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Literature Review

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Natural Compounds of the Birch Polypore *Piptoporus betulinus* (Bull.) P. Karst: An Overview of Biological Activities

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Piptoporus betulinus (Bull.) P. Karst, commonly known as the birch polypore, is a medicinal fungus traditionally used in Europe and Asia for the treatment of various ailments, including infections, inflammations, and gastrointestinal disorders. Recent scientific interest has highlighted the rich phytochemical composition and pharmacological potential of this polypore. The mushroom contains a wide range of bioactive compounds such as polysaccharides, triterpenoids, phenolics, and lectins, which contribute to its anti-inflammatory, antioxidant, antimicrobial, and anticancer activities. These effects are mediated by diverse mechanisms, including immunomodulation, suppression of inflammatory signalling, inhibition of microbial proliferation, and induction of apoptosis in tumour cells. This review synthesises current knowledge on the biological properties of *P. betulinus*, drawing on both ethnopharmacological data and modern biomedical research. Preliminary results from investigations into the antioxidant properties of the fungus are also presented. The therapeutic versatility of *P. betulinus* suggests its potential role in the prevention and treatment of chronic and degenerative diseases, especially those related to oxidative stress and inflammation. Furthermore, the integration of *P. betulinus*-derived natural products into functional foods, dietary supplements or topical formulations may offer novel approaches to support health and well-being. With the growing interest in evidence-based natural remedies, this species is a promising candidate for the development of alternative or complementary therapies. However, well-designed *in vivo* studies and clinical trials remain essential to establish standardised use, safety parameters, and bioavailability of their active compounds.

Keywords: *Piptoporus betulinus*, birch polypore, medicinal mushroom, bioactive compounds, antioxidant activity, anti-inflammatory, antimicrobial, anticancer, traditional medicine

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Introduction

In recent years, there has been a resurgence of interest in the medicinal applications of traditionally used mushrooms, driven by modern scientific efforts to verify their health benefits (Hobbs, 1995; Chang et al., 2006; Lindequist et al., 2010). While traditional mycological products are highly valued and widely used in Asia, the advent of synthetic drugs in Central Europe has led to a decline in the traditional knowledge and use of medicinal mushrooms in the region (Peintner et al., 1998; Pöder and Peintner, 1999). In regions such as Asia, the USA, Canada, Mexico, and Venezuela, mushrooms have long played a role in the treatment of disease in various folk medicines (Hobbs, 1995; Chang, 1999; Garibay-Orijel et al., 2007). They are still widely used in traditional Chinese medicine (Chang, 1999). Polypore fungi, in particular, are an integral part of the pharmacopoeia and medicinal practices of indigenous peoples worldwide. In addition to their medicinal uses, polypores have also been used as food, tinder, and commodities (Blanchette et al., 1992; Kreisel, 1998; Comandini et al., 2012).

The birch polypore, scientifically known as *Piptoporus betulinus* (Bull.) P. Karst or *Fomitopsis betulina* (Bull.) B.K. Cui, M.L. Han & Y.C. Dai, is a medicinal mushroom with a long history of use in traditional medicine in various cultures. Commonly found on birch trees, this fungus has received considerable attention in recent years due to its rich array of bioactive compounds and diverse pharmacological properties (Pleszczyńska et al., 2017; Sułkowska-Ziaja et al., 2018). Throughout history, indigenous peoples around the world have used *P. betulinus* for its purported therapeutic benefits. From Europe to Asia, traditional healers have used this fungus to treat a wide range of ailments, including inflammation, infection, and gastrointestinal disorders (Pleszczyńska et al., 2017). With advances in scientific research, modern investigations have begun to unravel the molecular mechanisms underlying the medicinal properties attributed to *P. betulinus*. In this review, we provide an overview of the biological activities associated with natural products derived from *P. betulinus*. This article aims to review the existing literature on the health benefits and bioactive compounds of *P. betulinus*, an important polypore in Central European folk medicine. In addition, we will present preliminary results of our study on the antioxidant properties of this mushroom.

Materials and Methodology

A systematic literature search was conducted to identify relevant studies on the biological activities of natural products derived from *P. betulinus*. Electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, were searched for articles published up to 2024. The search terms used included "*Piptoporus betulinus*", "birch polypore", "fungus", "bioactive compounds", "biological activities", and various combinations thereof. The search was not restricted by language or publication type.

Data from eligible studies were extracted, including information on the bioactive compounds identified, experimental models used, methods of extraction and isolation, biological assays used, and results related to pharmacological activities. The extracted data were synthesised to provide a comprehensive overview of the biological activities associated with natural products from *P. betulinus*.

Results

P. betulinus is a basidiomycetous polypore fungus that grows on birch trees (*Betula* sp.) (Wasson, 1969). It is characterised by a strong, pleasant odour and an astringent, bitter taste. This fungus was traditionally used for various medicinal purposes before the advent of modern medicine. In regions such as Siberia, the Baltic, and Finland, it was used to treat various types of cancer, and was also consumed for its anti-fatigue, calming, and immune-boosting properties (Peintner and Pöder, 2000). It was believed that only young, sterile fruit bodies (those without developed hymenial layers) were effective, and these were said to develop on birch trees only under certain environmental conditions, particularly when the trees grew on low ground (Lucas, 1960).

In Poland, oral administration of birch polypore extracts to female dogs with vaginal tumours resulted in complete disappearance of the tumours after five weeks (Utzig, 1957). Externally, strips of *P. betulinus* fruit bodies have been used as a styptic, and charcoal derived from this polypore has been valued for its antiseptic properties (Thoen, 1982; Hobbs, 1995). In addition, a powder made from the fruiting bodies of *P. betulinus* has been used as a snuff in Austria. Similar uses have been reported in North America and Siberia, where snuff made from the ash of *P. betulinus* was used as a painkiller (Rutalek, 2002).

Bioactive Metabolites

Significant research efforts have focused on the primary metabolites derived from polypores (Xu et al., 2011a; Zhang et al., 2011). Fungal polysaccharides can be divided into α-glucans (such as starch, cellulose, or chitin) and β-glucans and their derivatives (Moradali et al., 2007; Jiang et al., 2010). While α-glucans show minimal bioactivity, β-glucans are known for their diverse biological properties. These β-glucans, which are major components of the fungal cell wall, are composed of glucose residues linked by β-(1,3) glycosidic linkages with side chain glucose residues linked by β-(1,6) linkages (Moradali et al., 2007). The branching frequency of these glucans varies, resulting in a diverse array of these metabolites (Mattila et al., 2000; Vannucci et al., 2013). The biological effects of fungal polysaccharides include immunoregulatory (Jiang et al., 2010), anti-tumour (Chen et al., 2008), antiviral (Seo and Choi, 2021; Guo et al., 2022), anti-inflammatory (Moro et al., 2012), antioxidant (Sun et al., 2012; Klaus et al., 2013) and hypoglycaemic activities (Cha et al., 2009; Hwang and Yun, 2010). Notably, polysaccharides have no reported adverse effects and help the body adapt to biological and environmental stress (Jiang et al., 2010).

Carboxymethylated α-(1,3)-D-glucans from the fruiting bodies of *P. betulinus* have been shown to have cytotoxic effects (Wiater et al., 2011). In addition to polysaccharides, bioactive proteins in fungi are another abundant group of primary metabolites with antitumour, antiviral, antimicrobial, antioxidant, and immunomodulatory properties (Kang et al., 1982; Xu et al., 2011b). Structurally, fungal proteins can be classified as classical proteins/peptides (including enzymes) or lectins, which are carbohydrate-binding proteins. Several bioactive primary metabolites have been isolated from *P. betulinus*. For example, nucleic acids extracted from its fruit bodies have been shown to reduce vaccinia virus plaques in chick embryo fibroblast (CEF) tissue culture by inducing interferon production *in vivo* (Kandefer-Szerszen et al., 1979).

In *P. betulinus*, about 75% of the secondary metabolites are triterpenoids, comprising about 100 different structures, while other classes of secondary metabolites are less abundant. Triterpenes, mainly lanostanes, can be further subdivided into acids, esters and lactones, alcohols, ethers and peroxides, aldehydes and ketones, glycosides and miscellaneous triterpenes. Lanostanes are triterpenes with 30 carbon atoms and a characteristic tetracyclic structure and are biosynthetically derived from lanosterol, along with dammaranes, tirucallanes, euphanes, and cucurbitanes. The second largest group of secondary metabolites in *P. betulinus*, accounting for 14%, is organic acids, with approximately 20 different types described, including aliphatic, aromatic, and related compounds.

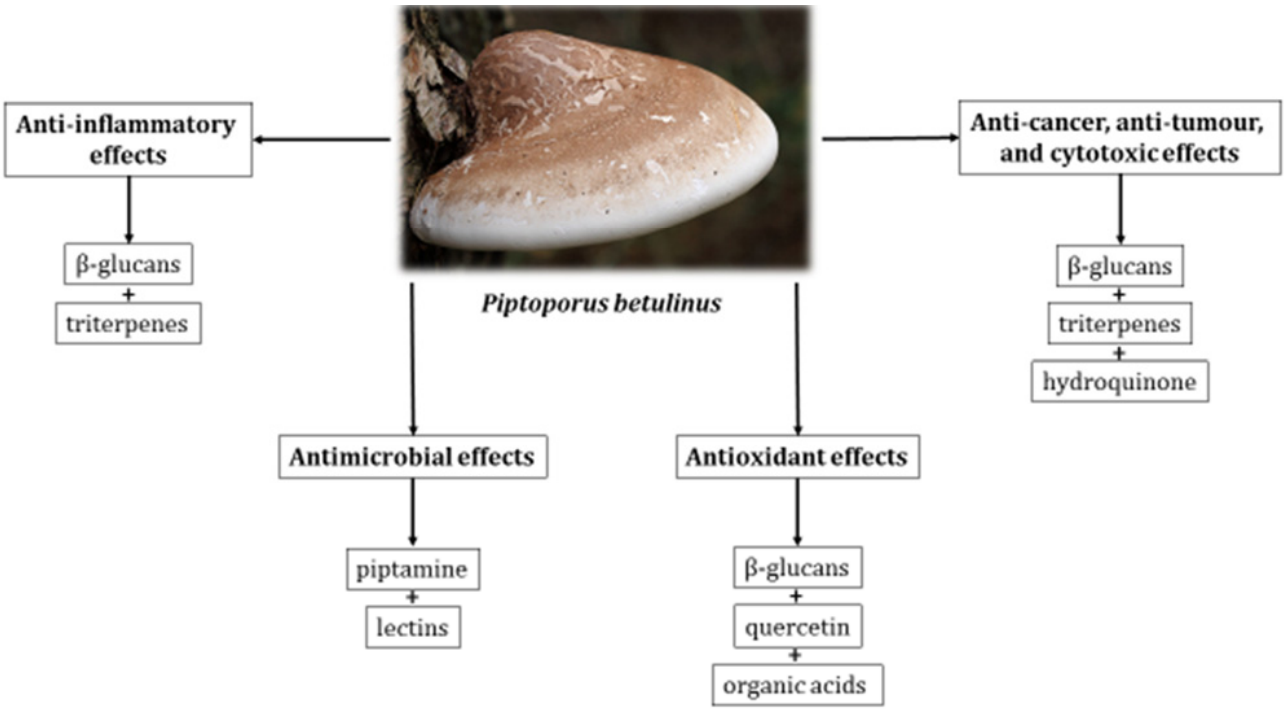

Figure 1 Chemical composition and biological activity of the birch polypore *Piptoporus betulinus* (Bull.) P. Karst.

In addition to the primary triterpenes and organic acids, this polypore also contains other compounds such as benzofurans, flavonoids, coumarins, and nitrogen-containing compounds.

Importantly, numerous triterpenes isolated from *P. betulinus*, particularly lanostane-type derivatives, exhibit a broad spectrum of pharmacological activities, including cytotoxic, anti-inflammatory, antibacterial, antiviral, antioxidant, hepatoprotective and neuroprotective effects (Kam et al., 2003; Wangun et al., 2004; Tohtahon et al., 2017; Khalilov et al., 2019). Recent studies have identified these compounds as potent inhibitors of cancer cell proliferation, inducers of apoptosis, and modulators of key signalling pathways involved in oxidative stress, immune regulation and inflammation (Czerwonka et al., 2019; Muszyńska et al., 2020; Nowotarska et al., 2024a,b). Consequently, triterpenoids from *P. betulinus* are currently considered promising lead compounds for the development of new anticancer, anti-inflammatory and immunomodulatory agents (Li et al., 2024; Nowotarska et al., 2024b). The chemical composition and biological activity of the birch polypore *P. betulinus* are shown in Figure 1.

As *P. betulinus* grows on wood, such as tree trunks or fallen logs, it is uncertain whether some of these minor constituents are produced by the fungus itself or are derived from the substrate, namely the bark of the host tree (Grienke et al., 2014).

Biological Activities

Anti-inflammatory Effects

Birch polypore contains compounds such as polysaccharides, triterpenoids, and phenolic compounds that can inhibit the production and release of pro-inflammatory mediators, including cytokines [such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β)], prostaglandins, and leukotrienes. By suppressing the expression of these inflammatory molecules, birch polypore helps to attenuate the inflammatory response (Li et al., 2021; Kozarski et al., 2024). Certain bioactive compounds found in birch polypore, such as polysaccharides and lectins, have immunomodulatory effects. These compounds may regulate the activity of immune cells, including macrophages, neutrophils, and lymphocytes, which are involved in the inflammatory response (Kozarski et al., 2024). Compounds derived from birch polypores may modulate the production of reactive oxygen species (ROS), nitric oxide (NO), and other inflammatory mediators by immune cells, thereby reducing inflammation (Anusiya et al., 2021).

Several signalling pathways, including the nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) pathways, are involved in the regulation of inflammatory gene expression. Compounds derived from birch polypore can inhibit the activation of these pathways, thereby suppressing the transcription of pro-inflammatory genes and reducing inflammation (Olędzka and Czerwińska, 2023). Emerging evidence suggests that the gut microbiota plays a critical role in modulating systemic inflammation. Birch polypore contains prebiotic compounds that may positively influence the composition and function of the gut microbiota. By promoting a healthy balance of gut microbiota, birch polypore may indirectly reduce inflammation (Jayachandran et al., 2017). Several lanostane-type triterpene acids from *P. betulinus* have been evaluated for their anti-inflammatory properties. While these triterpene acids showed weak inhibition of cyclooxygenase-1 (COX-1), they exhibited significant inhibitory activity against 3α-hydroxysteroid dehydrogenase (3α-HSD), an important enzyme in androgen metabolism. In addition, these four lanostanes showed potent selective inhibition of bacterial hyaluronidase (Wangun et al., 2004).

In addition, recent studies have confirmed that lanostane-type triterpenoids from *P. betulinus* and its polysaccharide fractions not only exert anti-inflammatory and immunomodulatory activities, but also have potent antiviral effects, including inhibition of influenza and herpes viruses. These effects are achieved both by direct inhibition of viral replication and by stimulation of interferon production, which enhances the host antiviral immune response (Kamo et al., 2003; Seo and Choi, 2021; Guo et al., 2022). This positions *P. betulinus* as a promising candidate for the development of multifunctional therapeutics with combined anti-inflammatory, immunomodulatory and antiviral properties.

Anti-cancer, anti-tumour, and Cytotoxic Effects

Birch polypore contains bioactive compounds such as polysaccharides and triterpenoids that can induce apoptosis, or programmed cell death, in cancer cells. These compounds activate signalling pathways that lead to the activation of caspases and the fragmentation of DNA, ultimately leading to the death of cancer cells (Pleszczyńska et al., 2016; Bożek et al., 2022). Compounds found in birch polypore,

including polysaccharides and triterpenoids, can inhibit the proliferation of cancer cells by arresting the cell cycle at various stages or by suppressing the expression of proteins involved in cell cycle progression. This inhibition of cell proliferation helps to slow tumour growth (Ajith and Janardhanan, 2003; Patel and Goyal, 2012). Compounds derived from birch polypore have been shown to inhibit angiogenesis, the process by which tumours develop new blood vessels to support their growth and metastasis. By suppressing angiogenesis, birch polypore inhibits the supply of nutrients and oxygen to tumours, thereby limiting their growth and spread (Lu et al., 2016; Wong et al., 2020). Birch polypore contains immunomodulatory compounds, such as polysaccharides and lectins, which can modulate the activity of immune cells, including natural killer cells, T cells, and macrophages. By enhancing immune surveillance and promoting anti-tumour immune responses, birch polypore helps the immune system to recognise and eliminate cancer cells (Pleszczyńska et al., 2017; Grunewald et al., 2018).

Birch polypore has anti-inflammatory properties by inhibiting inflammatory mediators and signalling pathways. By reducing inflammation, birch polypore may create an unfavourable environment for tumour growth and metastasis (Sułkowska-Ziaja et al., 2018). Compounds derived from birch polypore can modulate several signalling pathways involved in cancer cell survival, proliferation, and metastasis. These pathways include the PI3K/Akt/mTOR pathway, the MAPK pathway, and the Wnt/β-catenin pathway. By interfering with these signalling pathways, birch polypore inhibits cancer cell growth and promotes their apoptosis (Sun et al., 2019; Zughaibi et al., 2021). Kawagishi and colleagues (2002) reported that hydroquinone and triterpene acid isolated from *P. betulinus* act as matrix metalloproteinase (MMP) inhibitors. Specifically, compound 118 showed activity against MMP-1 (IC_{50} 28 mM), MMP-3 (IC_{50} 23 mM), and MMP-9 (IC_{50} 37 mM), whereas compound 35 showed only moderate inhibitory activity against MMP-1 (IC_{50} 126 mM) (Kawagishi et al., 2002).

In addition, recent research has highlighted the synergistic anti-cancer effects of lanostane-type triterpenoids and polysaccharides derived from *P. betulinus*. These bioactive compounds not only directly induce apoptosis and inhibit tumour proliferation, but also modulate the tumour microenvironment by enhancing the cytotoxic activity of immune effector cells and reducing immunosuppressive signals (Yadav et al., 2010; Tohtahon et al., 2017; Aly et al., 2024). Such combined effects have been demonstrated in models of breast, colon and liver cancer, suggesting the high potential of *P. betulinus* as an adjunct in integrative cancer therapies (Pleszczyńska et al., 2016; Sari et al., 2020; Nowotarska et al., 2024a,b). Furthermore, *P. betulinus* triterpenoids have been shown to increase the sensitivity of cancer cells to conventional chemotherapeutic agents, possibly by modulating drug resistance pathways (Vunduk et al., 2015; Cyranka et al., 2011).

Antimicrobial Effects

Birch polypore contains bioactive compounds such as triterpenoids and phenolic compounds that can disrupt the integrity of microbial cell membranes. These compounds interact with lipids in the cell membrane, leading to membrane destabilization, leakage of cellular contents, and ultimately cell death (Pleszczyńska et al., 2017). Some compounds found in birch polypore, such as polysaccharides, interfere with the synthesis of microbial cell walls. By inhibiting enzymes involved in cell wall biosynthesis, birch polypore prevents the formation of functional cell walls, leading to cell lysis and death (Schlegel et al., 2000). Compounds derived from birch polypore can interfere with the synthesis of nucleic acids (DNA and RNA) in microorganisms. By inhibiting enzymes involved in nucleic acid replication and transcription, birch polypore disrupts essential cellular processes, leading to microbial death (Pleszczyńska et al., 2017). Certain bioactive compounds in birch polypore, such as ribosome-inactivating proteins (RIPs) and lectins, inhibit protein synthesis in microorganisms. These compounds bind to ribosomes or interfere with translation factors, disrupting protein synthesis and causing cellular dysfunction (Landi et al., 2022; Iglesias et al., 2024). Birch polypore contains antioxidants that can generate reactive oxygen species (ROS) in microbial cells. The accumulation of ROS leads to oxidative stress and damage to cellular components, including DNA, proteins, and lipids, ultimately resulting in microbial death (Zandi and Schnug, 2022).

Compounds derived from birch polypore can modulate microbial signalling pathways involved in virulence and pathogenicity. By interfering with quorum-sensing systems or other signalling cascades, birch polypore disrupts microbial communication and coordination, reducing the ability of microorganisms to cause infection (Pleszczyńska et al., 2017). Birch polypore has immunomodulatory properties that can enhance the host immune response against microbial pathogens.

Compounds such as polysaccharides and beta-glucans stimulate immune cells, including macrophages and neutrophils, to phagocytose and kill microorganisms more effectively (Zhong et al., 2020, 2023).

The N-containing compound piptamine, isolated from *P. betulinus*, was tested against various Gram-positive bacteria, yeasts, and fungi using agar diffusion assays or standard antimicrobial susceptibility tests for aerobically growing bacteria and a broth dilution antifungal susceptibility test for yeasts (Schlegel et al., 2000). The most promising minimum inhibitory concentration (MIC) values for this compound were 0.78 $mg.mL^{-1}$ (2.35 mM) against *Staphylococcus aureus* and 1.56 $mg.mL^{-1}$ (4.70 mM) against *Enterococcus faecalis*. In addition, its haemolytic activity has been evaluated using heparinised blood from beagle dogs and was found to be between 10–50 $mg.mL^{-1}$ (30–150 mM) (Schlegel et al., 2000).

In addition, recent studies have shown that triterpenoids and polysaccharides from *P. betulinus* act synergistically, not only enhancing direct antimicrobial effects, but also effectively disrupting biofilm formation and persistence of multidrug resistant (MDR) bacterial and fungal strains. These compounds inhibit biofilm maturation by interfering with the production of extracellular polymeric substances (EPS) and reducing the expression of genes related to adhesion and biofilm architecture (Schlegel et al., 2000; Keller et al., 2002; Wangun et al., 2004; Krupodorova et al., 2019). In addition, they have been shown to sensitise resistant microbial strains to conventional antibiotics by impairing efflux pump activity and destabilising microbial membranes, offering a promising strategy to combat antimicrobial resistance (Keller et al., 2002; Pleszczyńska et al., 2017; Gaurav et al., 2023).

Antioxidant Effects

Birch polypore contains antioxidants that can neutralise reactive oxygen species (ROS) and free radicals, such as superoxide anion radicals ($O2\cdot^{-}$), hydroxyl radicals ($OH\cdot$), and peroxyl radicals ($ROO\cdot$). By donating electrons or hydrogen atoms, the antioxidants in birch polypore stabilise these highly reactive species, preventing them from causing oxidative damage to biomolecules such as DNA, proteins, and lipids (Vunduk et al., 2015). Some of the antioxidants found in birch polypore have metal chelating properties, enabling them to bind to transition metal ions such as iron and copper. Metal ions can catalyse the formation of free radicals through Fenton and Haber-Weiss reactions, leading to oxidative stress. By chelating metal ions, birch polypore prevents their involvement in these reactions and reduces the formation of free radicals (Reis et al., 2011; Stajić et al., 2013). Certain compounds in birch polypore, such as phenolic compounds, can regenerate other antioxidants, such as vitamin C and vitamin E, which are depleted in the process of scavenging free radicals. This recycling of antioxidants increases the overall antioxidant capacity of cells and tissues, providing sustained protection against oxidative damage (Sulkowska-Ziaja et al., 2012).

Compounds derived from birch polypore can stimulate the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). These enzymes play a critical role in detoxifying ROS and maintaining redox homeostasis within cells. By increasing the activity of these enzymes, birch polypore strengthens the cellular antioxidant defence system (Reis et al., 2011; Stajić et al., 2013). Oxidative stress results from an imbalance between ROS production and the body's antioxidant defence mechanisms. Birch polypore acts as an antioxidant by reducing oxidative stress, thereby mitigating the damage caused by excessive ROS production. This reduction in oxidative stress helps to maintain cellular integrity and function, promoting overall health and well-being (Vunduk et al., 2015). Oxidative stress and inflammation are closely linked, with each exacerbating the other. Birch Polypore has anti-inflammatory properties that contribute to its antioxidant effects by reducing the production of pro-inflammatory cytokines and mediators that promote oxidative stress. By suppressing inflammation, birch polypore helps to attenuate oxidative damage and maintain cellular homeostasis (Pleszczyńska et al., 2016; Bożek et al., 2022).

The antioxidant properties of *P. betulinus* are generally attributed to flavonoids such as kaempferol, quercetin, and (2R,3S)-(þ)-catechin, and organic acids such as gallic acid, *p*-coumaric acid, caffeic acid, and chlorogenic acid (Karunarathna et al., 2025). These widely known compounds are almost ubiquitous in natural products and are not unique to this particular polypore. Furthermore, their concentration in the fruit body material and their effect on antioxidant and radical scavenging activities are thought to be relatively low.

However, recent research has identified unique lanostane-type triterpenoids and specific polysaccharide-protein complexes found exclusively in *P. betulinus* that exhibit superior antioxidant capacity, particularly in protecting mitochondrial DNA (mtDNA)

from oxidative damage. These compounds not only scavenge ROS with high efficiency, but also stabilise mitochondrial membranes, improve mitochondrial respiration and prevent ROS-induced mitochondrial dysfunction – key mechanisms in slowing age-related cellular degeneration and protecting against neurodegenerative processes (Sułkowska-Ziaja et al., 2018; Li et al., 2024). These findings suggest that the antioxidant potential of *P. betulinus* may have been previously underestimated due to a focus on ubiquitous phenolic compounds, overlooking its unique bioactive matrix.

Conclusions

In conclusion, birch polypore (*Piptoporus betulinus*) is emerging as a promising natural source with diverse pharmacological activities and therapeutic potential. Through centuries of traditional use and modern scientific research, this fungus has been found to exhibit a wide range of biological activities, including anti-inflammatory, antioxidant, antimicrobial, and anticancer effects. The bioactive compounds present in birch polypore, such as polysaccharides, triterpenoids, phenolic compounds, and lectins, play a key role in mediating its pharmacological effects. These compounds act through various mechanisms, including modulation of immune responses, suppression of inflammatory pathways, scavenging of free radicals, inhibition of microbial growth, and induction of apoptosis in cancer cells. The diverse nature of birch polypore's pharmacological properties highlights its potential applications in the prevention and treatment of various diseases and health conditions. Its anti-inflammatory and antioxidant effects make it a promising candidate for the treatment of inflammatory conditions such as arthritis, inflammatory bowel disease, and dermatitis. In addition, its antimicrobial properties suggest utility in the control of infections caused by bacteria, fungi, and viruses. In addition, the anti-cancer potential of birch polypore offers hope in the field of oncology, where its ability to inhibit tumour growth, induce apoptosis, and modulate immune responses holds promise for cancer prevention and adjuvant therapy. However, further research, including preclinical and clinical studies, is warranted to elucidate the mechanisms of action, optimise dosing regimens, and assess safety and efficacy profiles. Overall, birch polypore represents a valuable natural resource with significant therapeutic implications. Harnessing its bioactive compounds and understanding their pharmacological effects may lead to novel pharmaceuticals, nutraceuticals, and functional foods developments to promote human health and well-being. Further exploration of the potential of birch polypore in integrative medicine and traditional healing systems may pave the way for its incorporation into mainstream healthcare practices, offering new avenues for disease prevention and management. Studies on the activities and mechanisms of action of fungal metabolites from European medicinal polypores are necessary to develop them into modern, evidence-based medicines. Consideration of dosage, bioavailability, and synergisms is crucial, as most existing studies are *in vitro* and lack clinical evidence. Advanced methods and sophisticated analytical techniques, integrated with biotechnology and other relevant fields, are needed. *In vivo* experiments with high-quality, long-term, double-blind clinical trials with large study populations are essential to confirm the safety and efficacy of mushroom-derived compounds. Therefore, future research should focus on characterising multi-component mixtures from well-identified fungal material, investigating their biological effects, including molecular mechanisms and bioavailability, to develop them as recognised therapeutic and health-promoting agents.

Conflicts of Interest

The authors have no competing interests to declare.

Ethical Statement

This article does not include any studies that would require an ethical statement.

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