kangai Injection

Kangai injection is mainly composed of extracts of ginseng, Astragalus and matrine, which has the effects of tonifying middle qi, clearing heat and dampness, dispersing tangles and relieving pain. It can enhance the immune function of the body, improve the state of the whole body, have specific killing effect on tumor cells, promote tumor cell apoptosis, inhibit tumor growth, reduce the toxic and side effects of radiotherapy and chemotherapy, and enhance immunity [39]. It is mainly used in NSCLC patients with spleen-lung-qi deficiency and spleen-kidney deficiency [40-41]. Wu Yaqin [42] discussed the clinical efficacy of Kangai injection combined with chemotherapy in the treatment of advanced non-small cell lung cancer (NSCLC). GP protocol was used as

group B, and Kangai injection was used as group A on the basis of group B. After 4 courses of treatment, It was observed that the CD4+ cell score, CD3+ cell score, CD4+/CD8+ cell ratio and NK in group A were higher than those in group B, the CD8+ cell score was lower than those in group B, and the side effects such as nausea, vomiting and leukopenia were less than those in group B. Due to the above advantages, according to the Quality of Life scale (FACT) score, It was observed that the quality of life in group A was significantly higher than that in group B after chemotherapy.

4.2.3 Shenmai injection

Shenmai injection is mainly composed of red ginseng and opopogon, which has the effect of nourishing Yin and promoting fluid and pulse, supplementing Qi and stabilizing dehydration, and is mostly used for Qi-Yin deficiency syndrome NSCLC. Combined with radiotherapy and chemotherapy can alleviate side effects. Some modern pharmacological studies have found that the active ingredients in Shenmai injection can not only inhibit the production of tumor vascular growth factor, but also improve microcirculation, anti-oxidation and enhance body immunity [43]. Song Xuewei et al. [44] observed through randomized controlled trials that compared with chemotherapy alone, the total effective rate, CD3+ and CD4+ ratio in patients with advanced NSCLC after treatment with Shenmai injection were higher than those in the control group. These results indicate that Shenmai injection combined with chemotherapy can effectively improve the clinical efficacy, improve the immune function and inhibit the adverse reactions of chemotherapy in patients with middle and advanced NSCLC.

4.3 Combined Application of Traditional Chinese Medicine Injection

4.3.1 Aidi Injection

Aidi injection is made of ginseng, Astragalus, Acanthopanax, cantharides and other traditional Chinese medicine. It has the effect of fuelling and dispelling evil, clearing heat and detoxifying. It has the effect of enhancing immune function and anti-tumor. Modern pharmacological studies and basic studies have shown that it mainly contains ginsenosides, astragalus saponins, Astragalus polysaccharides, Acanthopanax polysaccharide and norcantharidin, which can inhibit tumor growth and regulate immunity, enhance the efficacy and reduce the toxicity of tumor radiotherapy and chemotherapy, and can not only improve the curative effect of tumor treatment, but also improve the quality of life of patients [36]. Clinical studies have shown that the combination of Aidi injection with NSCLC can achieve good results, which can reduce the level of inflammatory factors, improve the quality of life, regulate immune function, alleviate adverse reactions, and even help alleviate cognitive impairment in patients with NSCLC brain metastases [45,46].

4.3.2 Kanglaite injection (KLT)

Kanglaite injection (KLT) is an anticancer injection made from coix seed of traditional Chinese medicine by modern scientific methods, and its main component is coix seed oil. It has the effect of invigorating qi and nourishing Yin,

eliminating disease and dispersing. Pharmacodynamics and clinical application study results show that it has inhibitory effect on a variety of tumors. It is suitable for NSCLC with both qi and Yin deficiency and spleen deficiency and dampness. Coix seed is beneficial to water detumescence, tonifying spleen and wetting. However, KLT can strengthen spleen qi and remove dampness and turbidity, which is consistent with the conclusion that it can inhibit the proliferation, invasion and metastasis of lung adenocarcinoma A549 cells by regulating cholesterol metabolism and related protein expression in cell experiments [47]. KLT combined with platinum-containing chemotherapy or targeted therapy has high efficacy and safety in NSCLC, which can prevent postoperative tumor recurrence and metastasis, reduce adverse reactions of radiotherapy and chemotherapy, improve patients' quality of life and immunity, and control malignant pleural effusion [48-49].

5. Summary and Prospects

As a modern Chinese medicine preparation, Chinese medicine injection has the characteristics of rapid efficacy, convenient use and rapid effect, and can effectively improve the efficacy of NSCLC, improve clinical symptoms and improve the quality of life of patients, showing a good development prospect of Chinese medicine injection and other Chinese medicine preparations involved in tumor treatment. With the in-depth study of modern pharmacology and cellular and molecular mechanisms, the use of anti-tumor proprietary Chinese medicines should not only stay in the empirical use, but should go from macro clinical symptoms to micro cellular and molecular changes, and scientifically apply traditional Chinese medicine to anti-tumor treatment to give full play to its greater advantages.

References

- [1] Oncology Society of Chinese Medical Association, Chinese Medical Association Publishing House. Chinese Medical Association guideline for clinical diagnosis and treatment of lung cancer (2023 edition) [J]. *Zhonghua Zhongliu Zazhi*, 2023, 45(7): 539-574.
- [2] Passaro A, Leighl N, Blackhall F, et al. ESMO expert consensus statements on the management of EGFR mutant non-small-cell lung cancer [J]. *Ann Oncol*, 2022, 33(5): 466-487.
- [3] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. *CA Cancer J Clin*, 2021, 71(3): 209-249.
- [4] Jin M H, Tang J, Qin J L, et al. Epidemiological analysis of lung cancer from 2002 to 2020 [J]. *Chinese Journal of Medicine*, 2019, 34(6):34-38.
- [5] Pi Weiping. Research on Chinese medicine evidence and identification and typing of non-small cell lung cancer [D]. Beijing: Beijing University of Chinese Medicine, 2017.
- [6] WANG Junhui, XIAO Meng, MA Gongxian, et al. Research progress in traditional Chinese medicine treatment of non-small cell lung cancer, [J]*Shaanxi Journal of Traditional Chinese Medicine*, , 2021, 34(6):34-38.

- [7] FU Xiaoqing, Dai Zhoujuan, XIA Tao-tao, et al. Correlation analysis between pathological staging of lung cancer and Chinese medicine evidence[J]. *Zhejiang Journal of Traditional Chinese Medicine*, 2024, 59(07):603-604.
- [8] Wang YL, Wang Q, Li H, et al. Sestrin2 mediates FOXM1 expression to block the EMT process in non-small cell lung cancer through the AMPK/YAP pathway[J]. *Neoplasma*, 2023, 70(1):46-57.
- [9] XIAO Zhenzhen, ZHU Yanjuan, YU Yaya, et al. Effect of Reduning Injection, Shenfu Injection Combined with Gefitinib on Proliferation, Stemness Characteristics and Metabolism of Non-small Cell Lung Cancer Cells[J]. *Chinese Journal of Experimental Traditional Medical Formulae*, 2023, 29(18):45-53.
- [10] Wei Xueqin. Inhibitory effect of Aidi injection combined with amlotinib hydrochloride on neovascularisation in non-small cell lung cancer based on VEGF/MAPK signaling pathway[D]. Tianjin: Tianjin University of Traditional Chinese Medicine, 2023.
- [11] ZHUO X F, JI Y H. Inhibition of matrine against proliferation, invasion and angiogenesis of lung cancer tumor A549 cell and its mechanism[J]. *Drugs & Clinic*, 2017, 32(5): 767-771.
- [12] YANG J, HE D, PENG Y, et al. Matrine suppresses the migration and invasion of NSCLC cells by inhibiting PAX2-induced epithelial-mesenchymal transition[J]. *OncoTargets and Therapy*, 2017, 10: 5209-5217.
- [13] FANG Chuanci, QIAN Yayun. Effect of Sodium Cantharidinate Injection Targeting PI3K/AKT/mTOR Signaling Pathway on the Migration Ability of Human Lung Adenocarcinoma Cell A549[J]. *Acta Chinese Medicine*, 2021, 36(9):1954-1958.
- [14] Liu Qiaozhen, Fan Renyan, Zhou Linping. Study on the therapeutic effect of Aidi injection combined with TP Regimen on non-small cell lung cancer [J]. *Contemporary Medicine*, 2020, 26(07):139-141.
- [15] ZHOU Juan, FU Ping, HAN Hui, et al. Effect of Kanglaite Injection adjuvant chemotherapy on lung function and cancer pain in patients with advanced non-small cell lung carcinoma[J]. *Journal of Hubei University of Chinese Medicine*, 2021, 23(4):34-36.
- [16] Tang Zhongming, Huang Naixin, Guo Hengzhao. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine[J]. *Practical Chinese and Western medicine combined clinic*, 2019, 19(01):148-149.
- [17] Guo Chunhui, Dong Jianchun, Yin Yanhai, et al. Analysis of the efficacy and safety of Aidi injection combined with chemotherapy in the treatment of elderly patients with non-small cell lung cancer[J]. *Journal of China Prescription Drug*, 2020, 18(10):119-120.
- [18] Yi Fei, Liu Lei, Zhang Jun. Sensitization effect and mechanism of Brucea Javanica oil emulsion on cisplatin chemotherapy in lung cancer A549 cells[J]. *Shandong Medical Journal*, 2024, 64(5):40-43.
- [19] PAN Pengyu, ZHOU Huan, XU Ming, et al. Study on Kang'ai injection regulating Beclin 1-dependent autophagy-apoptosis interaction and improving cisplatin resistance in A549/DDP cells[J]. *Academic Journal of Shanghai University of Traditional Chinese Medicine*, 2022, 36(4):41-51.
- [20] ZHOU Huan, SUN Ye, LIU Chunying, et al. Study on Improvement of Cisplatin Resistance of A549/DDP Cells by Kang'ai Injection Based on FOXO3a Regulated Glycolysis Pathway[J]. *Journal of Liaoning University of Traditional Chinese Medicine*, 2022, 24(5):13-18.
- [21] WU Qihang, ZHANG Xiaoli, SONG Yanping. The Current Situation and Outlet of Traditional Chinese Medicine Injection[J]. *CHINESE AND FOREIGN MEDICAL RESEARCH*, 2019, 17(36):185-188.
- [22] Chen Minghui, Liu Tao, Su Yuxia, et al. Efficacy and safety of different dosages of Cinbufosin injection combined with chemotherapy in treatment of advanced lung cancer [J]. *Chinese Remedies & Clinics*, 2019, 20(19):3241-3243.
- [23] Wu Weilong. Efficacy of huachunin injection combined with vincristine + cisplatin chemotherapy regimen for advanced non-small cell lung cancer[J]. *Chronic Pathematology Journal*, 2022, 23(11):1718-1720.
- [24] MI Suicai, WU Lingyan, CHEN Zhiming, et al. Objective to Compare The Clinical Efficacy of Arotinib Combined With Cinobufacin or Cisplatin in The Treatment of Non-small Cell Lung Cancer With Malignant Pleural Effusion[J]. *Medical Innovation of China*, 2021, 18(4):81-84.
- [25] FAN Xinyue, YANG Luming, FU Jiali, et al. Research Progress in Chemical Components and Pharmacological Action of Brucea [J]. *Chinese Pharmaceutical Journal*, 2022, 57(14):1137-1145.
- [26] DU Chongwei, LIU Xi, ZHANG Jiali. Effects of Sijunzi Tang combined with Crowberry Oil Milk Injection on immune function, tumour marker levels and lung function in patients with non-small cell lung cancer[J]. *Modern Journal of Integrated Traditional Chinese and Western Medicine*, 2023, 32(9):1277-1281.
- [27] HE Hua, ZHOU Yujie, LI Tian. Effect of bruceolic oil emulsion adjuvant PC regimen chemotherapy on immune function and inflammatory factors in NSCLC[J]. *Chinese Journal of Lung Diseases (Electronic Edition)*, 2023, 16(5):697-699.
- [28] LI Bin, BAI Huihui, ZHANG Yi, et al. Observation of the clinical effect of brucea javanica oil emulsion injection combined with gefitinib in treating non-small cell lung cancer and its effect on patients' serum indicators[J]. *Oncology Progress*, 2021, 19(10):1011-1014.
- [29] WANG Lei, ZHANG Meng, YU Lijie, et al. Research progress of compound Kushen injection in the adjuvant treatment of non-small cell lung cancer[J]. *World Clinical Drug*, 2023, 44(02):117-121.
- [30] Li K, Xiao K, Zhu S, et al. Chinese herbal medicine for primary liver cancer therapy: perspectives and challenges[J]. *Front Pharmacol*, 2022, 13: 889799.
- [31] Ye Z, Yao X, Chen Z, et al. Exploring the nucleotide molecular mechanism of compound Kushen injection for lung adenocarcinoma based on network pharmacology and molecular docking[J]. *Front Oncol*, 2022, 12: 1013052.
- [32] Chen Jiayi, Song Jian, He Jiajian, et al. Research progress of Chinese medicine injection in adjuvant treatment of non-small cell lung cancer[J]. *World Clinical Drug*, 2024, (6): 673-677.
- [33] Zuo Nian, Liang Liang. Effect of compound bitter ginseng injection combined with AP regimen on

- immune function and serum IL-6, IL-10 and TNF- α levels in patients with non-small cell lung cancer[J]. *The Journal of Medical Theory and Practice*, 2021, 34(24):4290 - 4291.
- [34] YING Weiping, ZHONG Guomei. Clinical Study on Compound Kushen Injection Combined with Osimertinib Mesylate Tablets for Epidermal Growth Factor Receptor Gene Mutation in Advanced NonSmall Cell Lung Cancer[J]. *New Chinese Medicine*, 2024, 56(2):147-150.
- [35] Kuang Yunfeng, Chen Gaofeng, Huang Zhongdeng, et al. Clinical Observation of Sanhuang Wuxue Acupuncture Method Combined with Shen Qi Fuzheng Injection for the Treatment of Fatigue in Lung Cancer Patients with Qi and Blood Deficiency Syndrome[J]. *Journal of Guangzhou University of Traditional Chinese Medicine*, 2022, 39(12):2847-2854.
- [36] Chen Weixia, Niu Yao-fei, KANG Yan, et al. Research status of antitumor Chinese patent medicine injection [J]. *Chinese Journal of Gerontology*, 2021, 41(23):5439-5444.
- [37] LIU Jingjing, YI Liangjie. Clinical Efficacy of Shenqi Fuzheng Injection Adjuvant Carrelizumab Combined with Chemotherapy in the First-Line Treatment of Advanced Non-Small Cell Lung Cancer[J]. *Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease*, 2024, 32(2):29-33.
- [38] Zhang Jingxian. Clinical study on the treatment of driver gene-negative non-small cell lung cancer with shenqi fu zheng injection combined with endu and PD-1 inhibitor[D]. Tianjin: Tianjin University of Traditional Chinese Medicine, 2023.
- [39] Zhang Hongyan, Bi Hongyu. Research Progress of Kangai Injection [J]. *Drug Evaluation*, 2022, 12 (3): 189-192.
- [40] Zhu Shicong, Wang Heling, Xu Ya, et al. Clinical Study of Kangai Injection Combined with PP Regimenin the Treatment of Advanced Lung Adenocarcinoma Patients with Spleen-Lung Qi Deficiency[J]. *Herald of Medicine*, 2020, 39(4):572-576.
- [41] YAO Yilin, LI Hegen, CHEN Zhiwei, et al. Clinical study on Jianpi Wenshen Ruanjian Jiedu formula, Kang'ai injection and low-dose chemotherapy in the treatment of advanced non-small cell lung cancer of spleen kidney deficiency type in the elderly[J]. *Shanghai Journal of Traditional Chinese Medicine*, 2020, 54(3):67-71.
- [42] Wu Y Q. Clinical effect of Kangai injection combined with chemotherapy in the treatment of advanced non-small cell lung cancer [J]. *Chinese Journal of Clinical Rational Drug Use*, 2021, 14(18):76-78.
- [43] Yan Dixue. Clinical effect of Shashen Maodong Decoction combined with etoposide and cisplatin in the treatment of patients with small cell lung cancer [J]. *Chinese Journal of Clinical Rational Drug Use*, 2012, 15(20):71-75.
- [44] Song Xuewei, Zhang Kuisong. Effect of Shenmai Injection Combined with chemotherapy on middle and Advanced Lung Cancer of Qi-Yin Deficiency Type [J]. *World Journal of Complex Medicine*, 2019, 9(11):104-107.
- [45] Li Hongyu. Efficacy of Aidi injection combined with gefitinib in patients with non-small cell lung cancer[J]. *Henan Medical Research*, 2021, 30(10):1878-1880.
- [46] LIU Guiju, LI Lu, ZHAO Qingqing, et al. Clinical efficacy of Aidi Injection combined with conventional chemotherapy in patients with lung cancer brain metastasis[J]. *Chinese Remedies & Clinics*, 2024, 24(2):102-106.
- [47] ZHU Guanghui, ZHENG Qi, GAO Ruike, et al. Kanglaite injection regulates cholesterol metabolism to inhibit the malignant biological behavior of lung adenocarcinoma A549 cells[J]. *Chinese Journal of Cancer Biotherapy*, 2023, 30(11):973-980.
- [48] WANG Xiaozhen, YANG Lixin, LI Danqing, et al. Clinical effect of intensity modulated radiotherapy combined with Kanglaite injection in the treatment of elderly patients with non-small cell lung cancer and its effect on immune function[J]. *China Medicine*, 2024, 19(2):198-201.
- [49] ZHANG Hengli, ZHANG Zhengwei. Clinical observation of Conrad combined with thoracic hypotonic retention perfusion paclitaxel plus loproressor in the treatment of malignant pleural effusion complicated by non-small cell lung cancer[J]. *Journal of Clinical Internal Medicine*, 2022, 39(7):472-474.