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Original plant of Coriolus Versicolor



Dried Coriolus Versicolor

Name

Latin Name: Coriolus versicolor, synonym Trametes versicolor

Common Name: Turkey tail / Cloud mushroom **Scientific Name**: Polystictus versicolor (L.) Fr.

Chinese Name: 雲芝/彩絨革蓋菌

Pinyin Name: yun zhi

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Origin

The sporophore (fruiting body) or mycelium of Polystictus versicolor (L.) Fr., family Polyporaceae [1].

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Where Does It Grow?

The wide giant fungal plant can be found on the spruces that located in 3000 meter attitude and distributed throughout most of China. Nowadays, the supply is mainly sourced from cultivation [1].

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Nature and Flavor

Sweet and bland in flavors, slightly cold in nature, and mainly manifests its therapeutic actions in the <u>spleen</u>, <u>lung</u> and <u>liver meridians</u> [2].

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Identified Active Components / Major Chemical Constituents

Cloud mushroom contains several saccharides including polysaccharide peptide (PSP) and polysaccharide-K (PSK, krestin). The protein bound polysaccharides have been found to be immune-modulating and anti-tumor, and their polypeptide moieties are rich in aspartic acid and glutamic acid. By gas chromatography and HPLC, PSP has proved that in addition to glucose, it also contains five other monosaccharides - mannose, xylose, galactose, rhamnose and arabinose. The polysaccharide peptides can be found in the mycelium, while the fruiting body mainly contains polysaccharides [3].

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Drug actions in TCM

Replenish <u>essence</u> and <u>gi (vital energy)</u>, general enhancement and regulate immune functions [1].

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Traditional Uses in TCM

Invigorating <u>spleen</u> and eliminating <u>dampness</u>: for symptoms like general weakness, poor appetite and loose bowels. Modern used for <u>hepatitis</u>, hepatic cirrhosis, nephritis, and rheumatoid arthritis, etc. [2]

Arresting cough and easing breath difficulty: for conditions like chronic cough and asthma. [2]

Stimulating the immune system: for chronic fatigue syndrome, adverse effects of chemotherapy or radiotherapy and improving quality of life in <u>cancer patients</u>. [4]

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Pharmacological Actions

PSP is classified as a biological response modifier which is capable of modifying the biological response by stimulating the immune system and thereby inducing various therapeutic effects. Extensive pharmacological studies have demonstrated that it exerts anti-tumor and immunoregulatory activities.

1. Anti-tumor functions

In vitro and *in vivo* studies reported that PSP possesses selective anti-cancer activity against certain cancer cells. PSP was reported to exert potent anti-carcinogenic effects evidenced by suppression of cell proliferation, gene modulation, cell cycle arrest and induction of apoptosis in different malignant cell lines.

Cell growth and prostate specific antigen production of LNCaP prostate cancer cells
Alcoholic extracts of PSP in 70% ethanol significantly reduced the androgen-dependent
human prostate cancer cell LNCaP growth and down-regulated prostate specific antigen
(PSA) production. [5]

Cell proliferation and cell cycle progression of human HL-60 leukemia cells

An *in vitro* experiment showed that both 70% ethanol and water extracts of PSP resulted in dose-dependent cell growth suppression in the human promyelocytic HL-60 leukemic cells after 3-day incubation in 0,1,3,5,7.5 and 10 ul/ml of extracts. In addition, incubation of HL-60 cells with either extracts resulted in significant change in the cell cycle distribution through the G 1/S cell cycle arrest. The water extracts exert more potent growth inhibition and apoptotic effect compared to the alcoholic extracts. [6]

Control of cell proliferation and cell cycle arrest in human U-937 leukemia cells Aqueous extracts of PSP inhibited cell proliferation and cell cycle progression and induced apoptosis in human U-937 leukemia cells. At low dose (0.1mg/ml), cell cycle arrest occurred at the G 1/S phases. While at higher concentration (0.5 and 1mg/ml), increase in G 2/M phases of the cell cycle was observed. [7]

Induction of apoptosis in HL-60 and U-937 leukemia cells

Treatment with high dose (1mg/ml) of water extracts PSP for three days resulted in the induction of apoptosis in both HL-60 and U-937 human leukemia cells, as shown by the appearance of cells displaying fractional DNA content in flow cytometric analysis and the cleavage of DNA repair enzyme poly (ADP-ribose) polymerase (PARP) .[7]

Other study demonstrated that PSP induced apoptosis of human promyelocytic leukemia HL-60 cells but not of normal human T-lymphocytes. The apoptotic machinery induced by PSP was associated with a decrease in Bcl-2/Bax ratio, drop in mitochondrial transmembrane potential, cytochrome c release, and activation of caspase-3, -8 and -9.

Effect of PSP on the cytotoxicity of cyclophosphamide on HepG2 liver cancer cells PSP enhanced the cytotoxic effect of cyclophosphamide in HepG2 cells. The combination of cyclophosphamide and PSP (10µM) decreased cell viability by 22% and 10% when compared with cyclophosphamide and PSP alone. [9]

Anti-tumor effect in tumor bearing mice models

In vivo anti-tumor activity of PSP has also been extensively studied. Significant tumor size reduction was shown after prolonged administration of PSP in the tumor bearing mice

models such as scaroma 180, lung adenocarcinoma and Lewis lung cancer. [10]

2. Immunoregulatory Activities

Effects of PSP extracts on secretion of the immunomodulating cytokines

Both water and ethanol extracts of PSP at concentration of 5μ I/ml significantly increased the secretion of interleukins, IL-1 β and IL -6 in HL-60 leukemia cells after 3-day incubation, with the water extract eliciting a more pronounced change. Production of IL-8 decreased in response to the addition of both extracts of PSP. [6]

PSP restored cyclophosphamide-induced immunosuppression in rats

Effects of PSP on cyclophosphamide-induced immunosuppression were investigated by determining lymphocyte proliferation, natural killer cell function, IgG and IL-2 concentration. The results showed that PSP could restore cyclophosphamide-induced immunosuppression in male Wistar rats by stabilizing lymphocyte proliferation, NK cell function, white blood cell count, IgG and IL-2 secretion. [11]

Immunomodulative effect of PSP in tumor bearing mice

PSP was found to be able to significantly raise serum half hemolysin concentration (HC50) and to retard the process of thymus atrophy in tumor S180 sarcoma bearing mice. Serum levels of immunological globulin (IgG) and alexin C3 in the mice were also significantly increased. [12]

3. Clinical Studies Overview

Breast Caner

The effect of PSP on peripheral blood counts was evaluated on 11 Chinese breast cancer patients and 13 patients from the historical control were used as the control. Results: Five patients in the treatment group noticed an increase in appetite. [13]

Non-small cell Lung Cancer (NSCLC)

The use of PSP in slowing down disease progression in patients with advanced NSCLC was assessed in double-blinded controlled trials in which 68 patients (treatment n=34, placebo n=34) were treated for four weeks. After 28-day treatment, there was a significant improvement in blood leukocyte and neutrophil counts, serum IgG and IgM levels in the treatment group. PSP treatment appeared to be associated with slower deterioration in patients with advanced NSCLC. [14]

Gastric Cancer (Adenocarcinoma)

The use of PSP in easing the side effects associated with chemotherapy and radiation in patients with stage I to IV gastric cancer was assessed in double-blinded controlled trials in which 60 patients (treatment n=30, placebo n=30) were treated for two months. PSP is safe and can help lessen the degree of side effects that chemotherapy and radiation produces. It also improved or maintained the immunological profiles of gastric cancer patients. [15]

Esophageal Cancer (Squamous cell carcinoma)

The use of PSP in easing the side effects associated with chemotherapy and radiation in patients with stage I to IV esophageal cancer was assessed in double-blinded controlled trials in which 61 patients (treatment n=31, placebo n=30) were treated for two months. PSP is safe and can help lessen the degree of side effects that chemotherapy and radiation produces. It also improved or maintained the immunological profiles of esophagus cancer patients. [15]

Hepatitis B

Clinical trial of total 75 patients (male or female) with acute or chronic hepatitis B has demonstrated that PSP treatment, which is assigned to 33 patients, can effectively improve the hepatic functions and shorten the treatment duration if it is used adjunctively with the regular treatment to hepatitis B (1.02g, three times daily). [16]

Another clinical study of total 60 subjects (male or female) with chronic hepatitis B has shown that PSP can significantly reduce the Hepatitis B surface Antigen (HBsAg) and the Hepatitis Be Antigen (HBeAg) in bloodstream after 30-day of oral treatment (1.02g, three times daily). [17]

4. Herb-Drug Interactions

A clinical study was to investigate the ability of PSP to inhibit or induce the drug metabolism of CYP450 3A 4 in healthy adult human subjects by using a diagnostic CYP450 3A4 specific assay, the erythromycin breath test (EBT). The 14-day course of PSP in 12 healthy subjects (eight women and four men) was not associated with any clinically significant CYP450 3A4 inhibition or induction. This suggests that administration of PSP with other medications and dietary supplements which are primarily metabolized by the CYP450 3A4 pathway is not expected to be associated with significant herb-drug interactions. [18]

Toxicology

PSP or PSK have an extremely low level of toxicity. The no-effect dose level after oral administration of PSP to mice was 20g/kg/day. A dose of 1.5g/kg/day PSK in mice for 60 days, which is approximately 130 times of the therapeutic dose in humans, did not cause any toxic effect. PSP has shown no evidence of reproductive toxicity. [1]

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Administration and Dosage

Crude herb for decoction used 9 -27g each time. [19]

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Adverse Effects, Side Effects and Cautions

Not in detail, and no interactions are known. [4]

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