

A Potent Pharmacological Mushroom: *Pleurotus eryngii*

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Abstract

Pleurotus eryngii, commonly known as the king oyster mushroom, has been used extensively in North Africa, Europe and Asia. A great deal of work has been carried out on therapeutic potential of *Pleurotus eryngii*. The edible fungi perform multiple bioactivities: anticancer, antiviral, antioxidant, antimicrobial, anti-leukaemia, hypolipidemic, immuno-modulating and estrogen-like activity. These bioactive properties depend on its bioactive compounds such as polysaccharides, eryngiolide A, ubiquinone-9, pentacyclic triterpenoid and so on. The present review focuses on the potential pharmacological activities and provides reference for the study of *Pleurotus eryngii* in the future.

Keywords Edible fungi; *Pleurotus eryngii*; Pharmacological effects

Introduction

As a kind of popular traditional food in Asia, mushrooms have been valued as a resource to support health for thousands of years. Even so, Many species of mushrooms have not been greater tapped in the field of medicine. In recent years, many macromolecules (e.g. polysaccharides, polysaccharide-proteins/peptides and proteins) and low-molecular-weight molecules (e.g. cerebrosides, isoflavones, catechols, amines, triacylglycerols, sesquiterpenes, and steroids) are considered as the major biological constituents in edible/medical mushrooms.



Figure 1: The fruit body of *Pleurotus eryngii*.

Pleurotus eryngii (Figure 1) cated by Italian initially, is cultivated for commercial use in USA, Thailand and Taiwan [1-3]. It has rapidly become a highly valued species in North Africa, Europe and Asia. *Pleurotus eryngii* attracted attention and many extracts from *Pleurotus eryngii* have been studied *in vivo* and *in vitro*. The results have shown many interesting biological activities of the fungus: antitumor,

anticancer, antioxidant, antimicrobial, hypoglycemic and immuno-stimulating activity. Though much information on bioactivities of *Pleurotus eryngii* is available, there were no existing references to summarize the pharmacological properties of it. Hence, to facilitate discussion of this issue, the present review aims to examine the existing scientific knowledge which demonstrates the pharmacological activities about *Pleurotus eryngii*.

Anticancer activity

Cancer is a worldwide disease which is causing serious damage to human health, how to conquer cancer is one of the most important research topics on the medicine. Recently, some natural active component have been discovered and purified from *Pleurotus eryngii*, including polysaccharide, polysaccharide-protein, diterpenoid, triterpene. These components exhibited the significant anti-cancer activity [1-10].

Biological studies have demonstrated that polysaccharides from *Pleurotus eryngii* played a main role in the enhancement of the antitumor activity. Jing et al. [3] reported that exopolysaccharides from *Pleurotus eryngii* exhibited higher antitumor ability of human hepatoma cells. The antitumor activity increased in a concentration-dependent manner and reached to 61.4% at the concentration of 400 µg/ml.

In addition, Ma et al. [9] also found polysaccharides in *Pleurotus eryngii* could suppress the proliferation of HepG-2 cells and enhance lactate dehydrogenase (LDH) in a dose- and time-dependent manner [10-14]. A water-soluble polysaccharide isolated from *Pleurotus eryngii* significantly suppressed the tumor growth in Renca-bearing mice at the doses of 50, 100 and 200 mg/kg [2].

Besides, Cui et al. investigated the changes of the chemical components and cytotoxicity potency at 5 developmental stages of *Pleurotus eryngii* fruiting body. Their findings proved that mature fruiting body of *Pleurotus eryngii* which contained polysaccharide-proteins possessed the highest antiproliferative effect on SGC-7901 and HepG-2 cells *in vitro* [5]. These results suggested that the

polysaccharides obtained from the *Pleurotus eryngii* might be suitable for use as potential therapeutic agents for human cancer disease.

Eryngiolide A (Figure 2) is a previously undescribed C20 diterpenoid with the skeleton deriving from a cyclododecane core fused with two lactone units, isolated from the solid culture of *Pleurotus eryngii*. The compound showed moderate toxicities against two cell lines with IC₅₀ values of 20.6 μ M and 28.6 μ M at the concentration of 100 μ M, respectively [1]. The discovery of Eryngiolide A will definitely attract interest from synthetic chemists and biosynthetic researchers.

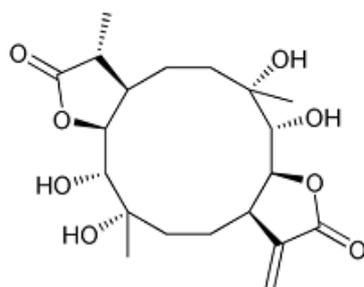


Figure 2: The structure of Eryngiolide A.

There was a research shown an acetic ether (EtOAc) fraction from the sporocarp of the edible mushroom *Pleurotus eryngii* exhibited significant tumour cell growth inhibition both *in vitro* and *in vivo*. Three pentacyclic triterpenoid compounds 1-3 (Figure 3) were isolated from EtOAc extracts and showed significant inhibitory activity against breast cancer MCF-7 cell lines *in vitro*. The compound 1 exhibited greatest activity with the IC₅₀ values of 15.71 μ M [8].

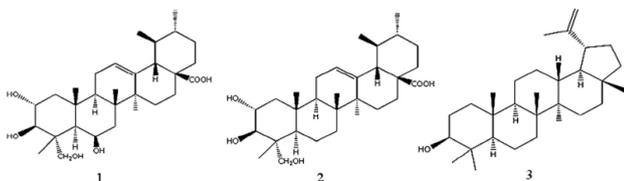


Figure 3: The structure of Pentacyclic triterpenoid (1. 2, 3, 6, 23-tetrahydroxy-urs-12-en-28 oic acid 2. 2, 3, 23-tetrahydroxy-urs-12-en-28 oic acid 3. 2, 3, 6, 23-tetrahydroxy-urs-12-en-28 oic acid).

As is reported, angiogenesis has been considered as an important factor of impacting tumour growth and metastasis. Through the chorioallantoic membrane assay, the extracellular polysaccharide (EPS) of *Pleurotus eryngii* exerted a significant inhibition in neo-vascularization at a concentration of above 500 μ g. Besides, ubiquinone-9 (Figure 4), a chloroform extract of *Pleurotus eryngii*, was demonstrated the property of inducing apoptotic cell death through inhibiting the activity of mammalian DNA topoisomerase I.

Topoisomerase I was considered as an attractive target for antitumor agents. The inhibition activity of the topoisomerase I was clearly observed at drug concentrations above 50 μ M.

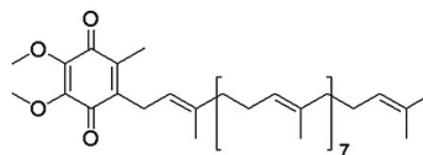


Figure 4: The structure of ubiquinone-9.

Antiviral activity

The prevention and treatment of viral diseases remains an urgent problem in modern medicine. Virus infection is one of the challenging global issues with regular widespread epidemics or pandemics resulting in high mortality worldwide. A laccase from *Pleurotus eryngii* was examined by HX Wang and Ng for inhibitory activity against HIV [10]. The result demonstrated that the laccase was active against HIV-1 growth with an IC₅₀ of 2.2 μ M by inhibiting HIV-1 reverse transcriptase. A protease designated pleureryn, isolated from fresh fruiting bodies of the edible mushroom, caused (23.1 \pm 0.6)% and (91.4 \pm 3.2)% inhibition of HIV-1 reverse transcriptase at 3 and 30 mM, respectively. These results indicated that there was a dose-dependent relationship for protease showing anti-HIV protease activity. What's more, Krupodorova et al. [11] investigated the *in vitro* antiviral activity of the mycelia of *Pleurotus eryngii* against influenza virus type A (serotype H1N1). Extracts from *Pleurotus eryngii* mycelia inhibited the reproduction of influenza virus strain A/FM/1/47(H1N1) in MDCK cells reducing the infectious titre by 2.0 lg ID₅₀. The result has not previously been presented in the literature.

Antioxidant

Many studies have reported that one of bioactivities about *Pleurotus eryngii* extracts is attributed mainly to antioxidant activity and the major effective content are polyphenols and polysaccharide. The antioxidant activity was evaluated through reducing power (Folin-Ciocalteu and Ferricyanide/Prussian blue assays), free radical scavenging activity (DPPH assay) and lipid peroxidation inhibition (b-carotene/linoleate and TBARS assays).

The polysaccharide from mushrooms has currently been found to perform the significant antioxidant capacities of scavenging free radicals. Many reports concerning to the polysaccharide are mainly focused on the exopolysaccharide (EPS) of fermentation broth and intracellular polysaccharide (IPS) of fruiting bodies. Two groups of EPSs (the weight average molar masses are 4.098 \times 10⁴ and 1.114 \times 10⁴ g/mol, respectively) were obtained from the culture broth [3], and pharmacology experiment *in vitro* indicated small molecular weight had stronger antioxidant capacities than larger molecular weight. It is suggested that the molecular-bioactivity relationship of the polysaccharide from *Pleurotus eryngii* might be attributed to the different molecular weights and chemical compositions [3,6]. However, the problem about the IPS of *Pleurotus eryngii* and its antioxidant activity *in vitro* was seldom reported. Liu et al. firstly reported that the *in vitro* hydroxyl radical inhibition percentages of IPS was 16.1 \pm 1.5%, the scavenging effects on superoxide anion radical and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical were 16.3 \pm 1.3% and 16.8 \pm 1.4% [15]. The results provided a reference for study about antioxidant activity of IPS from *Pleurotus eryngii*.

Numerous significant positive correlations were observed between phenolic compounds and detected antioxidative potential. The result proved *Pleurotus eryngii* has currently been found to possess antioxidant activity which was also correlated with their total phenolic content [16-19]. *Pleurotus eryngii* contained 69.67% DPPH scavenging activity and 70.82% chelating activity, which increased with increase in concentration [20]. Besides, Li and Shah [21] investigated all free and bound phenolic extracts for their antioxidant activities by 3 different assays. Free phenolic extracted from freeze dried and oven dried *Pleurotus eryngii* samples showed strongest DPPH radical scavenging activity (IC₅₀ at 32.61 µg/mL) and strongest reducing power (IC₅₀ at 26.31 µg/mL), respectively, and boiling treated one showed strongest superoxide anion radical scavenging activity (IC₅₀ at 14.07 µg/mL) [21].

Immuno-modulating effects

As is known, activated macrophages, NK cells, cytotoxic T cells, and their secretory products, such as tumour necrosis factor, reactive nitrogen and oxygen intermediates, and interleukins are involved in immunomodulatory responses [12]. And many of studies about edible mushroom almost refer to the function of immunoregulation. In 2008, Jeong et al. reported endo-biopolymers produced from submerged mycelial cultures of *Pleurotus eryngii*, which can increase the natural killer (NK) cell activity of splenocytes [4]. This result suggested *Pleurotus eryngii* was closely related to the immune system. In order to further study the immuno-modulating effect of *Pleurotus eryngii*, Kazunori Ike et al. assessed the effect on interferon-gamma (IFN-γ) and interleukin (IL-4) productions in mice. They found that the hot-water extract increased significantly in serum IFN-γ levels, the high-level production of IFN-γ in the culture supernatant from can enhance immunity in the trial immunogen group mice [13]. Furthermore, purified acidic glycosphingolipids (AGLs) from *Pleurotus eryngii* were reported that AGL could induced interleukin-2 (IL-2) release from invariant natural killer T (iNKT) cells and induced prolonged retention of IL-4 in serum *in vitro* and *in vivo* [14]. These indicated that *Pleurotus eryngii* AGLs might be involved in the maintenance of immunohomeostasis through iNKT cell activation.

Anti-allergic property

The anti-allergic drug research recently seldom have considered the natural defence mechanisms of the body or the causative factors, while *Pleurotus eryngii* extract (PEE) showed anti-allergic activity through inhibiting allergy markers. Han et al. [22] evaluated the inhibitory effect of PEE on antigen-stimulated RBL-2H3 mast cells and found that PEE inhibited degranulation and histamine release, transcriptional activation of IL-4, the activation of NFAT and NF-κB, pro-inflammatory cytokines (TNF-α, IL-1 and IL-6) and inflammatory (COX-2, ROS) mediators and regulated FcRI-mediated signaling events [22]. Moreover, PEE has also been demonstrated the inhibitory property of atopic dermatitis (AD)-like skin lesions in NC/Nga mice, which reduced thickness of the dermis and dermal infiltration of inflammatory cells and mast cells in histopathological examination [23]. After continuous treatment of PEE, allergic contact dermatitis was inhibited through the modulation of T helper Th1 and Th2 responses. Although PEE provide insight into the prevention and treatment of allergic and inflammatory diseases, its clinical effectiveness remains to be determined in an *in vivo* model, as does the identification of the active components in *Pleurotus eryngii* extract.

Hypolipidemic

Many studies have reported the hypolipidemic effect of *Pleurotus eryngii* in kinds of animal models. Alam et al. investigated dietary effect of *Pleurotus eryngii* on biochemical function and histology in hypercholesterolemic rats [24]. After administrating 5% powder of *Pleurotus eryngii* to hypercholesterolemic rats, plasma lipid profiles (plasma TC, TG, HDL-C, LDL-C, VLDL-C, TL and PL in HC rats) decreased significantly compared with control group, whereas total lipid and cholesterol excretion increased in faeces. In addition, the feeding of dietary supplementation with 3% *Pleurotus eryngii* powder to apolipoprotein E-deficient mice reduced serum total cholesterol (TC) concentrations at 12 weeks [25]. It is suggested *Pleurotus eryngii* powder intake can provide health benefits by modulating physiological functions that consist of various atherogenic lipid profiles.

However, Mizutani et al. [26] investigated the mechanism underlying anti-lipase activity of *Pleurotus eryngii* extract (PEE) *in vitro* and its hypolipidemic property in fat-loaded mice. The results showed that PEE suppressed the elevations of plasma and chylomicron triacylglycerol levels and inhibited pancreatic lipase at concentrations of 50-300 µg/ml, indicating the hypolipidemic effect of PEE was owed to pancreatic lipase inhibition resulting in low-absorption of fat. Besides, the purified *Pleurotus eryngii* polysaccharide performed a strong ability of inhibiting lipid accumulation in foam cells, resulting in only about 28.06% of lipid content left inside the cell compared to 100% in the control [27]. These results showed that *Pleurotus eryngii* could be recommended as a potent prophylactic against hypercholesterolemia, hyperlipidemia.

Antimicrobial activity

The antimicrobial properties of the medicinal mushrooms have been well recognized for many years, and the effect of *Pleurotus eryngii* extract (PEE) on microbia has recently been investigated. Wang and Ng isolated a peptide, designated as eryngin, from fruiting bodies of the mushroom *Pleurotus eryngii* and tested the antifungal activity. They found the peptide inhibited mycelial growth in *Fusarium oxysporum* and *Mycosphaerella arachidicola* at the IC₅₀ values of 1.35 ± 0.15M and 3.5 ± 0.4M, respectively [28]. Certainly, some studies reported that *Pleurotus eryngii* extracts also performed inhibitory property against a group of bacterial reference strains of medical relevance [19,29,30]. According to results of the antimicrobial screening assay, PEE showed weak activities against *Staphylococcus aureus* and *Escherichia coli*, but inhibited obviously the growth of the 2 *Helicobacter pylori* test strains (ATCC43504 and SS1) with MIC values in most cases of ≤ 3.0 mg/mL. In particular, *Pleurotus eryngii* var. *Ferulae* and *Pleurotus eryngii* var. *Elaeoselinii* extracts were able to inhibit the growth of *S. epidermidis* at an MIC of ≤ 0.025% v/v and 0.05% v/v, respectively. The acidic extract of *Pleurotus eryngii* var. *Eryngii* was not as effective as the other species of *Pleurotus*, showing MIC values of 25% v/v [30]. By this taken, the antimicrobial property of PEE is not strong.

Besides, the gastrointestinal tolerance and the survival rates of the probiotic strains supplemented with *Pleurotus eryngii* polysaccharides (PEP) were examined, so the results showed PEP exhibited the capability of enhancing the gastric juice tolerance of probiotics, retarding the death of the probiotics and enhancing the survival rate of *Lactobacillus acidophilus*, *Lactobacillus casei* and *Bifidobacterium longum* subsp. *longum* during cold storage. Through

analysis with compare, it indicated that a symbiotic interaction occurred between the microbial bacteria and PEP [31].

Estrogen-like activity

Estrogens play an important role in menopausal women's lives, especially in bone maintenance and in the central nervous system [32,33]. After menopause, women who are in a state of estrogen deficiency are at risk for osteoporosis and neurological symptoms such as depression and memory impairment. However, researches have shown that *Pleurotus eryngii* extracts (PEE) could improve these problems caused by estrogen deficiency [34-37].

To investigate whether *Pleurotus eryngii* extracts (PEE) plays a role in postmenopausal osteoporosis, Shimizu et al. regarded ovariectomies of young rats as models and feed with PEE [36]. The results demonstrated PEE protected against the bone loss in calcium deficient ovariectomized rats and the trabecular BMD of PEE group was higher by 14% in comparison to the control group by the *ex vivo* peripheral quantitative computed tomography analysis. More importantly, further study showed that the ALP activity increased significantly, the expression level of the Runx2 gene increased 100%, and the OPG gene expression level increased 70% at a PEE concentration of 10 μ L/mL. These proved PEE stimulated the activity of bone forming osteoblasts, while inhibiting the generation and activity of bone resorbing osteoclasts [38].

There are some researches related to estrogen-like drugs which improved neurological symptoms such as depression and memory impairment caused by surgical or natural menopause [36-38]. To determine whether the ethanol extracts of this *Pleurotus eryngii* (PEE) has estrogen-like activity, Minami et al. [39] fed the extracts to the OVX rats and observed the immobility time of the OVX rats with the treatment of the extracts was significantly shortened during a forced swimming test. The Morris water maze test showed that spatial memory impairment in OVX rats was improved by PEE. These results suggested that PEE has estrogen-like activity, which can improve depression-like behaviour and memory impairment in OVX rats [40-42].

Conclusion

Pleurotus eryngii, a common edible and medicinal mushroom, contains various beneficial bioactive compounds, which have health promoting benefits to cure various diseases and maintain good health by activating our immune systems for a multitude of defensive functions. A summary of the therapeutic effects and its corresponding bioactive compounds of *Pleurotus eryngii* reported in the literature have been presented in Table 1. Many *Pleurotus eryngii* extracts perform a significant effect on anticancer activity/antiviral activity, hypolipidemic activity and immuno-stimulating activity through immune regulatory factors. Although direct intervention trails of *Pleurotus eryngii* consumption in humans are lacking, *Pleurotus eryngii* and their extracts are generally well tolerated with few, if any, side effects. So, *Pleurotus eryngii* may be developed as functional food and potential therapeutic agent for human disease, especially for cancer disease. In the search for active compounds from *Pleurotus eryngii*, the majority of research had been focused on *Pleurotus eryngii* extracts and there have been fewer studies on identified bioactive compounds. It appears that more studies are necessary to explore their complete structural characteristics, structure-activity relationship and

the mechanism of their antitumor activity. As a result, the future research may be oriented in that direction.

Source	Bioactive Compound	Therapeutic Effects	References
Fruiting body	Polysaccharide	Anticancer activity/ Antioxidant/Immuno-Modulating effects/ Hypolipidemic/Antimicrobial activity	[2,9,16-18,30,32,34]
	Polysaccharide-protein	Anticancer activity	[5]
	Phenolic	Antioxidant	[23,24]
	Eryngin	Antimicrobial activity	[31]
	Laccase	Antiviral activity	[10]
	Acidic glycosphingolipids	Immuno-modulating effects	[15]
	Water extracts	Immuno-modulating effects/ Hypolipidemic	[13,14]
	Methanol extracts	Antioxidant	[22]
Mycelial	Ethanol extracts	Antimicrobial activity/Anti-Allergic Property, Estrogen-like activity	[21,25,26,37,38,42]
		Water extracts	Antiviral activity
Sporocar p	Pentacyclic triterpenoid	Anticancer activity	[8]
Culture medium	polysaccharide	Anticancer activity/Antioxidant	[3]
Solid culture	Eryngiolide A	Anticancer activity	[1]

Table 1: Therapeutic effects and bioactive compounds of *Pleurotus eryngii* reported in the literature.

Conflict of Interest

The authors declare that there is no conflict of interest.

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