

Research Progress in the Treatment of Prostate Cancer with Single Drug Extracts: A Meta-analysis

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Abstract: Prostate cancer one of the most common malignant tumors in elderly men, has occupied a major position in the diseases that threaten the health of middle-aged and elderly men, and its mortality rate ranks second among male tumors. It is found that traditional Chinese medicine plays an important role in the treatment of prostate cancer. This article reviews the research progress of traditional Chinese medicine extracts in the treatment of prostate cancer in recent years. Through the analysis of the etiology and pathogenesis of prostate cancer in Chinese medicine, the extracts of Chinese medicine (Polyphyllin I, PolyphyllinVII, PP7), glycyrrhizin, glycyrrhizin, licorice extract (glycyrrhetic acid, glycyrrhizin, glycyrrhizin, etc.), baicalin extract (baicalin, baicalin, etc.), triptolide extract (triptolide, triptolide, etc.) and cantharidin extract (norcantharidin, etc.) in the treatment of prostate cancer are summarized and summarized, which reflects the advantages of traditional Chinese medicine in the treatment of prostate cancer. It is expected to provide a certain basis for the experimental research and clinical practice of traditional Chinese medicine in the treatment of prostate cancer, and lay a solid foundation for further exploration.

1. Introduction

As one of the common cancers that threaten to men's health, the incidence of prostate cancer has increased significantly year by year with the change of population age structure, bad living habits, genetic inheritance and the rise of hormone level^[1]. With the increasing number of patients and the limited screening degree of Pca, especially the poor understanding of Pca in rural patients, leading to the obvious increasing mortality rate of crude prostate cancer with age and the mortality rate of urban prostate cancer is higher than that in rural^[2]. Androgen deprivation therapy as the premier therapy for advanced prostate cancer is the current consensus of the international oncology community. However, due to the change of hormone levels in the body during treatment, endocrine therapy has a certain impact on lipid metabolism, insulin resistance, and even some neurological and mental aspects. ADT extends survival while gradually transforming into castration-resistant prostate cancer^[4]. In addition, surgery, chemistry and radiotherapy are also the main means of treatment, but some patients are difficult to accept surgical treatment, and the side effects caused by

conventional chemotherapy drugs and radiotherapy will also affect the quality of life of patients. Compared with the disadvantage of modern medicine in the treatment of prostate cancer, finding feasible treatment means is the primary task of the current medical community. In the treatment of PCA, traditional Chinese medicine contains a variety of active ingredients, which can achieve its effect on multiple channels and targets through a single drug. In the treatment, it has many advantages, such as improving urinary incontinence, reducing the toxic side effects of radiotherapy and chemotherapy, preventing tumor recurrence and metastasis, and improving the symptoms of tumor-related complications^[5]. With the continuous exploration of Chinese medicine, a certain extract of a single TCM can be used in the treatment of Pca. In this paper, the research progress of prostate cancer has been reviewed in recent years, hoping to help TCM in basic research and clinical practice.

2. The cause of the disease

Prostate cancer belongs to the categories of "accumulation", "lymphatic syndrome", "lung closure", "urine blood", "low back pain" and so on. Professor Jia Yingjie believes that the basic pathogenesis of prostate cancer is the coexistence of vital qi deficiency, bladder dampness and heat, poison and blood stasis. Among them, deficiency, poison, blood stasis and dampness are the pathogenic elements of prostate cancer, "poison" is the inducement, "deficiency" is the internal cause, "blood stasis" and "dampness" are not only the pathological products but also the pathogenic factors^[6]. Professor Wang Xixing^[7] believes that prostate cancer is based on kidney Yin deficiency, dampness and heat and toxic stasis. Kidney deficiency is the right to bladder gasification, phlegm, dampness, heat evil, stasis and poison, the accumulation of sepsis, hindering the operation of three coke liquid, blood stasis and heat knot, dampness and disease is the direct cause, but its root lies in kidney Yin deficiency. Professor Zhang Yaqiang believes that the total pathogenesis of prostate cancer is positive and evil^[8]. Lack of positive Qi, the body's viscera function disorders, Qi blood semen operation is not smooth easy to cause evil endogenous, while the positive qi deficiency resistance to external evil ability is insufficient, foreign evil easy to take advantage of the opportunity to enter, evil gas invasion, condensation in the essence chamber, it is easy to produce cancer; The evil spirits such as dampness, phlegm, stasis, heat and poison remain in the body for a long time, depleting qi, blood and semen, and further leading to the deficiency of healthy qi. Professor Jia Liquan^[9] believes that prostate cancer is a false mark. The body is senescent, the kidney qi is insufficient, the disease pathogen is easy to invade the body is the basic deficiency; The five tastes of overeating hurt the spleen and stomach, the phlegm and dampness, and the accumulation of the two are entangled with each other, affecting the course of the disease. To sum up, the internal cause of the disease is the lack of healthy qi, especially diet injury and spleen and stomach, old kidney qi deficiency caused by deficiency is the key, the external cause is mainly from the feeling of six evil qi, distemper poison, accumulation of phlegm dampness, damp-heat, blood stasis and so on stop in the essence chamber, resulting in prostate cancer disease, evil Qi long lived in the body, continue to consume the injury of healthy Qi, thus affecting the further development of the disease course.

3. Chinese herbal extract for prostate cancer

3.1 Heavy building extract

According to the contents recorded in the Pharmacopoeia of the People's Republic of China, it can be divided into Yunnan Heavy Building, also known as Yunnan Heavy Building, and a flower, also known as Huazhong Building, which has swelling, pain relief, anti-tumor and other functions

[10]. The active components of Chonglou are becoming more and more popular in the study of anti-tumor. Their main components play an important role in inducing tumor cell apoptosis, regulating the expression of pro-oncogenes and tumor suppressor genes, inhibiting tumor cell metastasis and inhibiting tumor cell proliferation [11]. Liu Shuai^[12] found that collifloor saponin VII could upregulate p21 protein expression in PC3 cells and inhibit the expression of cyclin D1 cycle regulatory protein, thus blocking the cycle of prostate cancer cells in the G1 phase and hindering their proliferation. Shen Zhengchao and ^[13] confirmed that dionfloor saponin could regulate P21 / CDK2 / RB signaling pathway and activate apoptosis proteins, thus inhibiting the proliferation and growth and inducing apoptosis of prostate cancer cell lines. Xia Chengxing^[14] experiment proved that the long column total saponin inhibited the proliferation, invasion and metastasis of prostate cancer cells by downregulating the expression of IQGAP3. Liu^[15] experiment found that the active monomer PP-26 could significantly inhibit the proliferation of prostate cancer human prostate cancer cells in vitro. Zou Peiliang et al. ^[16] found that chongfloor saponin I could inhibit the expression of specific protein 1 and Zese gene enhancer homolog 2 by mediating and extracellular regulatory protein kinase 1 / 2 pathway, thus inducing early apoptosis of castration-resistant prostate cancer cell line DU145 cells, and then inhibiting cell growth. Xiang Yuchen and other ^[17] experiments found that PPI might inhibit the growth, metastasis and reversal of epithelial-stromal cell transformation through the downregulation of CIP2A / PP2A / ERK signaling pathway. The ^[18] experiment of Zou et al found that PPI may inhibit the protein expression of nuclear transcription factor kappa B / p65 and DNA methyltransferase 1 by mediating the ERK 1 / 2 pathway, induce early apoptosis in castration-resistant human prostate cancer PC3 cells, and then inhibit cell proliferation. Liu^[19] experiments demonstrated that PPI might inhibit the growth, invasion and EMT of PC cells by inhibiting the CIP2A / PP2A / ERK signaling axis. Zhang^[20] showed that the heavy ethanol extract exerts its effect against prostate cancer by inducing apoptosis and cell cycle arrest.

3.2 Licorice extract

Licorice is also called "medicine" in Chinese herbal medicine, which has the effect of tonifying spleen and qi, clearing heat and detoxification, removing phlegm and relieving cough, relieving pain, and blending various medicines^[21]. Its chemical components mainly include triterpenoid saponins, flavonoids and polysaccharides, and its main pharmacological effects are anti-inflammatory, anti-tumor, antibacterial, antiviral, antioxidant and immunomodulatory effects^[22]. Its anti-cancer pharmacology in prostate cancer research and treatment plays an important role, Lu Ting ^[23] experiment found that 18 β -glycyrrhizin hypoic acid inhibit adrenal androgen-sulfate deHEA through the organic anion transport peptide 2B1 transport, and reduce the generation of androgen, and with androgen receptor antagonist amine to reduce the generation of ligand and inhibit the purpose of androgen receptor, common resistance castration against prostate cancer progression. Yang Boya^[24] confirmed that the apoptosis of C4-2B cells by inhibiting the PI3K / AKT / AR pathway. Wang Xuefeng ^[25] experiment found that licorice hormone could inhibit the PI3K / AKT pathway, thus reducing cyclin D1 expression, promoting the expression of the cycle negative regulator protein P21, blocking the cell cycle G1 / S conversion, and finally inhibiting the growth of prostate cancer cell line PC3. Chen Fu ^[26] experiment observed the proliferation, apoptosis of PC3 cells and the expression of BLM helicase in prostate cancer, found that the concentration of 0.15 mol/L, can downregulate the transcription of BLM gene in the 0.12mol/L~0.36mol/L, the proliferation, invasion and migration, and promote the apoptosis of PC3 cells. Zhang^[27] experiments confirmed that the antitumor effect of liquine in prostate cancer is attributed to reactive oxygen species-mediated inactivation of Akt, thereby inhibiting the PI3K / Akt

signaling pathway. Katerina et al^[28] experiments confirmed that licorice fortified extract can interfere with the autophagy and apoptosis mechanism of prostate cancer PC-3 cells, affect their proliferation, and combine with doxorubicin to reduce the toxic side effects of licorice extract. Sun^[29] found that 18 β -GA could induce tumor suppressor miR-488 and transcriptionally downregulate AR by controlling E2F3 α and SRF function on the androgen receptor (androgen receptor AR) promoter, thus inhibiting androgen and survival response in prostate cancer cells and achieving anti-tumor effects. Chen^[30] experiments confirmed that neoglyridin inhibited the proliferation of AR-dependent prostate cancer cells in vitro and in vivo through negative regulation of AR expression and activity, thus supporting the tumor suppressive role of neoglyridin in AR-dependent prostate cancer.

3.3 Baicalein extract

Scutellaria baicalensis is divided into withered baicalensis and edible baicalensis, and has the effect of clearing heat and dampness, reducing fire, detoxification, hemostasis and relieving fetus^[31]. According to study^[32], there are many effective components in the chemical components of Scutellaria baicalensis, including baicalein, berberine, hyphanin A and baicalein. Tang Zhao et al^[33] found that baicalin could upregulate the expression of the pro-apoptotic genes bax and caspase-3 in PC cells, and inhibit the expression of the anti-apoptotic gene bcl-xl; and promoted the expression of autophagy-related genes beclin-1 and LC3B-in PC3 cells, thus promoting apoptosis and autophagy, increase the expression of E-cadherin, and inhibit the proliferation and invasion ability of PC3 cells. Liang Kun^[34] confirmed that baicalin could promote the expression of the tumor suppressor miR-485-5p in cells, thus reducing the expression of the target gene JAK 3 and affecting the proliferation of prostate cancer cells. Yangning^[35] found that baicalein reduced Ezrin protein expression and stimulated tumor cell apoptosis by reducing the Bcl-2 / Bax ratio, thus inhibiting the proliferation and invasion of human prostate cancer PC-3 cells. After animal experiments, Wu^[36] confirmed that baicalin could antagonize prostate cancer stem cells by inhibiting the Notch1 / NF- κ B signaling pathway. Sun^[37] experiment found that there are two reasons for baicalein against prostate tumors, one is that it can regulate AKT-SREBP1-FASN signaling network to induce apoptosis in human prostate cancer cells; the other is that it can destroy fatty acid metabolism, thus playing a role of anti-tumor. Yu^[38] experiments confirmed that prostate cancer cell growth was inhibited by baicalin-mediated regulation of cyclin expression, which was mainly affected by the CDK 6 / FOXM 1 axis, promoting the synthesis of DNA in S phase, and affecting cell apoptosis. Ma^[39] measured the relative level of Ezrin by inducing PC3 cells in vitro and in nude mice with prostate cancer, and found that the proliferation of prostate cancer cells, inhibit cell cycle and stimulate cell apoptosis. Wei^[40] experiments confirmed that baicalin inhibits prostate cancer cell growth and metastasis by regulating Wnt / β -Catenin pathway and epithelial-stromal transformation.

3.4 Lei Gong rattan extract

Tripteryfordii has the effect of dispelling wind dampness, promoting blood circulation and dredging collaterals, reducing swelling and relieving pain, killing insects and detoxifying. The study found that tripterygiide and^[41-42] in the extract of Tripterygifordii can inhibit a variety of malignant tumors^[41-42]. The recent studies of triptolide extract in prostate cancer are summarized as follows: Zhang Junqiang et al.^[43] found that triptolide upregulated the expression level of PC-3 miR-320b in prostate cancer cells and downregulated the expression level of AR, so as to inhibit the malignant biological behaviors such as cell proliferation, invasion and EMT transformation. Sun Qiang^[44] confirmed that triptolide could downregulate the expression levels of cyclin D1, VE GF and

MMP-9 in human prostate cancer DU-145 cells, and then inhibit the proliferation, invasion and migration of human prostate cancer DU-145 cells, and promote apoptosis. Mengyuan^[45] study confirmed that it inhibited the proliferation of T24 cells and 5637 cells by simultaneously inhibiting cell proliferation and regulating cell membrane ion transport channels. Zeng Can et al.^[46] found that triptolide could inhibit tumors by regulating the expression level of the tumor suppression gene p53, and triptolide-loaded exosomes could enhance the effects. Song Zhenguo^[47] experiment proved that the effect of lipool on PC3 cells could downregulate the content of vascular endothelial growth factor in tumor cells and inhibit the new growth of tumor blood vessels, thus inducing cell apoptosis and inhibiting cell growth and proliferation. Wang^[48] confirmed that triptonide could inhibit the differentiation function of Th 17 cells to block the Th 17-IL-17 pathway, thus achieving anti-prostate cancer effects. Arisan^[49] placed prostate cancer cells in triptolide dishes at different concentrations and observed that they could affect LAMP-1 and liin-1 in PC3 cells and affect the PI3K / AKT / mTOR signaling axis to trigger apoptosis and autophagic response in prostate cancer cells. Dong^[50] injected triptolide alcohol in nude mice and in different concentrations, found to inhibit the phosphorylation of mTOR and its downstream protein p70s6k and related downstream signaling pathway, make prostate cancer cells in vitro and in vivo to inhibit cell growth, promote apoptosis and maintain cell cycle arrest in the G2 / M phase.

3.5 Extracts of the presence of maculae

Spot has the effect of breaking blood and removing blood stasis, reducing swelling and relieving pain, and attacking poison and erosion sores. It is closely related to cancer / tumor, inflammation and infection, nervous system and pain, metabolism and immunity and other diseases^[51]. Yohko and^[52] screened the fermentation broth of 50,000 microorganisms, and found that deoxydemycin can inhibit androgen receptor-dependent transcriptional activity and AR nuclear translocation, thus inhibiting AR function leads to the inhibition of the activity of androgen-dependent cells, thus reducing the incidence of prostate cancer. Luo Xiangning observed the effect of norcantharidin on the growth inhibition rate of PC-3 cells through cell experiments, and found that norcantharidin affected the proliferation and apoptosis of prostate cancer PC-3 cells by inhibiting the proliferation of tumor cells, promoting apoptosis of tumor cells, inhibiting DNA replication of tumor cells, interfering with cell cycle of tumor cells, and inhibiting the invasion and metastasis of tumor cells^[53]; Further experiments on the changes in the expression of MMP-9 protein and the number of pseudopods on the surface of PC-3 cells at different concentrations confirmed that norcantharidin can down-regulate the MMP-9 mrna content and protein expression of PC-3 cells, reduce the pseudopods on the surface of PC-3 cells, and thus reduce the peripheral migration and invasion of PC-3 cells^[54]; After a deeper study, the results of controlled experiments confirmed that norcantharidin can also down-regulate the content and protein expression of cortical actin binding protein and MMP-9m RNA in PC-3 cells, inhibit the formation of pseudopods on the surface of PC-3 cells, and reduce the peripheral migration and invasion of PC-3 cells^[55]. Lou Tiantian^[56] found that porein had an inhibitory effect on PC-3 cell proliferation, and within a certain range, the greater the concentration, the stronger the inhibitory effect. The^[57] experiments confirmed that it can inhibit the assembly of the prereplication complex in the G1 phase of the cell cycle before DNA replication, leading to the synthesis of DNA in DU145 cells. At the same time, it can induce mitotic catastrophe in DU145 cells, thus inhibiting the growth and apoptosis of hormone 145 DU145 cells. Nazim^[58] experiments confirmed that porkinin downregulates c FLIP and upregulates DR 5, enabling TRAIL-mediated apoptosis of prostate cancer cells through the autophagy pathway. Mo^[59] demonstrated in vitro studies that it inhibits Akt activation and activates FOXO 1 transcription, thus producing pro-apoptotic effects on prostate cancer cells; in vivo studies showed that vaccine

treatment combined with NCTD can reduce the number of tumor-infiltrating Tregs and increase the number of CD4 + and CD8 + T cells to enhance the effect of vaccine inhibiting tumor growth.

4. Conclusion

In recent years, the incidence of Pca in China has increased significantly with various factors, so enough attention should be paid to the prevention of Pca, including refining the basic screening and treatment. For the current clinical surgical surgery, chemotherapy, radiotherapy, endocrine therapy and other treatment means can play a certain role in anti-tumor and prolonged survival for Pca, but it will lead to the disease development to castration resistance, and there are serious adverse reactions. Therefore, the research on new means of Pca is highly anticipated. Chinese medicine not only has the characteristics of small use and easy to accept, but also can extract a variety of active ingredients from its single drug, and can act on different targets and signaling pathways respectively. Through the collection of Pca treatment of single Chinese medicine extracts in recent years, it is found that many active substances in Chinese medicine extracts have certain effects on cancer cells, which mainly change: 1. induce apoptosis of cancer cells; 2. interfere with cell growth cycle; 3. Inhibit self-replication of stem cells to prevent rapid proliferation of cells. It can be predicted that the monomer extract of traditional Chinese medicine will have great potential in the field of treating PC. In addition, this paper also summarizes the mechanism of action of anti-PCa related TCM monomer extract, in order to provide a theoretical basis for its application to PCa therapy, and provide a new idea for the development of PCa therapy drugs.

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