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Open Access Journal of Pharmaceutical Research
ISSN: 2574-7797

Anti-Inflammatory agents from Mushrooms: A Review

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Review Article
Volume 7 Issue 2
Received Date: March 08, 2023
Published Date: April 24, 2023
DOI: 10.23880/oajpr-16000278

Abstract

Mushrooms can be highlighted as alternate sources of anti-inflammatory drugs. In recent years, natural resources have come into spotlight due to their enormous potential to be utilized in the discovery/development of novel bioactive chemicals. The anti-inflammatory properties of mushroom extracts and the bioactive metabolites that contribute to this bioactive action are reported in this review. Also, a study of the most popular assays used to gauge the anti-inflammatory effects of mushrooms was conducted.

Keywords: Edible mushroom; Anti-inflammatory Agents; *Pleurotus* Species; *Agaricus blazei, Grifola frondosa*; Therapeutic values

Introduction

Mushrooms create a wide range of secondary metabolites, including physiologically active chemicals, in addition to having a high quantity of micro and macronutrients. About 700 of the 14,000 or so species of known mushrooms are thought to be pharmacologically active. Some of these mushroom species are used as functional foods and food supplements as well as for direct consumption.

In addition to their gastronomic and nutritional qualities, mushrooms are highly valued for their pharmacological significance as sources of significant bioactive compounds, such as anti-inflammatory. Since ancient times, people have employed mushrooms as a food source and for their medical (mostly anticancer) effects. The secondary metabolites found in the fruit bodies, cultured mycelium, and cultured broth of basidiomycetes and ascomycetes are what make mushrooms more advanced. For many years, people have used mushrooms in a variety of human endeavors [1-15]. Mushrooms engage in a variety of potent biological processes that may help humans fight off sickness. Due to the diverse morphological, physiological, and ecological traits that also contribute to their diversity, several of these mushrooms have been dubbed medicinal mushrooms [16-20]. Researchers have recently focused more on the uses of mushrooms for food and medicine. Certain mushrooms and other filamentous fungi's fruiting bodies are edible or non-edible in the wild, and they are a good source of many secondary metabolites with therapeutic benefits [21-25]. With a high level of proteins, vitamins, minerals, fibers, and trace elements as well as minimal or no calories and cholesterol, mushrooms have a rich nutritional value. They enhance the diet and give individuals access to additional high-quality vegetables, both of which are directly beneficial to human health and fitness. The bioactive substances that may be extracted from medicinal mushrooms will strengthen the immune systems of people and raise their quality of life. Among the most frequent substances discovered in mushrooms are phenolics, flavonoids, glycosides, polysaccharides, tocopherols, ergothioneine, carotenoids, and vitamins [26-34].

An injury's physiological response is called inflammation, and it is characterized by loss of function as well as pain, heat, redness, and swelling. It is frequently linked to the development of conditions like diabetes, arthritis, obesity, metabolic syndrome, cancer, and a number of cardiovascular disorders. Our diet has included mushrooms for many years since they are a nutritious food. This review focuses on some significant edible, wild, and medicinal mushrooms that are found all over the world [35].

The anti-inflammatory compounds identified in mushrooms and mode of action

Eating and using edible therapeutic mushrooms as medicine have long been common practices among higher fungi. These species have physiologically active compounds with a wide range of possible health benefits for people. Several mushroom species have been shown to contain a variety of biologically active substances, including polysaccharides, vitamins, terpenes, steroids, amino acids, and trace elements [35,36].

Polysaccharides, mainly a- or b-glucans, protein-bound polysaccharides, or glycoproteins, demonstrated immunomodulatory activities through (i) increased production of cytokines (IL-10, IL-12p70 and IL-12p40) by dendritic cells (DC), (ii) activation of natural killer (NK) cells, and (iii) increased production of TNF-a, IL-1, IL-6, IL-8, IL- 12p40, and NO, and expression of iNOS by macrophages [37]. *Agaricus blazei*, *Grifola frondosa*, *Phellinus linteus*, and *Ganoderma lucidum* were some of the edible or medicinal mushrooms used in the bulk of these investigations. *Agaricus bisporus*, an edible white button mushroom, has recently been shown to increase NK cell activity in mice by increasing the production of TNF-a and IFN-g, which in turn induces the maturation of dendritic cells and IL-12 [37].

In addition to their nutritional benefits, oyster mushrooms (*Pleurotus* species) are eaten mushrooms that exhibit health-promoting (anti-atherosclerotic, antioxidant, immunomodulatory, and anticancer) activities [38]. While b-glucan showed an anti-inflammatory response in a model of acute colitis in rats when isolated from *Pleurotus pulmonarius*, and when isolated from *Pleurotus ostreatus*, it inhibited leukocyte migration to tissues damaged by acetic acid [39,40], glycosphingolipid, which was isolated from *Pleurotus eryngii*, induced secretion of IL-4 from T-cells and IFN-g [41].

The majority of investigations on the pharmacological potential of mushrooms concentrate mostly on crude extracts. But it's also critical to pinpoint the bioactive substances behind each of the claimed bioactivities. Terpenes, Polysaccharides, steroids, phenolic acids, fatty acids, and other metabolites have all been found to be anti-inflammatory substances in mushrooms. Several research have shown that among them, terpenoids, polysaccharides, and phenolic chemicals appear to be the most significant contributors to the anti-inflammatory effect of mushrooms [42-44].

Pleurotus floridanus has been shown to be a good source of antioxidants, phytoconstituents, and anti-inflammatory qualities; as a result, it can be employed in the therapy of oxidative stress-induced disease, according to Bains [45]. The strongest anti-inflammatory potential was found in the extracts of *Pleurotus ostreatus*, *Boletus impolitus, Macrolepiota procera*, and *Agaricus bisporus* [46]. These extracts (EC50 values 96 ± 1 to 190 ± 6 μg/mL, also contained the highest concentration of cinnamic acid (656 to 156 g/g), which was also the compound with the highest anti-inflammatory activity.

There are numerous pharmacologically potent substances found in *Ganoderma lucidum*. There are mainly nucleotides and nucleosides (*Adenosin, guanosin*, 5'-GMP, 5'-XMP, and 5'-deoxy-5'-methylsulphinyl adenosine which is a strong platelet aggregation inhibitor), steroids (*ergosterol*, *ganodesteron*, *24-methylcholesta-7,22-dien-3*, or *-6-ol*), proteoglycans and glycanes (polysaccharide protein complexes Ganoderan B and C) with hypoglycemic activity, peptidoglycan with blood pressure stabilizing effect, lectins, and cytotoxic polysaccharides (various hetero-(-8-Dglycans) and triterpenoids (Ganoderic acids) (5,17). This mushroom also contained various vitamins, coumarine-glycosids, lipids, and inorganic ions like Mg, Zn, Ca, Cu, Fe, and Ge. Thus, *Ganoderma lucidum* was discovered by Stavinoha et al. to be a powerful anti-inflammatory drug with positive effects [47].

A wide range of bioactive substances, including proteoglucans, polysaccharides, phenolic compounds, terpenoids, steroids, and lectins, are produced by edible mushrooms. These substances can operate as immune-modulating, antiviral, anticarcinogenic, antioxidant, and anti-inflammatory agents, among other therapeutic actions [48,49]. The species of mushroom, the substrate used, the culture and fruiting circumstances, the stage of development, the age of the fresh mushroom, the storage conditions, and the processing and cooking techniques all affect the concentration and effectiveness of the bioactive chemicals [50]. Many bioactive substances present in mushrooms have strong anti-inflammatory effects.

Coidgens's Mycoamaranthus (Pat.) An edible fungus called *Trappe*, which is naturally found in the jungles of Thailand and several other countries in Southeast Asia, was named for *S. Lumyong, P. Lumyong,* Sanmee, and Zhu L. Yang. It belongs to the Hyme-nogasteraceae family. The mushroom's thin outer membranous covering is yellowish. When it matures, its white gleba turns dark brown. This fungus is used in Thai traditional medicine to promote health, treat cancers, and assist women have regular menstrual cycles. *Mycoamaranthus combodgensis* extract had anti-oxidative, anti-inflammatory, and anti-estrogenic properties, according to Fangkrathok, et al., [51], which may be partly explained by its chemical makeup, which includes phenolics, flavonoids, and D-mannitol. These findings suggest the potential for natural product development and support the use of *Mycoamaranthus combodgensis* as a traditional medicine.

Lactarius rufus fruiting bodies' water and ethanol extracts shown strong anti-inflammatory action [52]. Water and ethanol extracts of *Pleurotus pulmonarius* showed anti-inflammatory action [53]. Both the whole mushroom extracts of *Agaricus blazei* and *Agaricus bisporus* have been shown to have anti-inflammatory properties [54,55]. Rats with Paw edema showed anti-inflammatory effects after taking *Agaricus blazei* powder in capsule form [56]. *Elaphomyces granulatus* and *Caripia montagnei* extracts in ethanol and methanol were found to have anti-inflammatory properties [57].

Smiderle, et al. [58] examined the *Cordyceps militaris* medicinal mushroom's anti-inflammatory capabilities. Several effects related to their monosaccharide content were displayed by the polysaccharide extracts from this mushroom. By inhibiting the expression of TNF-a, IL-1b, and COX-2, the alkaline extract from which a linear b- (1R3)-D-glucan was isolated demonstrated a stronger anti-inflammatory activity. The b-(1R3)-D-glucan demonstrated the same results, proving that it is the most effective anti-inflammatory substance in the *Cordyceps militaris* polysaccharide extracts. Furthermore, noted were the isolated b-(1R3)-D-antinociceptive glucan's and anti-inflammatory effects on mice with LPS- and formalin-induced nociception-induced peritonitis [58]. Mushroom native to Brazil called *Polyporus dermoporus*.

The mushrooms were dehydrated using chloroform: methanol (2:1 v/v) mixture, extracted using water at 100 °C, fractionated with ethanol, and then centrifuged. The ethanol precipitate contained 1% protein and a high quantity of total sugar (64.8%). High levels of glucan were seen in this precipitate. A signal at 103.25 ppm in the 13C NMR spectrum of these mushroom extracts indicated the presence of -glucose. These glucans have been the subject of studies to clarify their anti-inflammatory and antioxidant properties. At 67 g/mL, this glucans extract reduced both superoxide radicals (83.3%) and lipid peroxidation (42.9%). However, the mushroom extract's 96% hydroxyl radical inhibition at 267 g/mL level. At 30 mg/kg, this extract reduced polymorphonuclear cells by 92.5% and nitric oxide by 68.7% in experiments on induced pleurisy.

Overall, this polysaccharide demonstrated anti-inflammatory activity in *Polyporus dermoporus* mushrooms and had good antioxidant characteristics [59]. *Pleurotus ostreatus* is one of the most often grown culinary mushrooms, making the *Pleurotus* genus a good representation of medicinal mushrooms. In our research, we investigated the anti-inflammatory and antioxidant activities of lesser-known *Pleurotus* species. Extracts of the mushrooms were made by Stastny [60], who then examined them using HPLC-HRMS, GC-MS, and 1H-NMR. The biological activity of the *Pleurotus* spp. extracts exhibited noticeable differences. While a chloroform extract of *P. flabellatus* demonstrated considerable anti-inflammatory COX-2 activity, a MeOH extract of the species was the most effective as a radical scavenger with the highest ORAC. Ergothioneine, ergosterol, and mannitol were present in the highest concentrations in the *P. flabellatus* extract prepared with 80% MeOH. The *P. ostreatus* Florida 80% MeOH extract was the most effective in the NF- B inhibition experiment and contained the most -glucans. *P. flabellatus* has anti-inflammatory and antioxidant capabilities, thus its potential therapeutic value should be assessed through in-depth research and confirmed by clinical trials [60].

Mushrooms with Anti-Oxidant Properties

Several types of edible mushrooms have been found to have antioxidant properties. It is widely acknowledged that fungus extracts contain a variety of components, each of which has distinct biological effects [61]. Flavonoids, Phenolics, polysaccharides, glycosides, ergothioneine, carotenoids, tocopherols, and ascorbic acid were identified as the antioxidant substances present in fruit bodies, mycelium, and broth [62]. For example, techniques based on the exchange of electrons and hydrogen atoms, the ability to chelate cupric (Cu2+) and ferrous (Fe2+) particles, erythrocyte hemolysis, the electron spin resonance (ESR) strategy, and the observation of the action of SOD, CAT, and GPx are among the methods used to measure the anti-oxidative properties of mushroom compounds or concentrates [63,64].

It has been demonstrated that different stages of the oxidation process and different processes can cause mushroom agents to display their protective qualities. Primary (chain breaking, free radical scavengers) and secondary or preventive anti-oxidants are the two main categories of mushroom antioxidants [63-65]. Secondary antioxidants are created when lipid hydroperoxides are restrained or broken down, metals are deactivated, and antioxidants are recovered. Certain compounds found in mushrooms that have antioxidant properties operate as inducers and cell signals, causing changes in quality expression that lead to the activation of catalysts that destroy ROS [66-67].

Mushrooms with Analgesic Properties

When damaging excitation and primary afferent nociceptive C and A fibres are activated, the central nervous system begins to send pain signals. This is commonly brought on by the activation of various types of etabotropic receptors and ionotropic channels [68]. In addition to being a strong source of analgesics, mushrooms are also widely used to treat pain as it is a by-product of inflammation. The list of mushrooms used as analgesic are long. But the mostly used edible mushrooms are *Pleurotus pulmonarius* with active compound β-glucans [69], *Pleurotus florida* with active compound *Hydroethanolic* extract [70], *Pleurotus eous* with active compound Methanol and aquous extract [71], *Agaricus brasiliensis* with active compound Fucogalactan [72], *Agaricus bisporus var. hortensis* with active compound Fucogalactan [72], *Agaricus macrospores* with active compound Agaricoglycerides [73], *Coriolus versicolor* with active compound Polysaccharopeptides [74], *Cordyceps sinensis* with active compound Cordymin [75], *Termitomyces albuminosus* with active compound Crude saponin and polysaccharide extract [76], *Inonotus obliqus* with active compound Methanol extract [77], *Phellinus linteus* with active compound EtOH extract [78], *Lactarius rufus* with active compound Soluble β-glucans, and *Grifola frondosa* with active compound Agarucoglycerides. There are numerous mushrooms with known pain-relieving ingredients. These mushrooms also have fewer negative effects than other commercially available synthetic medications, especially the edible varieties.

Conclusion

This article focuses on the anti-inflammatory properties of certain significant edible, wild, and medicinal mushrooms that are found around the world, as well as the bioactive metabolites they contain that confer this property. Many studies have focused on the anti-inflammatory properties of both edible and inedible mushroom species; these conclusions have been made primarily based on the data from the extract rather than the bioactive chemicals themselves. *Agaricus bisporus, Phellinus linteus, Cordyceps species, Antrodia camphorate, Pleurotus* species, and *Ganoderma lucidum* have undergone the most in-depth research among the currently recognized mushroom species.

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