# Discussion on the Nature and Flavor of the Chemotherapy Drug Paclitaxel Based on the Theory of Yin and Yang

Wei Wang<sup>1,a</sup>, Dejun Wang<sup>1,b,\*</sup>, Jingya Fu<sup>2,c</sup>, Yingtao Liu<sup>1,d</sup>, Yumei Huang<sup>1,e</sup>

<sup>1</sup>Hunan University of Traditional Chinese Medicine, Changsha, Hunan, 410208, China <sup>2</sup>Shaanxi University of Traditional Chinese Medicine, Xiangyang, Shaanxi, 712046, China <sup>a</sup>2717429934@qq.com, <sup>b</sup>36497062@qq.com, <sup>c</sup>1031633021@qq.com, <sup>d</sup>873702894@qq.com, <sup>e</sup>2336031698@qq.com
\*Corresponding author

**Keywords:** Traditional Chinese Medicine Properties, Paclitaxel, Four Qi, Five Flavors

**Abstract:** Paclitaxel is one of the commonly used chemotherapeutics in clinical practice, but some patients cannot tolerate related treatments due to the side effects of chemotherapy. This article analyzes the chemotherapeutic drug paclitaxel from the four qi, five flavors, ups, and downs, and return meridian. It is believed that paclitaxel is cold and cold, and the five flavors are bitter and salty. Through the discussion of the properties of paclitaxel, it is of guiding significance to prevent its side effects of chemotherapy and to treat tumor diseases with integrated traditional Chinese and western medicine.

#### 1. Introduction

Chinese medicine believes that everything can be divided into yin and yang. "Su Wen Yin-Yang Yingxiang Great Theory," says: "Yin-yang is the way of heaven and earth, the principle of all things, the parent of change, and the origin of life and death." The theoretical basis is also the methodology to guide the clinical practice of traditional Chinese medicine [1]. The return of nature and flavor to the meridian is the basic content of the theory of traditional Chinese medicine. Can the chemotherapy drug paclitaxel be used to analyze the return of nature and flavor to the meridian to better guide clinical practice?

Paclitaxel is a metabolite isolated and purified from the bark of Taxus Chinensis. It is a diterpene alkaloid compound with anticancer activity. It is a white crystalline powder and has a strong killing effect on various tumors. Approved by the US FDA for clinical use in 1992, it has a history of nearly 30 years. Its mechanism of action is to specifically bind to the β-position of tubules, causing tubulin and tubulin dimers that makeup microtubules to lose the dynamic balance, causing microtubules to aggregate into clumps and bundles and promoting their stability, thereby inhibiting the normal function of tubulin, and inhibit the mitosis of cancer cells and trigger apoptosis, interfering with cell division and proliferation, thereby effectively preventing the proliferation of cancer cells, thereby playing an anti-tumor effect [2].

#### 2. Second Section

## 2.1 Four Properties of Paclitaxel - Cold, Cool

Four Qi refers to the four medicinal properties of cold, heat, warm and cool. Four qi is one of the basic contents of traditional Chinese medicine. It can be found in "Shen Nong's Materia Medica" for the first time. The preface says: "The medicine has five flavors of sour, salty, sweet, bitter, and pungent, as well as for qi of cold, heat, warm and cool." The Da Lun says: "Control qi with heat, use heat without offense, manage qi with cold, use cold without offense, manage qi with coolness, use cool without offense, manage qi with warmth, use warm without offending." It is summed up by the reaction of the drug acting on the body, which is opposite to the cold and heat nature of the disease being treated. Therefore, the four properties of paclitaxel can be inferred through the mechanism of paclitaxel acting on the human body and the side effects after chemotherapy. The theory of "cancer poison" was put forward by Professor Zhou Zhongying, who believed that the essence of cancer poison is a class of specific pathological products and pathogenic factors that can lead to the occurrence and development of malignant tumors [3]. Pathogenesis changes in the process are mostly positive and deficient and evil, endogenous dampness, phlegm aggregation, blood stasis block, and heat and toxin accumulation [4]. Professor Zhou Lan believes that cancer poison has the characteristics of depleting human nutrition, easy to flow, and blocking the flow of human qi and blood [5]. Modern medicine believes that tumor cells have the characteristics of high energy metabolism, strong proliferation ability, and easy metastasis and spread [6]. In the theory of yin and yang, everything that is moving, outward, rising, warm, and bright belongs to yang; that which is relatively static, inward, descending, cold, and dark belongs to yin. "Su Wen Yin-Yang Yingxiang Great Theory," says: "Yang prevails and heat prevails, and yin prevails leads to cold." In the early stage of tumor cell survival, with the deficiency of human righteousness, tumor cells grow rapidly. According to "Su Wen Zhizhen Yao Da Lun": "The cold is hot, and the hot is cold." It can be inferred that the properties of paclitaxel tend to be cold. In addition, we can also infer the drug properties through the adverse reactions after paclitaxel chemotherapy. First, the common adverse reaction of paclitaxel chemotherapy is neurotoxicity (mainly peripheral neuropathy), accounting for about three-fifths of clinical cases. Ni Kaiwen et al [7] believe that cancer patients are inherently positive and false. Paclitaxel is a poisonous product, which can easily damage the yang qi of the human body, causing the collaterals and collaterals to be cold and stagnant. Secondly, myelosuppression is also one of the common adverse reactions of paclitaxel chemotherapy. Many patients may appear with white blood cells and neutropenia manifested as general fatigue, muscle pain, and so on. Chemotherapy drugs belong to the category of "drug poison" in traditional Chinese medicine. Modern medicine [8] believes that chemotherapy is a double-edged sword, which not only kills cancer cells but also damages normal cells of the human body, thereby reducing human immunity. After chemotherapy with paclitaxel, most patients show symptoms of yang deficiency such as loss of appetite, fatigue, and consumptive fatigue. Again, it can be inferred that paclitaxel is cold.

## 2.2 The Five Taste Properties of Paclitaxel - Bitter and Salty

The five flavors are the five flavors of the medicine: sour, bitter, sweet, pungent, and salty. The taste of a drug is mostly based on its taste and the effect of the drug on the human body. "Simple Questions: Yin-Yang Yingxiang Great Theory," says: "The smell is pungent and sweet, which is yang, and the sour and bitter rushing out is yin." Tumor diseases are classified in the categories of "accumulation" and "shi jiao" in traditional Chinese medicine, and they are systemic diseases. The pathogenesis and pathogenic factors are more complex. In Zhu Danxi's "Danxi Heart Method", he

said: "Mortal people with lumps in the middle and lower body are mostly phlegm." He believes that the accumulation of masses is caused by "phlegm-drinking, qi stagnation, and blood stasis" [9]. Bitterness, diarrhea, and dryness. Diarrhea is to relieve, reduce and clear the discharge; the bitter medicine can clear the phlegm and drink, regulate qi and remove blood stasis, to dissipate the accumulation. The dry is wet. Phlegm is transformed from dampness, and dampness aggregates into phlegm. Chinese medicine believes that "the spleen is the source of phlegm." There is also "the spleen controls the transportation and transformation." If the spleen's transportation and transformation functions are not good, the dampness will be endogenous and condense into phlegm for a long time. Bitter herbs remove dampness and phlegm to remove the pathogenic factors of tumors. Salty, can be soft. Some patients may have gastrointestinal reactions such as diarrhea after chemotherapy with paclitaxel, which may be related to the laxative effect of salty drugs. Modern pharmacological studies have shown that the efficacy of salty drugs is related to anti-tumor, antiinflammatory, and diarrhea-causing effects 10. Salty medicines have the effect of softening firmness and dispersing knots and can be used to treat scrofula, galls, and scabies[10]. Patients treated with paclitaxel may have imaging manifestations of shrinking tumor lesions, which may be due to the effect of salt to soften hard, suggesting that paclitaxel has a salty taste. Furthermore, traditional Chinese medicines such as seaweed and oysters have a salty taste and are often used in the treatment of tumor diseases.

## 2.3 The up-and-Down Properties of Paclitaxel—Sedimentation

The ups and downs of traditional Chinese medicine are relative to the trend of disease [11]. Medicines have the properties of ups and downs, which can adjust the disorder of zang-fu qi and restore normal physiological functions, or act on different parts of the body to make the best use of the situation, expel pathogens and go out, to achieve the purpose of curing diseases. In clinical practice, it is necessary to select the appropriate drug according to the difference between the upper part and the lower part and the outer part in the disease occurrence part, and according to the different characteristics of the medicine with ups and downs. "Plain Questions: Yin and Yang Yingxiang Great Theory," says: "The higher ones are therefore overtaken; the lower ones are drawn and exhausted." It clarifies that the disease situation and disease position of the disease should be produced according to the obstacles of the ascending and descending of qi., and take corresponding treatment methods, which lays a theoretical foundation for the emergence and development of the theory of lifting and sinking of traditional Chinese medicine. Ascending means ascending, ascending, and ascending descending means descending and descending inversely, floating means ascending and floating, ascending and divergent, and sinking means sinking and descending to release profit. The rising and floating properties are upward and outward, while the sedimentation properties are downward and inward. The rising and floating are mostly yang, and the subsidence is mostly yin. The characteristics of rapid growth and strong metastasis of tumor cells can be classified as positive diseases, so negative drugs are required for treatment. In terms of the nature, taste, and thickness of medicines, all medicines with acrid and sweet taste (thin taste) and warm and hot (thickness in gas) are mostly floating medicines, and all tastes are bitter, sour, salty (thick taste), cold and cool (thin qi) medicines are mostly sedimentation medicines. Paclitaxel is extracted from the bark, which is derived from heavy materials. Heavy things tend to settle. Furthermore, the medicines with the functions of diarrhea, clearing of stagnation, and heat-clearing can go down and inward, which also shows that the up-and-down property of paclitaxel is sedimentation.

### 2.4 The Meridian of Paclitaxel - Spleen, Liver, Kidney

Gui Jing is based on the theory of zang-fu organs and meridians, and closely links the action of

drugs with the zang-fu organs and meridians of the human body. Mastering the meridian of the drug will help to improve the accuracy of clinical drug use and further guide the rationalization of clinical drug use. Gui Jing has first seen in "Plain Questions: Xuanming Five Qi Chapter": "The five flavors enter, the sour enters the liver, the pungent enters the lung, the bitter enters the heart, the salty enters the kidney, and the sweet enters the spleen, which is called the five entrances." In different types of tumors in there are also differences in the selection of chemotherapy drugs. If the theory of meridian return in traditional Chinese medicine is better used in chemotherapy, it can guide doctors to use drugs according to the laws of visceral and meridian lesions. "Su Wen Jinkuizhen Statement": "So the back is yang, and the yang in the yang is the heart. The back is yang, and the yin in the yang is the lung. The abdomen is yin, and the yin in the yin is the kidney. Yin, the yang in the yin is also the liver. The abdomen is yin, and the yin in the yin is also the spleen." Paclitaxel is the first-line drug for the treatment of advanced ovarian cancer and is also commonly used for head and neck tumors, bladder tumors, metastatic breast tumors, etc., return to the spleen, liver, and kidney channels.

# 2.4.1 Taxol Returns to the Spleen Meridian

Bone marrow suppression is one of the common adverse reactions of paclitaxel, which generally occurs 8-10 days after administration. Bone marrow suppression belongs to the category of "blood deficiency" and "consumption of labor" in traditional Chinese medicine. Most patients have symptoms such as pale complexion and weakness of limbs. The main pathogenesis of the disease is a deficiency of the spleen and kidney and a lack of qi and blood. During treatment, Chinese medicines such as Diyu Shengbai Tablets and Yiqi Shengbai Decoction can be taken orally to nourish Qi and blood [12]. Chinese medicine believes that the kidney is the foundation of the innate and the spleen is the foundation of the acquired. The spleen and stomach are the sources of qi and blood biochemistry. "Lingnan Secret Canon," says: "The spleen and stomach are the officials of the warehouse, and the five flavors come out." The function of the spleen and stomach is damaged, and the production of gi and blood raw materials is insufficient, which can lead to blood deficiency. In addition, gastrointestinal reactions, such as nausea and vomiting, may occur after paclitaxel chemotherapy. The spleen and stomach are damaged, which affects the abnormal rise and fall of the gi mechanism, the clear yang does not rise, and the biochemical sources of gi and blood are lacking, resulting in dizziness, mental fatigue, and fatigue; According to its bone marrow suppression and digestive tract reaction, it can be attributed to the spleen meridian.

#### 2.4.2 Taxol Returns to the Liver Meridian

The return of paclitaxel to the liver meridian can also be discussed by its adverse reactions. Paclitaxel is mainly metabolized in the liver and enters the intestine with bile, and its neurotoxicity is mainly manifested as numbness and pain in the hands and feet. In "Su Wen Liu Jie Zangxiang Lun", "the liver is the root of the extreme and the dwelling of the soul. Its beauty is in the claws, and its filling is in the tendons." Tremors, numbness of limbs, and even unfavorable flexion and extension. If the liver blood is full, the nails will be firm and thick, and the color will be moist. Optic nerve disorder with flash scotoma as a specific manifestation can also occur after paclitaxel chemotherapy, which is closely related to the "opening of the liver to the eyes". The essence and qi of the five viscera and six fu-organs are transmitted through the blood vessels and directed to the eyes. If the liver blood is insufficient, the eyes will lose nourishment, and there will be eye diseases such as blurred vision. "Lingshu 'Benson," says, "The liver stores blood and the blood gives up the soul." The liver stores blood so that the blood is collected in the meridians, so as not to overflow outside the meridians and cause bleeding. For the treatment of leukopenia after paclitaxel

chemotherapy, the clinical practice of traditional Chinese medicine mostly starts with tonifying qi and nourishing blood and nourishing the liver and kidney [12]. The above can be introduced that paclitaxel returns to the liver meridian.

### 2.4.3 Taxol Returns to the Kidney Meridian

The return of paclitaxel to the kidney meridian is also discussed in terms of efficacy and adverse reactions. "Simple Questions: Ancient Innocent Theory," says: "A woman is seven years old, her kidney qi is prosperous, and her teeth grow longer." This shows that the kidney qi plays an important role in the growth and development of the human body. Chinese medicine believes that the kidney stores essence. One is that the kidneys store the essence of water and grains in the five viscera and six fu-organs to maintain life and promote the growth and development of the body; the other is to store the essence of the kidneys, which is the basic substance for reproduction and reproduction and is related to human reproduction, growth, development, and aging. After paclitaxel chemotherapy, about 87% of patients can experience hair loss, and with the accumulation of chemotherapy drug doses, the whole body hair will also fall off [2]. "Kidneys govern stings, seal the foundation of storage, and are the place of the essence. Its beauty is in the hair, and its main body is in the bones." The dryness of hair is closely related to the sufficiency of kidney essence. Bone pain is also one of the most common adverse reactions after paclitaxel chemotherapy, which also coincides with the Chinese medicine concept of "kidney dominates the bone". Based on the above, it can be inferred that paclitaxel belongs to the kidney meridian.

## 3. Conclusions

To sum up, the four qi of paclitaxel are cold and cool, bitter and salty in taste, subsidence in nature, and return to the spleen, liver, and kidney meridians. Paclitaxel is the first-line drug against ovarian tumors and is also widely used in the treatment of other tumors, but some patients have severe side effects and cannot tolerate related treatments. Some scholars believe that the modern pharmacological results of traditional Chinese medicine can be directly used in Western medicine. For example, salidroside, an extract of Rhodiola Rosea, can induce dendritic cells by regulating the ERK pathway through extracellular signals to play an anti-tumor effect [13-14]. Sophora flavescens extract machine can inhibit the proliferation of tumor cells and induce tumor cell apoptosis [15], both of which can be directly used as tumor drugs for clinical use. Western medicine can also be based on its properties and functions, according to the characteristics of traditional Chinese medicine, such as antibacterial drugs and blindly heat-clearing and detoxifying agents [16]. Based on the theory of yin and yang theory, after clarifying the traditional Chinese medical properties of paclitaxel, the side effects of paclitaxel can be prevented before chemotherapy. For the prevention of myelosuppression after paclitaxel chemotherapy, it can be added in advance to nourish the liver and kidney, and to nourish qi and blood. Paclitaxel is known to be cold, and for the prevention and treatment of neurotoxicity, it can be used to warm the yang and nourish the blood, dispel cold and relieve stagnation. Paclitaxel belongs to the spleen meridian, and can be added to the spleen and stomach products such as Atractylodes and Chinese yam to prevent nausea and vomiting due to damage to the spleen and stomach; for the prevention of hair loss, use Shenqi Pills, herbal selections Psoraleae, Epimedium and other products to nourish the kidney and warm the yang. In addition, clarifying the nature and taste of paclitaxel can also guide the diet of chemotherapy patients. "Su Wen Zang Qi Law Time Theory," says: "Poisons attack evil, five grains are for nourishment, and five fruits are for help... The smell is combined and taken to replenish the essence and replenish the Qi." It shows the importance of diet therapy in the side effects of chemotherapy drugs. . There is also "Su Wen Xuanming Five Qi", see: "The five flavors are forbidden: salty blood, blood disease

does not eat more salty." Therefore, during the chemotherapy of paclitaxel, you can eat less salty food. Furthermore, it can be used to guide the treatment of clinical acupuncture. For patients with neurotoxic manifestations such as numbness of hands and feet, muscle pain, etc., acupuncture on the liver meridian of foot Jueyin and the kidney meridian of foot Shaoyin can be selected. Discussing the traditional Chinese medicine properties of paclitaxel, combined with the characteristics of traditional Chinese medicine, has guiding significance for the advantages of integrated traditional Chinese and Western medicine in the prevention and treatment of tumor diseases, to better guide clinical practice and benefit more tumor patients.

#### References

- [1] Yu Y, Cheng W. X., Diao H.l., Ding N, Chen S.R., Xu L, Shi W, and Li S.Y. (2020)To explore the correlation between autophagy and endometriosis from the theory of yin and yang of traditional Chinese medicine [J]. Zhonghua Journal of Traditional Chinese Medicine, 38(6): 42-45.
- [2] Zhou Jichang. (2016). Practical medical oncology treatment [M]. Beijing: Beijing Science and Technology Press, 70-71.
- [3] Zhao Y. H., Zhao Z. Q., Wu M. H., and XU L.(2018) Professor Zhou Zhongying's view on the integration of traditional Chinese and Western medicine in the differentiation and treatment of malignant tumors [J]. China Journal of Integrated Traditional Chinese and Western Medicine, 38(6): 748-749.
- [4] Liao M.M., Wang Z.Y., Zhang F. X., and Wang N.(2021) Exploring the theory of cancer virus pathogenesis in traditional Chinese medicine based on tumor stem cells [J]. World Traditional Chinese Medicine.16(20):3058-3062.
- [5] Sun T, Zhou L. (2020) Zhou Lan's method of attacking poison and righting for the treatment of malignant tumor [J]. Clinical Journal of Traditional Chinese Medicine, 32(1): 19-24.
- [6] Gao Y, Du L, Xiao C, Yan R, You F. M., and Zhu J.(2021) Discussion on traditional Chinese medicine properties of the chemotherapeutic drug etoposide [J]. Hubei Journal of Traditional Chinese Medicine, 43(4): 50-53.
- [7] Ni K. W., Chen Y. L., Zhou L. S., Gao R.D., and Wang Z.(2020)Research progress on the mechanism of action of paclitaxel-induced peripheral neuropathy and discussion on differentiation and treatment of traditional Chinese medicine [J]. Journal of Zhejiang University of Traditional Chinese Medicine, 44(8): 818-824.
- [8] Yang X.Y. (2013) Research progress of traditional Chinese and Western medicine on chemotherapy-induced peripheral neurotoxicity [D]. Beijing University of Traditional Chinese Medicine.
- [9] Liu Y.X. (2005) Oncology of Integrated Traditional Chinese and Western Medicine [M]. Beijing: China Traditional Chinese Medicine Press, 4-5.
- [10] Chen W.W. (2008) Chinese Pharmacy [M]. Beijing: China Traditional Chinese Medicine Press, 28.
- [11] Li N, Wang Y.Y., and Zhang Q.(2015)A preliminary study on the clinical performance of cisplatin-based on the theory of "nature and flavor returning to the meridian" [J]. Journal of Traditional Chinese Medicine, 56(21): 1822-1825
- [12] Qi X.T., Zhang J.X., Zhang X.L., Huang N.N., Li X.Y., and Sun R. (2019) Research progress of traditional Chinese medicine in the treatment of chemotherapy-induced leukopenia [J]. Chinese Herbal Medicine, 50(20): 5088-5095.
- [13] Pan Z.L. (2018) Effects of Danggui Buxue Decoction combined with western medicine on cellular immune function and quality of life after colorectal cancer surgery [J]. Inner Mongolia Traditional Chinese Medicine, 37(9):60-61.
- [14] Pu W.L., Li W.H., Bai R.Y., Gao X.M., and Sun L.K. (2017)Research progress on the pharmacological effects of Rhodiola Rosea and its anti-inflammatory and anti-tumor active components [J]. Tianjin Traditional Chinese Medicine, 34(12): 856-859.
- [15] Zhang Y.L., Yue Q.j., Wen Z.X., Zhang X.W., Li P.F., Cui L, and Zhang M.(2019) Salidroside induces the antitumor effect of dendritic cells through extracellular signal-regulated protein kinase (ERK) pathway [J]. Journal of Cell and Molecular Immunology, 35 (11): 979-985.
- [16] Kong S.H., Zhang S.j., and Cheng B.l. (2016). "Overview of research on the anti-tumor mechanism of matrine." Journal of Shandong University of Traditional Chinese Medicine, 40.04: 377-379