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Application of Chinese Medicine Poria cocos in Anti-tumor

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Abstract:

Poria cocos is a type of traditional Chinese medicine which has rich pharmacological effects, including anti-tumor, liver protection, diuretic, anti-aging, anti-inflammatory, lowering blood lipids, and enhancing immunity. The chemical components of Poria Cocos mainly include polysaccharides, triterpenes, fatty acids, sterols and enzymes, among which Poria Cocos and triterpenes play an important role in antitumor, liver protection and antiaging. Modern research shows that poria can improve the therapeutic effect of chemotherapy drugs in cancer, reduce the negative effects of chemoradiotherapy and prevent the proliferation of cancer cells. Triterpenoid components, such as caroicimaric acid, can inhibit tumor cell proliferation by regulating the cycle and promoting tumor cell apoptosis. As a traditional Chinese medicine, poria has great potential in antitumor applications.

Keywords: Chinse traditional medicine; Poria cocos; Anti-tumor;

1. Introduction

Poria cocos (Schw.) Wolf, the scientific name of Poria cocos (SCHW.) Wolf, is a dried sclerotia of a fungus of the Poraceae family, which has a long medicinal history and rich pharmacological effects. Poria cocos contains a variety of chemical components, including polysaccharides, triterpenes, fatty acids, sterols, enzymes, etc. These components give poria a variety of pharmacological effects, such as anti-tumor, liver protection, diuretic, anti-aging, anti-inflammatory, lowering blood lipids, enhancing immunity, hypnosis, and so on [1]. Pachymaria polysaccharides and pachymaria triterpenoids play a major role in anti-tumor, liver protection, and anti-aging. Poria has been widely used in traditional Chinese medicine to treat various diseases. Its traditional uses mainly include rehydrating dampness, strengthening the spleen and stomach, calming the heart and calming nerves [2]

In recent years, Poria has shown a new role in the anti-tumor field. The significance of Poria cocos in modern anti-tumor research is mainly reflected in the anti-tumor activity of its polysaccharide and triterpenoid components and the regulatory effect on the immune system. Pachymaria polysaccharide and triterpenoid components have been confirmed to have extensive pharmacological effects, such as inhibiting the proliferation and inducing apoptosis of malignant tumors, inhibiting invasion and metastasis, regulating the immune function of patients and improving the quality of life of patients [3].

Pachymaran, as one of the main active ingredients in pachymaria, has been extensively studied and has

shown significant anti-tumor effects. Studies have shown that Pachymaran can help enhance the therapeutic effect of chemotherapy drugs on lung cancer and reduce the adverse reactions caused by radiotherapy and chemotherapy [4] In addition, pachymaran can significantly inhibit the proliferation of breast cancer cells and gastric cancer cells, and exert its anticancer mechanism by changing the biochemical characteristics of cell membranes [5]. The study of the compound Pachymaran oral liquid also showed that the drug could significantly inhibit the growth of solid tumors in mice, enhance the phagocytosis function of macrophages, promote the proliferation of lymphocytes and the activity of NK cells, and thus regulate the immune function of tumor-bearing mice [6].

In addition to polysaccharides, triterpenoids in Pachymaria also showed anti-tumor potential. For example, poria acid has been found to alter the cycle of breast cancer cells by down-regulating the cyclins Cycline D1, Cycline E, CDK2, and CDK4 and up-regulating the expression of p53 and p21 proteins, thereby inhibiting the proliferation of breast cancer cells. In addition, the effective part of pachygyria has different degrees of tumor inhibition on H22 ascites tumor mice and such tumor inhibition may be realized by regulating the immune function of the body and regulating Caspase-3 and Bcl-2 proteins to promote the apoptosis of tumor cells [7].

The significance of Poria Cocos in modern anti-tumor research lies in the anti-tumor activity of its various active components (especially the polysaccharide and triterpenoid components of Poria Cocos) and its positive regulatory effect on the immune system (Figure 1). These research results provided a scientific basis for the clinical application of poria cocos and laid a foundation for its further development and application in the field of tumor therapy.

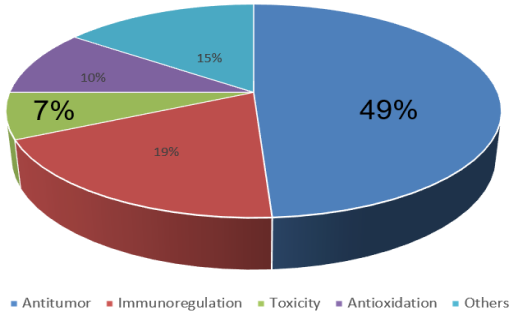

Figure 1. Pharmacological activities of Poria Cocos

2. Effective Chemical Composition of Poria Cocos

Poria cocos contain two main chemical components, namely triterpenoids and polysaccharides, as well as some other small molecular compounds, including steroids, amino acids, histidine etc [8].

Several triterpenoids have been isolated from Poria cocos (Figure 2), almost all of which are derived from the spines of Lanostans or Seco Lanostans. In the past decades, Tai et al and other Chinese and Japanese research groups have isolated important known compounds, including various triterpenes, from Poria cocos (Table 1). In 2007, Akihisa et al. [9, 10] 35 compounds, 20 known structures, and 15 new structures from this species; Zheng and Yang [11, 12] isolated 10 triterpenoids, including Pacharyone A and Pacharyone B-2 new compounds. The triterpenoids isolated from Pachymaria can be considered as the precursors of lanostane. However, some differences were observed. For example, many compounds with different structures are derived from aconite shells (lanostan C21).

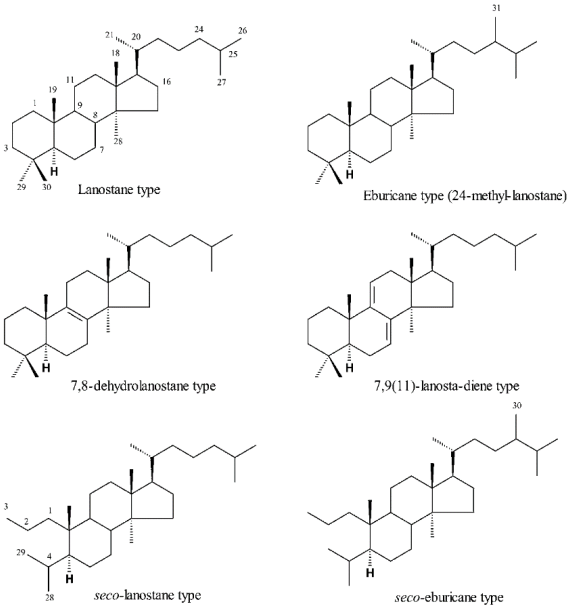

Figure 2 General structures of triterpenoids from Poria cocos [8]

Various polysaccharides have been isolated from Poria cocos. However, due to a lack of clear naming, these compounds have many different names. Before 1980, some authors isolated a compound called β-pure polysaccharide and identified it as a (1→3)-(1→6)-β-D-glucan. Later, other authors obtained information that later became known as pachymaran, carboxymethyl pachymaran, U-pachymaran f, and polysaccharide H11, which exhibit different characteristics and have been tested [13]. In recent years, other authors have isolated different polysaccharides from

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Pachymaria. As the definition of these polysaccharides becomes clearer, their chemical composition can be determined.

Scholar Wang and her colleagues extracted six types of polysaccharides from Poria cocos, including heteropolysaccharides containing D-glucose, D-mannose, D-fucose, and trace amounts of D-xylose [14]. However, these anhydrous configurations were isolated from the mycelium of Poria cocos and obtained through fermentation in a pilot plant.

3. Anti-tumor Mechanism of Poria

3.1 Effect of Poria cocos on tumor cell cycle

The cell cycle is generally divided into 4 phases. Current research results indicate that cyclic-dependent kinase inhibitors (Ck i), Cdk, and cyclin are three types of key cell cycle regulatory factors. Interact with others, and there are three types of key regulatory factors in the cell cycle. They interact with each other and are closely related to the pathways of cell proliferation, apoptosis and differentiation, forming a complex regulatory network. Cdk, a cyclin-dependent protein kinase, plays a central role in the cell cycle regulation network. The expression of Cyclins is time-specific and typically cyclic [15]. Through the activation of transcription factors and other factors, various signal transduction pathways inside and outside the cell can affect the action level of Cyclins and, thus, further affect the corresponding Cdk so as to regulate the cell cycle. Studies have confirmed that the contents of various cyclins change periodically in the cell cycle, but the expression of Cdk is relatively constant throughout the cell cycle. After the corresponding Cdk and Cyclin combine to form a complex and be activated, the specific substrate in the cell is phosphorylated and plays a corresponding role [16]. Cyclin A, which belongs to S phase and M phase, is the earliest cyclin found. In the S phase, Cyclin A binds to Cdk2, phosphorylates the substrate, and pushes the cell cycle into the G2 phase. Its high expression is closely associated with uncontrolled cell proliferation and tumorigenesis [17]. Jiang et al. found that poria can effectively reduce the expression of Cyclin A and affect the cell cycle [18].

The transition of cells from the G1 phase to the S phase requires the participation of cyclin E and Cdk2. When cells enter the S phase, cyclin E is degraded, and Cdk2, in turn, binds to cyclin A, causing cells to cross the restriction point from the S phase to the G2 phase. Studies have shown that poria can reduce the expression of Cdk2 protein in MCF-7 cells and block breast cancer cells in the S phase [18].

3.2 Effect of Poria Poria on apoptosis of tumor cells

The effect of Poria cocos and its different components on the apoptosis of tumor cells has been confirmed by many studies. These studies have shown that the active components of Poria cocos, including Poria acid and Poria polysaccharide, can induce apoptosis of tumor cells through different mechanisms. In tongue squamous cell carcinoma cell CAL-27, pachymaric acid can decrease cell survival rate and expression of CyclinD1 and CDK2, increase cell number in the G0-G1 phase, and decrease cell number in the S phase and G2-M phase. Increased the apoptosis rate of CAL-27 cells, Cleaved PARP and Cleaved caspase-3 protein expression, and decreased CXCR4 protein expression [19]. In addition, pachymaric acid can also induce apoptosis of human breast cancer MDA-MB-231 cells by activating polyadenosine diphosphoribose polymerase (PARP). For human cervical cancer HeLa cells, Pachymaria polysaccharide could significantly inhibit the proliferation and induce the apoptosis of HeLa cells. The mechanism of apoptosis may be related to the down-regulation of p-ERK1/2 expression and inhibition of phosphorylation of the ERK signaling pathway. Studies on human gastric cancer transplanted in nude mice also showed that Pachymaran could inhibit tumor growth, and the mechanism might be to promote tumor cell apoptosis by improving immunity and regulating Bcl-2/Bax protein[20].

3.3 Effect of Poria Cocos on immune function

English tumor has several triggering factors, among which the main factor is that tumor precursor cells escape immune surveillance due to a decrease in immune function. In recent years, a large number of studies have shown that TCM polysaccharides can enhance the body's immunity and also improve the sensitivity of tumors to radiotherapy and chemotherapy [21]. Often used in combination with radiation therapy and chemotherapy, they can improve the toxic effects of tumor chemotherapy. Synergistically increase the healing effect [22-26]. Pachymaran, the active extract of pachymaria, one of the "four kings and eight treasures" of Chinese medicine, has noninflammatory and anti-tumor effects, the mechanism of which may be related to the activation of macrophages and T cells to promote the production of TNF- α and IL -2, regulate the body's immunity and increase the anti-tumor capacity [27-29]. Studies have shown that Pachymaran has a strong regulatory effect on immune factors IL-2 and TNF-α. IL-2 and TNF-alpha are potent immune activators. Upregulation of IL-2 and TNF-alpha can directly induce tumor cell apoptosis and inhibit tumor growth. In addition, Pachymaran can also increase the spleen index and the thymus index,

which indicates that it has a positive effect on the immune organs [30].

4. Challenges of Poria in Anti-tumor Therapy

Although studies have shown that Poria Cocos and its polysaccharides and triterpenoids have certain anti-tumor activities, the specific components are the main anti-tumor active substances, and the specific mechanism of action of these components is still not very clear. For example, pachymaric acid is considered to be one of the main active substances against breast cancer, but the mechanism and importance of other components need to be further studied.

Quality control and standardization of Chinese medicinal materials are key factors affecting their clinical efficacy. The cultivation method, drug site, growing environment, harvesting cycle, drug dosage form and processing method of Poria Cocos can all affect the content of different effective components of Poria cocos [31]. The lack of personalized and standardized quality control standards may affect the anti-tumor effect of Tucker to the greatest extent.

Poria exerts anti-tumor effects through "multi-component - multi-target - multi-pathway", and this complexity is both its potential advantage and challenge. How to accurately understand and utilize this complexity, and how to translate this complexity into specific therapeutic strategies, is a problem that needs to be solved [31]

5. Conclusion

The application of Poria Cocos in anti-tumor therapy shows great potential; its polysaccharide and triterpenoid components have remarkable anti-tumor effects and enhance anti-tumor ability by regulating the immune system. However, the anti-tumor active components and specific mechanism of action of Poria Cocos still need to be further studied. Quality control and standardization of Chinese medicinal materials are crucial to ensure clinical efficacy, and the "multi-component - multi-target - multi-pathway" mechanism of Poria Cocos is both an advantage and a challenge. Future studies need to address how to accurately understand and utilize this complexity and translate it into specific therapeutic strategies to promote further development and application of Poria in the field of tumor therapy.

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