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Open Access Journal of Pharmaceutical Research
ISSN: 2574-7797

Trametes Versicolor and *Dictyophora Indusiata* Champions of Medicinal Mushrooms

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Review Article

Volume 4 Issue 1

Received Date: December 28, 2019

Published Date: January 10, 2020

DOI: 10.23880/oajpr-16000192

Abstract

Overall, studies both on the chemistry and pharmacology of *Trametes versicolor* and *Dictyophora indusiata* extracts and compounds are increasing in recent years and show therapeutic potential for various pathologies. The purpose of this review was to investigate the biological activities of polysaccharide extracts prepared from fruiting bodies of *Trametes versicolor* and *Dictyophora indusiata.*

Keywords: Medicinal Mushrooms; *Dictyophora indusiata*; *Phallus indusiata*; *Trametes versicolor*; polysaccharide

Abbreviations: PSP: Polysaccharopeptide SFDA: State Food and Drug Administration; PSK: Polysaccharide K; WE: Water Extract; DIP: *Dictyophora Indusiata* Polysaccharides; NK cells: Natural Killer cells; CR: Complement Receptor; NO: Nitric Oxide; NOS: Nitric Oxide Synthase.

Introduction

Mushrooms have been valued throughout the world both as food and medicine; mushrooms possess high contents of qualitative protein, crude fibre, minerals and vitamins [1-3]. With the development of methods for the artificial cultivation of mushrooms, several mushrooms are now cultivated at a commercial scale and many of them have been developed as supplemental foods [4]. Apart from their nutritional potentials, mushrooms are also sources of physiologically beneficial bioactive substances that promote good health [5,6]. They produce a wide range of secondary metabolites with high therapeutic value [7]. Health promoting properties, e.g. antioxidant, antimicrobial, Antiviral, anticancer, cholesterol lowering and immunostimulatory effects, have been reported for some species of mushrooms [8-14]. Both fruiting bodies and the mycelium contain compounds with wide ranging antioxidant and antimicrobial activities [15-18]. As sources of antioxidants, edible mushrooms are desirable since they are safe to eat and known not to place additional stress on the body [6]. Mushrooms need antibacterial and antifungal compounds to survive in their natural environment. Hence, they are rich sources of natural antibiotics [19].

Mushroom Polysaccharides

Mushrooms, whether belong to the class Basidiomycetes or Ascomycetes, are considered precious food resources that widely distributed all over the world. For more than 2000 years, mushrooms have been greatly consumed due to their nutritional and medicinal values [20,21]. In eastern Asia, a wide variety of bioactive compounds have been isolated from various medicinal mushrooms, and these compounds have been widely used and extensively studied. Polysaccharides, lectins, alkaloids and terpenoids have been reported among the important bioactive compounds [22,23]. Among these bioactive compounds, polysaccharides are considered the main bioactive component for many mushroom species. The diverse activities displayed by polysaccharides return to their unique structure and properties. These activities include antitumor, antioxidative, immunomodulatory, hepatoprotective, antiviral and hypoglycemic as well as anti-inflammatory effects [22,23]. The polysaccharides compositions are directly related to their pharmaceutical activities, and increasing research attention has been directed to the structure-activity relationship [24,25]. Studying the various polysaccharides synthetic pathways as well as their regulatory mechanisms is of great importance in order to produce biologically and chemically uniform polysaccharides, hence obtaining reliable results. The polysaccharides biosynthetic pathways involve several steps starting with the synthesis of sugar precursors, followed by the assembly of repeating monosaccharide building units, and finally ending with the polymerization process [26,27].

Recently, many studies have addressed the structures as well as the numerous bioactivities of mushroom polysaccharides. Here, we review the various biological activities of the glucan polysaccharides isolated from *Trametes versicolor* and *Dictyophora indusiata* mushrooms.

Trametes versicolor (Turkey Tail)

Trametes versicolor which is also known as *Polyporus versicolor*, *Coriolus versicolor* and Turkey tail belongs to the Basidiomycetes (Figures 1 & 2). It is a common traditional medicinal polypore mushroom that spreads throughout the world and grows on tree trunks [28,29]. Many bioactive substances are isolated from this mushroom, such as polysaccharopeptide (PSP), amino acids, proteins, as well as other various compounds. PSP is considered the most biologically active compound that can be isolated from both mycelium or fermentation broth of *Trametes versicolor* [30].

Various strains of *T. versicolor* and different culture conditions greatly affect the produced polysaccharides properties including the structures and molecular weights [31,32]. In China PSP used form is mostly produced from the 'COV-1 strain' [33], while in Japan the polysaccharide K (PSK) form is the most common and it is produced from the 'CM-101' strain. Up to date, nearly thirteen types of *T. versicolor* based drugs and one *T. versicolor* based health products are used in different commercial and clinical products and they are authorized by the China State Food and Drug Administration (SFDA) [34]. These products include: *Coriolus versicolor* Gantai granules, Gansukang capsules, Polystictus Glycopeptide capsules, Posaverptidum capsules as well as other products.

As it was mentioned that PSP is the main active compound isolated can be obtained from the mycelium or fermentation broth of *C. versicolor*. The molecular weight of PSP significantly differs with different batches. Its molecular weight ranges from 36 kDa in the mycelium to 45 kDa in the fermentation broth. While its molecular weight in the fruiting body is about 75 kDa [34].

The extracellular PSP are mainly glucans without peptide where D-glucose content is about 99.2% of its structure. Its structure contains β (1–3) in the main chain and β (1–6) in the branches of the polysaccharide structure. However, the intracellular PSP from mycelium is formed of a glycopeptide with covalently linked peptides [35], its main monosaccharide compositions are glucose, mannose with β (1–4)-β (1–3) or β (1–4)-β (1–6) linked glucose backbone. The polysaccharide content is found to be 30–60%, while the protein content represents 10–30% [36,37]. PSK is a proteoglycan that consists of a β-glucan with β-(1,4) linked glucose backbone and β-(1,3) and β-(1,6) linked side chains. Its molecular weight is about 100 kDa [38].

Antitumor and Immunity Enhancement Effects

Currently, the bioactive glucans and proteoglycans isolated from variable mushroom sources are considered among the most promising sources of immunoceuticals, this is due to their ability to augment different pathways of host immunity. The experiments proved that PSP and PSK have potent effect on many pathways exist in the immune system. PSK can restore a proper immune response in cancer patients moreover it improves the immunosuppressive state. It was also reported that PSK is a Toll-like receptors agonist, especially in TLR2 and TLR4 mediated signaling pathways.

In a similar way, PSP is found to stimulate the expression of TLR4 and TRAF6 (its downstream signaling molecule) [39]. PSP also enhances the natural killer cells (NK cells) activity in tumor immunity [40]. It activates complement system and promotes antibody formation by activating T lymphocytes, B lymphocytes and macrophages [41]. Additionally, PSP plays an important role in declining the tumor resulting immune cell function as well as decreasing the adverse side effects related to the cancer treatment including pain, fatigue and vomiting.

As the studies show that PSK and PSP major biologically active component are β-glucans, which have different structures from various sources. TLR-2, TLR-4, TLR -6 and complement receptor (CR3) are found to be immune receptors for β-glucans, where β-Glucans is responsible for the activation of some immune cells that express these receptors, these include: natural killer cells, neutrophils, monocytes, macrophages and dendritic cells. Consequently, both the innate and adaptive responses will be modulated by β-glucans either directly or indirectly [42].

Figure 1: ***Trametes versicolor*** (Photographs taken by Walt Sturgeon, Locality: USA, Ohio, Columbiana Co., Beaver Creek State Forest, hosted by http://mycoportal.org).

Figure 2: ***Trametes versicolor*** (Photographs taken by Robert Chapman, Locality: USA, Arizona, Chiricahua Mountains, hosted by http://mycoportal.org).

Antihepatopathy Effect

Furthermore, PSP has been used in China as a traditional medicine for treating hepatitis [41]. It has been found that PSP reduces the serum level of ALT and AST and it also increase the negative conversion rate of HBVDNA, HBeAg, and HBsAg. In consequence, the combination of PSP with other hepatoprotective drugs such as, Mujimixture, Xinganbao capsule, Yiganle particles, as well as multivitamins, leads to better treatment comparing to the results of any single drug treatment [41-43].

Antioxidant Effect

Animal studies also show that PSP is able to scavenge free radicals in liver injured mice (induced by CCl_4). PSP increases the activity of antioxidant enzymes and glutathione (GSH) that result in acceleration of the free radicals scavenging by reducing the nitric oxide synthase (NOS) activity and reducing the nitric oxide (NO) content. Thus, enhancing the antioxidant capacity of the body [44]. Moreover, PSP itself shows an antioxidation activity, however its free radicals scavenging ability is still less than vitamin C [34]. A synergistic effect on eliminating free radicals in liver injury is also noticed when PSP is combined with vitamin E [44].

Antihyperlipidemia Effect

PSP can also be used in treatment of hyperlipidaemia (high levels of some or all serum lipids and Lipoproteins including low density lipoproteins, cholesterol and triglycerides) as it reduces the lipid level [45,46]. Antihyperlipidemia drugs such as statins and fibrate are highly effective, however they increase the risk of myopathyandrhabdomyolysis. Clinical trials showed that the administration of PSP reduced the lipid levels significantly 240 patients [45]. PSP also reduces the levels of total cholesterol, low density lipoprotein and triglyceride, it also increases the high density lipoprotein in hyperlipidaemia mouse model. Recently, PSP has been identified to have antiatherosclerosis effect by controlling serum lipid level [34].

Toxicity and Teratogenicity of PSP

The acute toxicity tests results have shown that PSP oral administration tolerance dose (LD_{50}) is 20 g·kg^{-1} while intravenous injection LD_{50} is 300.36 mg·kg^{-1} in mice. Indicating that PSP exhibits minimum acute toxicity. On the other side, the chronic toxicity tests have demonstrated that there is no visible chronic toxicity when PSP oral doses used in rat and monkey are increased 200 times and 100 times that of the clinical dose [29]. And interestingly, no mutagenic nor teratogenic effects are noticed in the used animal models [47].

Dictyophora Indusiata

Dictyophora indusiata (Vent.) Fisch. is an edible and medicinal mushroom that belongs to the family Phallaceae of the Agaricomycetes class (phylum Basidiomycetes) of fungi. In recent taxonomic literature, the synonym Phallus indusiata Vent. is the accepted name for the fungus though nearly all the scientific literature so far is available under the name entry of *Dictyophora indusiata*. As a saprophytic fungus, it grows in well-rotted woody trunk or rich soil of tropical Africa, Asia, Australia and the Americas, Figure 3. Its food and medicinal value are however much appreciated in the far eastern countries such as China where it grows on the wet roots of bamboo groves and in forests. Its common local names mainly in China and Japan include bamboo mushrooms, bamboo pith, long net stinkhorn, crinoline and stinkhorn basket, but perhaps the names most vividly associated with the morphologically distinctive feature of the fungus are bridal veil fungus, veiled lady or queen of the mushrooms [48].

Dictyophora indusiata and many other *Dictyophora* mushrooms distribute widely around the world. *Dictyophora indusiata* (Vent.) Desv. (*Phallus indusiatus* Vent.) is an edible mushroom that is considered a good delicacy by the Chinese. The species is also known as “Veiled Lady Mushroom” and belongs to the family of Phallaceae Corda. The fruiting body begins as an “egg” stage, from which the phallic-looking basidioma emerges over the course of just a few hours. Like other edible mushrooms, *Dictyophora indusiata* sourced both from the wild and commercial sources has nutritional value and its protein, carbohydrates, and dietary fibre contents have been extensively studied [49,50]. Likewise, the amino acids, vitamins and inorganic elements composition of *Dictyophora indusiata* have been reported [51].

Antioxidant and Antimicrobial Effect

The antioxidant property of methanolic extract from *Dictyophora indusiata* had been reported by Mau, et al. [52] due to the presence of water soluble phenolics in Water Extract. Trung Kien Nguyen, et al. [53] showed that *Dictyophora indusiata* extracts have excellent DPPH scavenging and chelating activity on the ferrous ions compared with positive control. Therefore, the experimental results suggested that methanol and hot-water extracts of *Dictyophora indusiata* fruiting bodies might be used for natural sources of antioxidant and anti-inflammatory agents. The antioxidant and antimicrobial properties of hot water extract (WE) obtained from *Dictyophora indusiata* were investigated by Oyetayo, et al. [17]. The free radical scavenging ability of *Dictyophora indusiata* Water Extract on DPPH was 97.35% at 2 mg/ml concentration. The reducing power of WE was moderate (1.22 at 2 mg/ml). Similarly, the WE displayed average scavenging effect on hydroxyl radical (52.28% at 2 mg/ml) and superoxide anion scavenging effect (48.64% at 2 mg/ml). Antimicrobial assay revealed that Water Extract from *Dictyophora indusiata* can inhibit both bacteria and fungi used as indicators for antimicrobial effect at concentration of 200 mg/ml. The results suggest that *Dictyophora indusiata* Water Extract possess good antioxidant and antimicrobial properties [17].

Dictyophora indusiata Polysaccharide

Owing to the outstanding healthy benefits, various bioactive substances from *Dictyophora indusiata*, including polysaccharide, amino acid, vitamin and protein, have been studied in recent years [54]. The superior health benefits of *Dictyophora indusiata* have attracted people’s attention. Modern studies suggested that *Dictyophora indusiata* polysaccharide is verified to own many biologically activities such as anticancer, antitumor, anti-proliferative and neuroprotection effect [55]. Nevertheless, there is little about the anti-hyperlipidemic effects of *Dictyophora indusiata* polysaccharides [56]. Polysaccharide is one of the most important substances reported throughout years, many studies reported that *Dictyophora indusiata* polysaccharides (DIP) shows antioxidant, anti-tumor and immunostimulatory activities [49, 54, 57,56]. Therefore Water Extract from *Dictyophora indusiata* hold promise as a good source of bioactive for biopharmaceutical exploitation.

Figure 3: *Dictyophora indusiata* **(**Photographs taken by Arturo Valencia: Mexico, Veracruz, Coatepec, Ver., México, hosted by http://mycoportal.org).

Conclusion

As a conclusion, the PSP importance as a drug depends mainly on its glucans and proteoglycans. Thus, more effort should be focused on discovering other active ingredients in PSP and PSK beside β-glucan and the covalently linked peptide. Also, the quality of the active components should be standardized in order to get reliable studies performed on PSP and PSK. Further researches and clinical trials have to be carried out to confirm *Trametes versicolor* and *Dictyophora indusiata* as sources of bioactive compounds responsible for antioxidant and antimicrobial and other biological agents in their extracts.

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