

Advances in the Pharmacological Mechanism of Polyporus Umbellatus in the Treatment of Chronic Glomerulonephritis

Sitong Liu^{1, a}, Junjian Xu^{2, *}

¹ Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712000, China

² Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi 712000, China

^a1658457451@qq.com, ^{*}1292069952@qq.com

Abstract

Chronic glomerulonephritis is a common glomerular disease in China, which will eventually develop into renal failure, seriously threatening human health and life, and the combination of Chinese and Western medicine has achieved certain curative effects. Modern pharmacological studies have also shown that Polyporus Umbellatus has diuretic, anti-tumour, hepatoprotective, renal protective, immune regulating, anti-infective, anti-mutagenic and anti-fibrotic effects, which have been widely used in clinical practice. However, the application of Polyporus Umbellatus in the treatment of chronic glomerulonephritis has not been systematically elaborated. Through reviewing relevant pharmacological research progress and animal experiments, this study elaborates the pharmacological mechanism of Polyporus Umbellatus in the treatment of chronic glomerulonephritis, showing that Polyporus Umbellatus plays a role in diuresis, renal protection, anti-fibrosis, immunomodulation, anti-mutagenesis and anti-inflammation, aiming to provide a basis for the clinical application of Polyporus Umbellatus in the treatment of chronic glomerulonephritis. The aim is to provide a basis for the clinical application of Polyporus Umbellatus in the treatment of chronic glomerulonephritis.

Keywords

Chronic Glomerulonephritis; Polyporus Umbellatus; Pharmacological Mechanism.

1. Introduction

Chronic glomerulonephritis (CGN) is a disease characterised by haematuria, proteinuria, oedema, hypertension and slowly progressive renal failure. It is a common glomerular disease in China. It is usually seen in young and middle-aged men and its clinical manifestations can be varied depending on the mode of origin, type and course of the disease. It is a progressive disease that eventually progresses to chronic renal failure [1]. Although glucocorticoids are commonly used in clinical practice, their immunosuppressive effects are not specific, and single-application glucocorticoid therapy does not provide the best clinical outcome, requiring higher doses and a longer treatment course. Some patients with glomerulonephritis are not very sensitive to hormone therapy, and long-term hormone therapy can lead to a series of adverse effects, such as femoral necrosis and interstitial lung fibrosis [2]. Therefore, reducing the toxic side effects of the drugs and enhancing the therapeutic effect are what we need to further study in our clinic. Zhang Shanshan et al[3] conducted a meta-analysis of 942 randomized cases of pigling soup combined with western conventional therapy in the treatment of chronic glomerulonephritis and concluded that pigling soup plus or minus combined with western conventional therapy in the treatment of CGN has certain advantages in improving clinical efficacy and reducing 24h urine protein. Li Siming et al[4] also demonstrated the good

pharmacological effects and clinical efficacy of pigling and pigling soup in the treatment of chronic glomerulonephritis. Therefore, this study provides an overview on the study of the pharmacological mechanism of Polyporus Umbellatus for the treatment of chronic glomerulonephritis.

2. Overview of Research on Polyporus Umbellatus

Polyporus umbellatus (Pers.) Fries is a dried mycorrhizal nucleus of the fungus Polyporus umbellatus (Pers.) Fries, family Polyporaceae. Its clinical applications are widespread and are well documented in ancient texts, such as the "Shen Nong Ben Cao Jing", where it is said: "Pigling, an ape, tastes sweet and flat and is born in the valley. It is used for treating malaria, detoxifying poison, and for treating inauspicious compulsions. It is light and resistant to old age when taken for a long time." [5] The "Materia Medica Jing Shu - Wooden Department in the Middle" considers it to be classified as a meridian: "Enters the foot sun and foot shao yin meridians." [6] "The Materia Medica - Volume II (Wooden Division)" states that it "rises and can descend, opens the coup and generates sweat, facilitates the flow of water, and treats typhoid fever and epidemic fever, anxiety and thirst, swelling and drenching, diarrhea and dysentery, and malaria." [7] "The New Compilation of Materia Medica - Volume 4 (Zhiji)" states that it is: "Bitter, sweet and light in taste, with a flat temperament. It is also descending and yang. Where water-dampness is in the intestines, stomach, bladder, limbs and skin, it is necessary for pig-ling to benefit them." [8] Professor Lu Renhe, a master of Chinese medicine, believes that kidney disease is mainly a deficiency of the kidney element as the basic pathogenesis, and therefore pays great attention to the cultivation of the body's vital energy and is good at treating chronic kidney disease from the point of view of "deficiency", while Professor Lu also attaches importance to modern pharmacology for use in Chinese medicine, so for patients with obvious weakness and poor mental health, pig ling is often used to To improve immunity and nourish the vital energy[9].

Modern pharmacological studies have found that the main chemical components of the medicinal parts of Polyporus umbellatus are mainly polysaccharides, ergosterol, ergosta-7,22-diene-3 β ,5 α ,6 β -triol and ergosta-4,6,8(14),22-tetraen-3-one (ergosterone), and other steroidal compounds, α -hydroxytetracosanoic acid, p-hydroxy-benzaldehyde, physcion, and other non-steroidal compounds, amino acids, vitamins and trace elements. [10, 11]. Its pharmacological effects mainly include diuretic, antitumour, hepatoprotective, renal protective, immunomodulatory, anti-infective, anti-mutagenic and anti-fibrotic effects [10, 11, 12]. However, the pharmacological studies on Polyporus umbellatus in chronic glomerulonephritis have not been systematically described. In this study, the pathogenesis of chronic glomerulonephritis and the pharmacological effects of Polyporus umbellatus were analyzed and studied in order to investigate the pharmacological mechanism of Polyporus umbellatus in the treatment of chronic glomerulonephritis.

3. The Pharmacological Mechanism of Polyporus Umbellatus in Chronic Glomerulonephritis

3.1 Diuretic Effect

Polyporus Umbellatus can reduce the levels of angiotensin II, aldosterone and antidiuretic hormone in the renin-aldosterone-angiotensin system. Its target of action may lie in the inhibition of angiotensin-converting enzyme (ACE) and antagonism of angiotensin II receptor 1, thus reducing the levels of related hormones in renin-aldosterone-angiotensin and producing diuretic effects [13]. One of the components, ergosta-4,6,8(14),22-tetraen-3-ergone, was not significantly different in urinary sodium excretion and Na⁺/K⁺ ratio between the treated and untreated groups, but was not significantly different via desoxycorticosterone acetate. However, a comparison of adrenalectomized rats treated with desoxycorticosterone acetate (DOCA) and normal rats produced a significantly lower Na⁺/K⁺ urinary ratio, demonstrating the diuretic effect of Polyporus Umbellatus by the aldosterone antagonism of lysergic acid, which affects Na⁺/K⁺ channels to produce diuretic effects [14].

3.2 Renal Protective Effect

Wang et al [15] confirmed in experiments on rats with experimental hyperoxaluria that *Polyporus Umbellatus japonica* ethyl acetate extract could inhibit urinary Ca^{2+} secretion, thus inhibiting the growth and aggregation of urinary calcium oxalate crystals, significantly reducing serum urea nitrogen and creatinine concentrations, reducing stone induced renal tubular dilatation, inhibiting swelling, degeneration, necrosis and shedding of renal tubular epithelial cells, and having a significant protective effect on renal function in rats, and also confirmed that ergosterol is the effective active site of *Polyporus Umbellatus* inhibiting the formation of urinary calcium oxalate stones.

3.3 Anti-fibrotic Effect

Hu Hehe et al [16] showed that adenine caused a decrease in renal function and interstitial fibrosis in rats with chronic kidney disease by significantly increasing serum creatinine levels, severe tubular damage and interstitial fibrosis in the kidneys. The intervention of *Polyporus Umbellatus* n-hexane extract (PPU) and its active ingredient ergosterone (ERG) significantly reduced the serum creatinine level and inhibited the secretion and deposition of extracellular matrix components; and the improvement of ERG was stronger than that of PPU, the mechanism of which may be to improve the disorder of lipid metabolites such as leukotrienes and bile acids and the dysregulation of lipid metabolism, thus improving the interstitial fibrosis of the kidney.

Zhao et al [17] used UPLC Q-TOF/MS to study the metabolomic profile of adenine induced chronic renal failure (CRF) and have been shown that the *Polyporus Umbellatus* component ergosta-4,6,8(14), 22-tetraen-3-one can prevent the progression of renal injury and subsequent renal fibrosis. *Paramecium nucleatum* polysaccharide showed significant protective effects against unilateral urethral obstruction (UUO)-induced interstitial renal fibrosis in a mouse model, improving renal function, the extent of renal collagen deposition and further fibrosis by a mechanism that may be related to inhibition of inflammation, inhibition of epithelial-mesenchymal transition, re-establishment of the balance of matrix metalloproteinases and tissue inhibitors of metalloproteinases, and promotion and anti-fibrotic factors [18].

3.4 Immunomodulatory Effects

Liu et al [19] proposed that *Polyporus Umbellatus* polysaccharide enhanced IFN- γ -stimulated RAW 264.7 macrophage activity, such as induction of nitric oxide synthase (iNOS) release, TNF- α and IL-6 secretion, phagocytic activity, and expression of M1 phenotypic indicators such as CD40, CD284 and CD86. *Polyporus Umbellatus* polysaccharides act upstream in the activation cascade of the nuclear factor (NF)- κ B signalling pathway by interfering with I κ B phosphorylation. In addition, *Polyporus Umbellatus* polysaccharide modulated NF- κ B (P65) signaling by interfering with Toll-like receptor (TLR)-4, iNOS and cyclooxygenase (COX)-2. This suggests that *Polyporus Umbellatus* polysaccharide activates macrophages through TLR4 / NF- κ B signalling pathway.

Li Yonghui [20] studied the immunosuppressed mouse model induced by cyclophosphamide and concluded that *Polyporus Umbellatus* polysaccharide at 200mg/kg could significantly increase the protein content in their serum as well as the number of white blood cells, red blood cells and platelets in their blood. It also enhanced the phagocytosis of macrophages in immunosuppressed mice, promoted the secretion of NO, TNF- α and IL-1 β cytokines by macrophages, and enhanced the activity of ACP (acid phosphatase) and LDH (lactate dehydrogenase) in spleen tissue homogenates. The results showed that *Polyporus Umbellatus* polysaccharide could significantly restore the immune function of cyclophosphamide-induced immunosuppressed mice, thereby enhancing the immune response ability of the immune system and strengthening the immunity of the organism.

3.5 Anti-mutagenic Effects

Wang Hong et al [21] established a mouse model with low, medium and high dose groups to study the anti-mutagenic effect of *Polyporus Umbellatus* polysaccharide on cyclophosphamide, and concluded that *Polyporus Umbellatus* polysaccharide not only reduced the high rate of micronuclei

induced by cyclophosphamide in mice between 31.77% and 84.28%, in which the low dose of *Polyporus Umbellatus* polysaccharide had the highest inhibition rate, but also reduced the high rate of sperm malformation induced by cyclophosphamide in mice between 13.62% and 60.40%. The inhibition rate was between 13.62% and 60.40%, which was positively correlated with the polysaccharide concentration. It showed that *Polyporus Umbellatus* polysaccharide has anti-mutagenic effect and has a significant effect on reducing the toxic side effects of cyclophosphamide.

3.6 Anti-inflammatory Effects

In a mouse model of simulated bladder cancer tumour microenvironment established by Li Shiqi et al [22], homogeneous *Polyporus Umbellatus* polysaccharide extracted from total *Polyporus Umbellatus* polysaccharide may promote the expression of anti-inflammatory factor IL-10 in RAW264. 7 cells through activation of PI3K/ AKT/ mTOR signalling pathway, and also promote anti-inflammatory factor SOCS3 and IL-1Ra expression and secretion through activation of IL-10 / JAK1 / STAT3 pathway , and synergize with IL-10 to exert anti-inflammatory functions.

The lipopolysaccharide (LPS)-induced inflammation model of J774 macrophages established by Jiang Zebo et al [23] was divided into blank group, LPS model group, LPS plus *Polyporus Umbellatus* low dose group, LPS plus *Polyporus Umbellatus* medium dose group and LPS plus *Polyporus Umbellatus* high dose group, and it was concluded that compared with the blank group, cytokines IL-1 β , IL-10, TNF- α , IFN- γ and IL-6 mRNA expression was significantly higher in the LPS model group compared with the blank group. The administration of *Polyporus Umbellatus* polysaccharide reduced the elevation of inflammatory factors induced by LPS and the expression of p38, ERK42/44 and p65 phosphorylation caused by LPS. This suggests that *Polyporus Umbellatus* polysaccharide can reduce the inflammatory response caused by LPS, possibly through the mitogen-activated protein kinase (MAPK) signaling pathway to reduce inflammatory damage.

4. Conclusion and outlook

Throughout the ages, *Polyporus Umbellatus* has been widely used in the treatment of kidney diseases, with *Polyporus Umbellatus* polysaccharides and ergosterone as the main pharmacological components also proven to play a role in diuresis, renal protection, anti-fibrosis, immunomodulation, anti-mutagenesis, anti-inflammation and other aspects, with good pharmacological effects and clinical efficacy. Although *Polyporus Umbellatus* has been widely used clinically in the treatment of chronic glomerulonephritis, and many breakthroughs have been made regarding its pharmacological mechanism in the treatment of chronic glomerulonephritis, and *Polyporus Umbellatus* and its extracts have been widely studied in diuresis, renal protection, anti-fibrosis and immunomodulation, studies have shown that the anti-tumour effects of *Polyporus Umbellatus* are more commonly applied to bladder cancer [24], breast cancer [25], lung cancer [26], etc. In the anti-tumour effects of *Polyporus Umbellatus* still need to be investigated. In addition, the study of the pharmacological mechanism of *Polyporus Umbellatus* is still at a preliminary stage, so the medicinal value of *Polyporus Umbellatus* and its herbal combinations in the treatment of chronic glomerulonephritis and other diseases needs to be further investigated to provide a more reliable basis and new progress for the clinical treatment of *Polyporus Umbellatus*.

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