Research Progress of Traditional Chinese Medicine in Non-small Cell Lung Cancer

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Abstract. This paper provides an in-depth look at the application of Chinese medicine in the treatment of non-small cell lung cancer (NSCLC) and its potential pharmacological mechanisms. NSCLC is one of the most common malignant tumors in the world, and despite the continuous progress of modern medical treatment, the quality of life and survival rate of patients still need to be improved. Traditional Chinese medicine (TCM), with its unique treatment concepts and methods, has shown potential in individualizing treatment and reducing side effects. Based on the basic theory of TCM, this paper expounds the etiology and pathogenesis of NSCLC in TCM, as well as the strategies of treating NSCLC in TCM, including fuzheng and dispelling evil, strengthening qi and reducing side effects. In particular, several commonly used TCM prescriptions, such as Liushenzi Decoction, Buzhong Yiqi Decoction, Shashen Madong Decoction, Baihe Gujin Decoction, etc. are mentioned, which can help to improve the symptoms and quality of life of NSCLC patients by promoting qi and Yin, clearing heat and eliminating phlegm, and strengthening the normal cultivation. In addition, the article also analyzed the main components of TCM, such as polysaccharides, alkaloids, flavonoids, etc., and their anti-tumor mechanisms, including immune regulation, antioxidant, direct anti-tumor effects. TCM is expected to play a more important role in the comprehensive treatment of NSCLC.

Keywords: Non-small cell lung cancer (NSCLC), Traditional Chinese medicine (TCM), Pharmacological mechanisms.

1. Introduction

Non-small cell lung cancer (NSCLC) is one of the most common malignant tumors in the world, with high morbidity and mortality. According to the World Health Organization (WHO), NSCLC accounts for about 85% of all lung cancer cases. At present, the main treatment methods for NSCLC are chemotherapy, radiotherapy, targeted therapy, and immunotherapy. Although modern medicine has made remarkable progress in the treatment of NSCLC, the survival and quality of life of patients still need to be improved. Therefore, the advantages of traditional Chinese medicine (TCM) in the treatment of NSCLC are increasingly being appreciated, especially in the potential of individualized treatment and reduction of side effects. TCM, with its unique therapeutic concepts and methods, provides new ideas and directions for the comprehensive treatment of NSCLC.

TCM prescription and the application of TCM is the main way to treat cancer. According to statistics, the most commonly used TCM prescriptions for NSCLC are Liushenzi Decoction, Buzhong Yiqi Decoction, Shashen Maodong Decoction and Baihe Gujin Decoction, all of which help to improve the symptoms of patients, improve the quality of life, reduce side effects, and enhance the therapeutic effect to a certain extent through different mechanisms. [1]

Not only have TCM prescriptions achieved remarkable results in the treatment of NSCLC, but recent studies have shown that TCM plays a significant anti-tumor role by regulating a variety of biological pathways. For example, studies have shown that some Chinese herbs and formulas containing "alkaloids" and "flavonoids" can inhibit the proliferation and migration of tumor cells by regulating the PI3K/Akt pathway, thus fighting the development of tumors. The PI3K/Akt pathway is a key cell signaling pathway involved in cell proliferation, survival, and migration. By affecting this pathway, tumor progression can be effectively slowed. [2]

In view of the advantages of TCM in the treatment of NSCLC, this review aims to reveal how TCM prescriptions play a role in NSCLC through comprehensive analysis. In addition, the potential

value of TCM in improving the prognosis of NSCLC patients will also be discussed to provide more reference for treatment.

2. Basic Theories of TCM

2.1. The Concepts of INSCLC in TCM

In the treatment of NSCLC, the TCM treatment strategy lays special emphasis on maintaining and enhancing the healthy qi of the human body, with the core concept of fuelling the healthy and dispelling the evil. In clinical practice, TCM treatment is usually based on drugs to supplement the positive qi, supplemented by heat-clearing phlegm and detoxification drugs, aiming to improve the therapeutic effect and reduce the adverse reactions that may be brought about by Western medicine

According to the characteristics of four qi and five taste, TCM can nourish different zang-fu organs, restore the balance of qi, blood and Yin and Yang, so as to achieve the purpose of strengthening the right and overcoming the evil. In the research of Hu Xiaowei, Luo Yingbin [1], Astragalus, licorice, white art, poria, ophiopogon and other Qi-nourishing tonics are the most widely used, they help to enhance the body's healthy qi. At the same time, with the use of white flower snake tongue, Schistoderma, Tangerine peel, pinellia and other drugs with the effect of clearing heat and detoxification, eliminating phlegm and relieving cough and asthma, in order to dissolve the heat toxin and phlegm dampness in the body, to achieve both symptoms and root causes.

2.2. TCM Compounds: Liujunji Dedoction, Buzhong Yiqi Decoction, Shashen Maidong Dedoction, and Lily Gujin Dedoction

Liujunzi Decoction and Buzhong Yiqi Decoction have the effect of beneficial qi, while Shashen Maodong decoction and Lilihe Gujin are the prescriptions for nourishing Yin, and these four compounds are used most frequently. Therefore, we can conclude that Qi-yin deficiency is the most common type of syndrome in NSCLC patients. This finding is highly consistent with statistical findings on drug use, with Qi-tonifying and yin-tonifying drugs being used most frequently in treatment. This indicates that enhancing patients' positive qi and regulating yin-yang balance are key therapeutic strategies in the TCM treatment of NSCLC. Supplementing positive qi and nourishing Yin fluid, it can effectively relieve the clinical symptoms of patients, improve the therapeutic effect, and may reduce the adverse reactions brought by Western medicine treatment [3,4].

3. Application of TCM in the treatment of NSCLC

3.1. Compound: The composition of Liushenzi decoction, Buzhong Yiqi decoction, Shashen Maidong decoction and Baihe Gujin decoction

Liushenzi Decoction, Buzhong Yiqi decoction, Shashen Maidong decoction and Baihe Gujin decoction are the most frequently used TCM prescriptions. Table 1 details the composition, efficacy, and response of these four formulations to NSCLC symptoms.

Table 1.Combination, efficacy and symptoms of NSCLC in Liushenzi Decoction, Buzhong Yiqi Decoction, Shashen Maodong Decoction and Baihe Gujin Decoction

Prescription	Liujunzi Decoction	Buzhong Yiqi Decoction	Shashen Maidong Decoction	Lily Gujin decoction
Constitution	Ginseng, Atractylodes, Honey-fried Licorice Dried Tangerine Peel Pinellia	Astragalus Ginseng Atractylodes Honey-fried Licorice Angelica Sinensis Dried Tangerine Peel	Adenophora Ophiopogon Polygonatum Licorice Mulberry Leaf White Hyacinth Bean	LilyBulb Rehmannia Ophiopogon White Peony Root
Efficacy	Tonify qi and strengthen the spleen,dry dampness and transform phlegm	tonify the middle and boost qi,raise yang and lift what has sunk	clear the lungs and nourish yin,generate fluids and moisten dryness.	moisten the lungs and clear heat,nourish yin and stop coughing
Corresponding to symptoms of NSCLC	To improve symptoms of spleen deficiency and phlegm-dampness caused by illness or treatment—such as fatigue and loss of appetite	Patients with NSCLC often present with symptoms of qi deficiency, such as fatigue and weak voice. The Bu Zhong Yi Qi Decoction can help improve these symptoms.	Patients with NSCLC, especially after radiotherapy or chemotherapy, often experience symptoms of yin deficiency and internal heat, such as dry mouth and throat. The Sha Shen Mai Dong Tang can effectively relieve these symptoms.	In the treatment of NSCLC, certain approaches may help alleviate respiratory symptoms such as dry cough and throat dryness.

3.2. Analysis of Main Components and Their Mechanism of Action

All the compounds introduced above have the effect of invigorating qi and nourishing Yin, and modern pharmacology shows that most of the invigorating and nourishing yin-strengthening TCMs have anti-tumor effects to varying degrees.

3.2.1 Polysaccharide substances

Most Chinese drugs containing polysaccharides are widely used in the treatment of NSCLC. Medicinal products containing polysaccharides (PPS) also showed significant anti-tumor effects. Its mechanisms include inhibiting the proliferation of tumor cells, inducing cell cycle arrest and apoptosis, and enhancing the immune system's ability to clear cancer cells. [5,6] In addition, Astragalus (APS) has been shown to enhance immune response and directly inhibit tumor growth in the treatment of non-small cell lung cancer. It has been found that Astragalus polysaccharide can effectively inhibit tumor growth by enhancing the activity of immune cells and inducing apoptosis of cancer cells. Astragalus polysaccharides from Astragalus showed remarkable effect on the proliferation of human lung cancer cell lines A549 and NCI-H358, and the mechanism of action may be related to the reduction of the transcriptional activity of nuclear factor κB (NF-κB), thereby inhibiting the expression of p65 and p50. [7]

In summary, the polysaccharide substances of these TCMs provide a beneficial auxiliary choice for the treatment of NSCLC through a variety of mechanisms, including immunomodulatory, antioxidant and direct anti-tumor effects.

3.2.2 Alkaloids

TCMs containing alkaloids, such as Coptis chinensis, Pinellia ternata, and Rehmannia glutinosa, have shown significant therapeutic potential for NSCLC.

The main alkaloid component in Coptis chinensis is berberine. Studies have shown that berberine fights NSCLC through multiple mechanisms. Its mechanisms include inhibiting tumor cell proliferation, inducing apoptosis, inhibiting tumor angiogenesis, and interfering with cancer cell signaling pathways. For example, berberine can induce apoptosis of tumor cells by inhibiting the PI3K/Akt signaling pathway and activating the p53 pathway. [8] The main alkaloid component in Pinellia ternata is pinellia. It has been found that pinellidine can inhibit the growth of NSCLC by regulating cell cycle, inducing apoptosis and inhibiting cancer cell migration. It causes apoptosis of cancer cells by blocking the progression of the cell cycle, and inhibits metastasis of tumor cells [9]. Rehmannia glutinosa is the main alkaloid in Rehmannia glutinosa, which also has a certain inhibitory effect on non-small cell lung cancer. Rehmanidine reduces oxidative stress through antioxidant effects and inhibits the growth of cancer cells by regulating cell signaling pathways. Rehmanine can inhibit the proliferation of tumor cells by affecting NF-kB and MAPK signaling pathways. [10]
TCMs of alkaloids have shown significant anti-tumor effects in the treatment of non-small cell lung cancer. These drugs provide beneficial adjuvant treatment options through a variety of mechanisms, including apoptosis, cell cycle regulation, antioxidant effects, and inhibition of tumor cell migration.

3.2.3 Flavonoids

Traditional Chinese flavones, including Sophora flavescens, Astragalus membranaceus and Eugenia caryophyllata, have shown remarkable efficacy in the treatment of NSCLC.

The main brass component in Sophora flavescens is matrine. Studies have found that matrine has a variety of anti-tumor mechanisms. First, it significantly reduces tumor volume by inhibiting tumor cell proliferation and inducing apoptosis. Matrine down-regulates the PI3K/Akt and NF-κB signaling pathways, thereby inhibiting the proliferation and migration of cancer cells and further weakening tumor growth by enhancing apoptosis [11]. These mechanisms make matrine play an important role in the treatment of non-small cell lung cancer. On the other hand, astragaloside IV, a brass-like component of Astragalus membranaceus, also showed significant anti-tumor effects. Astragaloside fights NSCLC in several ways, especially in inducing apoptosis and enhancing the immune response. Specifically, Astragaloside effectively inhibits the proliferation and metastasis of cancer cells by regulating apoptosis-related proteins, inhibiting oxidative stress, and improving antioxidant capacity [12]. These mechanisms of action make astragaloside an important candidate for the treatment of non-small cell lung cancer. In addition, eugenol, the brass-like component of cloves [Eugenia caryophyllata], has also shown significant anti-cancer effects. Eugenol fights NSCLC through multiple mechanisms, in particular by inhibiting NF-κB and MAPK signaling pathways, thereby reducing the proliferation and migration of cancer cells. At the same time, eugenol also has powerful antioxidant properties, which can reduce oxidative stress damage to cells [13]. These mechanisms make eugenol potentially useful in the treatment of non-small cell lung cancer. Details are displayed in the Table 2.

Table 2. Efficacy of Dyphyllin sinense and Oldenlandia diffusa, main active ingredients, and their anti-tumor mechanisms [14].

Medicine	Dyphyllin sense	Oldenlandia diffusa
Efficacy	**Clearing Heat and Detoxifying**: According to TCM, the formation of tumors is related to the accumulation of "heat toxins" in the body. Dyphyllin sinense is believed to have the ability to clear heat and detoxify, eliminating "evil heat" and "toxins" from the body, thereby improving the internal environment and inhibiting tumor growth. **Invigorating Blood and Resolving Stasis**: In TCM theory, blood stasis is considered a significant factor in tumor formation. Dyphyllin sinense is thought to promote blood circulation and resolve stasis, helping to improve blood flow and reduce the stasis condition in tumor tissues. **Promoting Dampness Removal and Detoxification:** Dyphyllin sinense also has the function of promoting dampness removal and detoxification, which can help clear internal dampness, improve organ function, and further reduce conditions that promote tumor growth.	**Clearing Heat and Detoxifying**: Oldenlandia diffusa is widely used to treat various diseases caused by "heat toxins." TCM theory holds that it has strong heat-clearing and detoxifying properties, capable of eliminating toxins from the body and reducing the occurrence and development of tumors. **Dissolving Nodules and Reducing Swelling**: TCM considers tumors to result from stagnant qi and blood in the body, leading to accumulation. Oldenlandia diffusa has the ability to dissolve nodules and reduce swelling, helping to alleviate the formation and development of tumor masses. **Harmonizing the Organs:** Bai Hua She She Cao also plays a role in harmonizing the organs, which can improve dysfunction within the organs and enhance the body's ability to resist disease, providing support for tumor treatment.
Major active ingredient	**Diphyllin**: One of the main active components of Diphyllin, it has various pharmacological effects, including antitumor activity. **Flavonoids**: Compounds like Diphyllin flavonoids are also considered to possess antitumor properties.	**Oldenlandia diffusa glycosides**: This component is abundant in Bai Hua She She Cao and has significant antitumor effects. **Oleanolic Acid:** Another effective antitumor ingredient that is widely found in Bai Hua She She Cao.
Antitumor mechanism	**Inducing Apoptosis**: Ban Zhi Lian Glycoside can promote cancer cell apoptosis by regulating apoptosis-related signaling pathways. For example, studies show that it induces apoptosis in cancer cells by activating the p53 pathway and inhibiting Bcl-2 family proteins. Inhibiting Proliferation: Ban Zhi Lian Glycoside can suppress cancer cell proliferation by interfering with proliferation-related signaling pathways, such as the PI3K/Akt and MAPK pathways. **Antioxidant Activity**: It possesses strong antioxidant activity, which can reduce oxidative stress damage to cells, playing a crucial role in inhibiting cancer cells.	**Induce cell apoptosis:** The main components of Oldenlandia diffusa can promote the apoptosis of cancer cells by regulating apoptosis-related proteins, such as caspases and Bcl-2 family proteins). **Inhibit tumor metastasis:** Oleanolic acid can inhibit the invasion and migration of tumor cells and reduce the risk of tumor metastasis by interfering with the adhesion and migration mechanism of tumor cells. **Regulate the immune response:** These active ingredients also enhance the body's ability to recognize and eliminate cancer cells by regulating the immune system.

4. Conclusion

In this review, the application of TCM in the treatment of NSCLC and its potential pharmacological mechanism were discussed, which provided a scientific basis for the role of TCM

in modern clinical tumor treatment. Through the analysis of the epidemiology and treatment status of NSCLC, we recognized the unique advantages of TCM in alleviating symptoms, improving quality of life, and reducing toxic and side effects of radiotherapy and chemotherapy.

Under the theoretical framework of TCM, NSCLC is regarded as "lung accumulation", and its incidence is closely related to TCM syndrome types such as qi and Yin deficiency. This review focuses on the relationship between Liushenzi Decoction, Buzhong Yiqi Decoction, Shashen Maodong decoction, Baihe Gujin Decoction and Qi-Yin deficiency syndrome, and reveals the role of these formulas in regulating Qi-yin, clearing heat and eliminating phlegm, strengthening and cultivating the essence. The detailed introduction of the composition of the prescription and the discussion of pharmacological action further elucidated the multi-target intervention ability of TCM compound in the treatment of NSCLC.

The significance of this review is that it not only provides theoretical support and practical guidance for the application of TCM in the treatment of NSCLC but also points out the direction for future pharmacological research and clinical application of TCM prescriptions. With an in-depth understanding of the mechanism of action of TCM prescriptions, we have reason to believe that TCM will play a more important role in the comprehensive treatment of NSCLC and bring greater clinical benefits to patients.

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