Fomitopsis betulina (formerly Piptoporus betulinus): the Iceman’s polypore fungus with modern biotechnological potential

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Abstract Higher Basidiomycota have been used in natural medicine throughout the world for centuries. One of such fungi is Fomitopsis betulina (formerly Piptoporus betulina), which causes brown rot of birch wood. Annual white to brownish fruiting bodies of the species can be found on trees in the northern hemisphere but F. betulina can also be cultured as a mycelium and fruiting body. The fungus has a long tradition of being applied in folk medicine as an antimicrobial, anticancer, and anti-inflammatory agent. Probably due to the curative properties, pieces of its fruiting body were carried by Ötzi the Iceman. Modern research confirms the health-promoting benefits of F. betulina. Pharmacological studies have provided evidence supporting the antibacterial, anti-parasitic, antiviral, anti-inflammatory, anticancer, neuroprotective, and immunomodulating activities of F. betulina preparations. Biologically active compounds such as triterpenoids have been isolated. The mushroom is also a reservoir of valuable enzymes and other substances such as cell wall (1→3)-α-D-glucan which can be used for induction of microbial enzymes degrading cariogenic dental biofilm. In conclusion, F. betulina can be considered as a promising source for the development of new products for healthcare and other biotechnological uses.

Keywords Biological activity · Cultivation · Fomitopsis betulina · Phytochemistry · Piptoporus betulinus

Introduction

In 1991, a mummified body was discovered in the Val Senales glacier in Italy. The man (named Ötzi the Iceman), who lived 5300 years ago, carried two fragments of a fruiting body of Fomitopsis betulina (formerly Piptoporus betulinus). Some scientists believe that Ötzi might have used the fungus for medical purposes (Pöder 2005) and, although the idea arouses some controversy (Pöder 2005), the long tradition of the use of F. betulina in folk medicine is a fact (Reshetnikov et al. 2001; Wasser 2010). Infusion from F. betulina fruiting bodies was popular, especially in Russia, Baltic countries, Hungary, Romania for its nutritional and calming properties. Fungal tea was used against various cancer types, as an immunoenhancing, anti-parasitic agent, and a remedy for gastrointestinal disorders (Grienke et al. 2014; Lucas 1960; Peintner and Pöder 2000; Semerdžieva and Veselský 1986; Shamsyan et al. 2004). Antiseptic and anti-bleeding dressings made from fresh F. betulina fruiting body were applied to wounds and the powder obtained from dried ones was used as a painkiller (Grienke et al. 2014; Papp et al. 2015; Rutalek 2002).

In the present paper, we have shown the current knowledge of the fungus F. betulina, including its lifestyle, chemical composition, and potential in biotechnology.
Taxonomy and characteristics

*Piptoporus betulinus* (Bull.) P. Karst. (known as birch polypore, birch bracket, or razor strop) is a common Basidiomycota brown rot macrofungus growing on decaying birch wood. Homobasidiomycetes were divided into eight clades. The family Polyporaceae with the genus *Piptoporus* was classified to the polyporoid clade, and then the antrodia clade—the *Fomitopsis-Daedalea-Piptoporus* group comprising brown rot fungi was identified within this clade (Hibbett and Donoghue 2001; Hibbett and Thorn 2001). Further studies of the phylogenetic relationships among members of the antrodia clade revealed polyphyly of the *Fomitopsis* genus and suggested that *P. betulinus* was phylogenetically closer to *Fomitopsis* than to *Piptoporus* (Kim et al. 2005; Ortiz-Santana et al. 2013). Recently, *P. betulinus* (Bull.) P. Karst. has been transferred to *Fomitopsis* (Han et al. 2016) and, according to Index Fungorum (2016), is classified in the genus *Fomitopsis*, family *Fomitopsidaceae*, order Polyporales, class Agaricomycetes, division Basidiomycota, kingdom Fungi, with the current name *Fomitopsis betulina* (Bull.) B.K. Cui, M.L. Han and Y.C. Dai, comb.nov. (MycoBank no.: MB 812646).

*Fomitopsis betulina* is characterized by annual, sessile to effused-reflexed, tough to woody hard basidiocarps, white to tan or pinkish-colored pore surface with mostly small and regular pores. Fruiting bodies grow singly or in small groups, are covered with a laccate, glabrous crust, never zonate, young cream to white, later ochraceous-brown to greyish brown (Fig. 1a). The mycelium of *F. betulina* developing on agar media is white, relatively homogeneous, downy-felt, with regular colony edges (Fig. 1b). The hyphae develop radially. The hyphal system is mostly dimitic. The clamped generative hyphae, 1.5–3.5 µm in diameter, are branched and hyaline whereas the skeletal hyphae with the diameter of 3–4 µm, are less branched and have thicker walls. No primordia or fruiting bodies of this species were found in vitro (Petre and Tanase 2013). Basidiospores are smooth, hyaline, thin-walled, and cylindrical (Han and Cui 2015; Han et al. 2016; Kim et al. 2005; Schwarze 1993).

The birch polypore grows mainly as a saprophyte on dead trees and occasionally as a parasite of living trees. It occurs in northern temperate forests and parks in Europe, North America, and Asia. The host range of the fungus is restricted exclusively to birch species, e.g. *Betula pendula* Roth., *B. pubescens* Ehrh., *B. papyrifera* Marsh., and *B. obscura* Kotula (Schwarze 1993; Žižka et al. 2010).

Wood decay

Wood rotting fungi are traditionally divided into white and brown rot species based on the structure and composition of residual wood. Brown rot fungi extensively degrade the carbohydrate fraction of lignocellulose but, in contrast to white rot fungi, leave lignin, although in a modified form. In these fungi, chemical depolymerization of cellulose, which precedes and supports its enzymatic degradation, is very important. They lack ligninolytic peroxidases and usually some other enzymes such as processive cellobiohydrolases used for degradation of crystalline cellulose, but contain H₂O₂-generating oxidases and Fe³⁺- and quinone-reducing enzymes used for non-enzymatic depolymerization of polysaccharides (Arantes and Goodell 2014; Baldrian and Valášková 2008; Hori et al. 2013). Modern phylogenetic evidence suggest, however, that there is no sharp distinction between the two groups of fungi (Hori et al. 2013; Riley et al. 2014).

*Fomitopsis betulina* is one of the most common brown rot species but its wood-decaying mechanism has been tested only fragmentarily (Meng et al. 2012) and is still poorly understood.

**Fig. 1** *Fomitopsis betulina*. a Basidiocarp of the wild fungus. b Mycelium on an agar plate. c Mature fruiting body cultured on birch sawdust in artificial conditions. (photographed by M. Siwulski)
understood. As other fungi of this type, it degrades wood to yield brown, cubical cracks easily broken down. Many factors, including microflora or compounds present in wood, contribute to this complex process (Przybył and Złobińska-Podejma 2000; Song et al. 2016; Zarzyński 2009). Shang et al. (2013) showed that wood samples decayed by F. betulina lost 57% of dry weight (dw) and 74% of hemicellulose after 30 days, whereas the fungus growing on wheat straw causes 65% loss of dw within 98 days of culture (Valášková and Baldrian 2006a). A set of enzymes of F. betulina involved in the degradation of lignocellulose was characterized in detail by Valášková and Baldrian (2006a, b). The fungus growing on straw produced enzymes with wide substrate specificities: (1→4)-β-endoglucanase, β-glucosidase, (1→4)-β-endoxylanase, (1→4)-β-endomannanase, (1→4)-β-xylosidase, and (1→4)-β-mannosidase. The activities of ligninolytic enzymes and cellobiose dehydrogenase for oxidoreductive cleavage of cellulose were not detected. Similar results were obtained in liquid cultures by Větrovský et al. (2013). When F. betulina grew in nature, β-glucosidase and β-mannosidase activity was associated with the fruiting bodies while endopolysaccharidases were detected in colonized wood (Valášková and Baldrian 2006a).

Cultivation

Carpophores of F. betulina from natural habitats or mycelium and culture liquid from submerged cultures were used as raw material to obtain extracts and bioactive substances with medicinal properties (Table 1) (Lomberh et al. 2002). Studies concerning the mycelium growth rate in the presence of various substances (metals, dyes) were conducted mainly on agar media or in liquid cultures (Baldrian and Gabriel 2002; Dresch et al. 2015; Hartikainen et al. 2016). The yield of F. betulina mycelium was established in liquid cultures with addition of some agricultural wastes or mycelia were inoculated into birch sawdust supplemented with organic additives. Mature fruiting bodies weighing from 50 to 120 g were obtained from only one strain, after 3–4 months of the cultivation in artificial conditions (Fig. 1c). The biological efficiency ranged from 12 to 16%. It was shown that extracts isolated from cultivated and naturally grown F. betulina fruiting bodies had comparable biological activity (Table 1).

Biotechnological uses

Phytochemistry and pharmacological activity

Comprehensive analyses of the chemical composition of the F. betulina fruiting body carried out under different conditions (Grishin et al. 2016; Hybelauerová et al. 2008; Reis et al. 2011) revealed the presence of 17 fatty acids, in it 22% saturated and 78% unsaturated (mainly oleic and linoleic acid); sugars (d-arabinitol, d-mannitol and α,α trehalose); biomolecules with antioxidant properties (tocopherols—0.578 mg/100 g dw, mainly β and γ; ascorbic acid—87.5 mg/100 g dw; β-carotene and lycopene). Among other identified compounds were betulonic acid, betulin, lupeol, fomefficinic acid, ergosterol peroxide, and 9,11-dehydroergosterol peroxide (Alresly et al. 2016; Jasicka-Misiak et al. 2010). Total content of phenolics was determined on 14 or 35 mg GAE/g dw whereas phenolic acids were not detected (Reis et al. 2011; Sułkowska-Ziaja et al. 2012). Product of hydrogenation of F. betulina fruiting bodies contained numerous volatile mono- and sesquiterpenes. Several compounds found, (+)-α-barbatene, (−)-β-barbatene, daucene and isobazzanene, have not been previously reported from other mushrooms. Alcohols, 3-octanol and 1-octen-3-ol, were the main flavour constituents of the fungus (Rapior et al. 1996; Rösecke et al. 2000). Although some authors considered young specimens of F. betulina edible (Wasson 1969), the fungus value is not the result of nutritional but therapeutic properties. The overview of the available literature concerning medical potential of birch polypore was presented in Table 1. Referring to the folk uses of the birch polypore, most of the presented research was based on crude extracts, which often have greater bioactivity than isolated constituents at an equivalent dose. This phenomenon is explained by mostly synergistic interactions between compounds present in mixtures. Furthermore, extracts often contain substances that inhibit multi-drug...
Table 1: Biological properties of extracts and compounds isolated from *Fomitopsis betulina*

| Biological activity | Mechanism of biological activity | Model [method of study] | Extract* | Active compound* | References |
|---------------------|----------------------------------|-------------------------|----------|------------------|------------|
| Bactericidal        | Inhibition of bacterial growth   | *Bacillus subtilis, Mycobacterium smegmatis, Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus aureus* [zone of inhibition, agar well diffusion assay] | Extracts | | Suay et al. (2000) |
|                     |                                  | *Brucella sp.* [zone of inhibition, agar well diffusion assay] | Benzene extracts | Polypropenic acid (suggested) | Utzig and Fertig (1957) |
|                     |                                  | *Bacillus sp., Rhodococcus equi, S. aureus* [zone of inhibition, disk-diffusion method] | Chloroform extracts | | Karaman et al. (2009) |
|                     |                                  | *B. subtilis, Escherichia coli* [zone of inhibition, agar well diffusion assay] | Dichloromethane extracts | | Keller et al. (2002) |
|                     |                                  | *Bacillus sp., R. equi, S. aureus, E. coli* [zone of inhibition, agar well diffusion assay] | Methanol extracts | | |
|                     |                                  | *B. subtilis, S. lutea* [zone of inhibition, agar well diffusion assay] | Ethanol extracts | Polypropenic acid A (suggested) | Kandel-Szerszeń et al. (1981) |
|                     |                                  | *B. subtilis, E. coli, S. aureus* [zone of inhibition assay] | Eter extracts | Polypropenic acid (suggested) | Kandel-Szerszeń and Kawecki (1974), Utzig and Fertig (1957) |
|                     |                                  | *B. subtilis, Enterococcus faecalis, E. coli, S. aureus* [zone of inhibition, agar well diffusion assay, NCCLS-method] | Piplamine isolated from submerged culture of *F. betulina* | | Schlegel et al. (2000) |
|                     |                                  | *B. subtilis, E. coli, S. aureus* [zone of inhibition assay] | Mycelium, culture liquid | | Krepodorova et al. (2016) |
|                     |                                  | *B. subtilis, S. aureus* [zone of inhibition assay] | Alkali extract | 3β-acetoxy-16α-hydroxyl-24-oxo-5α-lanosta-8-ene-21-oic acid | Arley et al. (2016) |
| Fungicidal          | Inhibition of fungal growth      | *Saccharomyces cerevisiae, Aspergillus fumigatus,* [zone of inhibition, agar well diffusion assay] | Extracts | | Suay et al. (2000) |
|                     |                                  | *Candida albicans, Kluyveromyces marxianus, Rhodosporidium rubra,* *Sporobolomyces salmonicolor,* *Penicillium notatum* [zone of inhibition, agar well diffusion assay, NCCLS-method] | Piplamine isolated from submerged culture of *F. betulina* | | Schlegel et al. (2000) |
| Larvicidal          | Induction of larva death         | *Aedes aegypti* [bioassay] | Dichloromethane extract | | Keller et al. (2002) |
| Antiviral           | Protection of CEF cells from *vaccinia virus* | Host/target cells: primary culture of chick embryo fibroblasts (CEF) | Ethanol extracts | | Kandel-Szerszeń et al. (1981) |
|                     | Induction of substance with properties similar to interferon (hot-stable, stable at pH 2, nondialyzing, insensitive to RNA-se, slightly sensitive to trypsin) [Plaque formation assays] | | Water extracts | polypropenic acid (suggested) | Kandel-Szerszeń and Kawecki (1979) |
|                     |                                  | Eter extracts | | nucleic acids (RNA and DNA) | Kandel-Szerszeń and Kawecki (1974), Kandel-Szerszeń et al. (1979) |
| Biological activity | Mechanism of biological activity | Model [method of study] | Extracta | Active compounda | References |
|---------------------|----------------------------------|-------------------------|----------|------------------|------------|
| Protection of HAT cells from *vaccinia virus* by induction of interferon | Host/target cells: human fibroblast culture (HAT) challenge virus: *vaccinia virus* [plaque formation assay] | | | RNA | Kawecki et al. (1978) |
| Mice protection from lethal infection with TBE | Host/target: Swiss mice Challenge virus: *tick borne encephalitis* (TBE) virus | Ethanol extracts | | | Kandefer-Szerszeń et al. (1981) |
| Water extracts induced substance with properties similar to interferon (stable at pH, nondialyzing, sensitive to trypsin) | [Neutralization test] | Water extracts | Ethanol extracts | Nucleic acids (RNA and DNA) (suggested) | Kandefer-Szerszeń and Kawecki (1979); Kandefer-Szerszeń et al. (1979); Kawecki et al. (1978) |
| Mice protection from lethal infection with HSV-2 | Host/target: Swiss mice Challenge virus: *herpes simplex virus* type 2 (HSV-2) [neutralization test] | | | RNA | Kawecki et al. (1978) |
| Anti-inflammatory | Angiotensin I-converting enzyme inhibitory activity | | Alkali extract | | Vanduk et al. (2015) |
| Strong inhibition of 3α-hydroxysteroid dehydrogenase (3α-HSD), hyaluronicase and weak inhibition of cyclooxygenase-1 (COX-1) | [Enzyme-based assays: (3α-HSD)- assay according to the method of Penning; N-cetyl-N-trimethylammonium bromide assay according to the method of Ferrante; COX-1 assay] | | | Polyporenic acid C; (3α,12α,25S)-12-hydroxy-3-(3-methoxy-1,3-dioxopropoxy)-24-methylene-lanost-8-en-26-0ic acid; (3α,12α,25S)-3-(acetoxy)-12-hydroxy-24-methylene-lanost-8-en-26-0ic acid | Wangun et al. (2004) |
| Mice protection from ear edema induction by 12-O-tetradecanoylphorbol-13-acetate (TPA) | Mice ear edema model | | | Polyporenic acid A; polyporenic acid C; (3α,12α,25S)-3-[(carboxyacetyl)oxy]-12-hydroxy-24-methylene-lanost-8-en-26-0ic acid; (3α,12α,25S)-12-hydroxy-3-[(3 S)-3-hydroxy-5-methoxy-3-methyl-1,5-dioxopentyl]oxy]-24-methylene-lanost-8-en-26-0ic acid; (+)-12α,28-dihydroxy-3α-(30-hydroxy-30-methylglutaroyloxy)-24-methyllanosta-8,24(31)-dien-26-0ic acid | Kamo et al. (2003) |
| Antioxidant | Antioxidant capacity | [DPPH scavenging activity, FRAP method] | Water extracts | | Vanduk et al. (2015) |
| Antioxidant capacity | [DPPH scavenging activity, reducing power, α-carotene bleaching inhibition] | | | α-, β-, γ-, δ-tocopherols; ascorbic acid; β-carotene; hydroxy | Reis et al. (2011) |
| Antioxidant capacity | [FRAP method] | Water extracts | | | Sulkowska-Ziaja et al. (2012) |
| Immunomodulation | Activation of neutrophils to production of reactive oxygen forms | Neutrophils from human peripheral blood [LDCL method] | Water extracts from fruiting bodies and mycelium | p-hydroxybenzoic acid; protocatechonic acid; vanillic acid | Shamsyan et al. (2004) |
| Anticancer | Antimigrative properties | Cancer cell lines: A549, HT-29, T47D, TE671 [wound assay] | Ethanol extracts | | Płoszczynska et al. (2016); Zwołińska (2004); Zyla et al. (2005) |
| | | Cancer cell line: TE671 [wound assay] | Ethanol extracts | | Zwołińska (2004) |
| Biological activity | Mechanism of biological activity | Model [method of study] | Extracta Active compounda | References |
|---------------------|----------------------------------|------------------------|---------------------------|------------|
| Cancer cell lines: A549, C6, HT-29, T47D [wound assay] | Water extracts | | | Pleszczynska et al. (2016), Lemieszek et al. (2009) |
| Cancer cell lines: A549, HT-29, T47D [wound assay] | Water and ethanol extracts of cultivated fruiting bodies | | | Pleszczynska et al. (2016) |
| Decrease in tumor cell adhesion | Cancer cell line: LS180 [crystal violet assay] | Ethanol and ether extracts of in vitro grown mycelium | | Cyranek et al. (2011) |
| Apoptosis induction | Cancer cell line: T47D [ELISA] | Ethanol extracts | | Zwolinska (2004) |
| Cancer cell line: A549 [ELISA] | Ether extracts | | Zyla (2005) |
| Cancer cell line: A549, C6 [ELISA, May Grünwald Giemsa staining] | Water extracts | | Lemieszek et al. (2009) |
| Cancer cell line: A549, T47D, TE671 [May Grünwald Giemsa staining] | Ethanol extracts | | Zyla et al. (2005), Zwolinska (2004) |
| Decrease in cancer viability | Cancer cell line: HeLa [MTT test] | | Carboxymethylated (1→3)- α-D-glucans | Water et al. (2011) |
| Decrease in cancer viability | Cancer cell line: LS180 [MTT test] | | Ethanol and ether extracts of in vitro grown mycelium | Cyranek et al. (2011) |
| Inhibition of MMP-3, MMP-9, MMP-14 | Cancer cell line: A549 [zymography] | Ethanol and ether extracts of in vitro grown mycelium | | Zwolinska (2004) |
| Inhibition of MMP-9 | Cancer cell line: HT-29 [zymography] | Water extracts | | Lemieszek (2008) |
| Inhibition of MMP-1, MMP-3, MMP-9 | [Hydrolysis of MMP protein substrates—labeled synthetic peptides] | Ethanol extracts | (E)-2-(4-hydroxy-3-methyl-2-butenyl)hydroquinone | Kawagishi et al. (2002) |
| Inhibition of MMP-1 | [Hydrolysis of MMP protein substrates—labeled synthetic peptides] | | Polyporenic acid C | Kawagishi et al. (2002) |
| Inhibition of cancer cells proliferation | Cancer cell lines: A549, C6, HEp-2, HT-29, Jurkat E6.1, RPMI 8226, T47D, TE671 [MTT test] | Ethanol extracts | | Pleszczynska et al. (2016), Wasyl (2006), Zyla et al. (2005), Zwolinska (2004) |
| Cancer cell lines: A549, HT-29, T47D [MTT test] | Ethanol extracts of cultivated fruiting bodies | | | Pleszczynska et al. (2016) |
| Cancer cell lines: A549, C6, FTC238, HEp-2, HEp-2, HT-29, Jurkat E6.1, RPMI 8226, SK-N-AS, T47D, TE671 [MTT test] | Ether extract | | | Wasyl (2006), Kaczor et al. (2004), Zwolinska (2004) |
| Cancer cell lines: A549, HT-29, Jurkat E6.1, T47D [MTT test] | Water extracts | | | Pleszczynska et al. (2016), Lemieszek et al. (2009), Zwolinska (2004) |
| Cancer cell lines: A549, HT-29, T47D [MTT test] | Water extracts of cultivated fruiting bodies | | | Pleszczynska et al. (2016) |
| Cancer cell lines: A549, T47D [MTT test] | Polyporenic acid A | | | Zwolinska (2004) |
| Inhibition of DNA synthesis | Cancer cell line: C6 [BrdU test] | Ethanol extracts | | Wasyl (2006) |
| Cancer cell line: A549, C6 [BrdU test] | Water extracts | | | Lemieszek et al. (2009) |
| Alterations in cell cycle progression—accumulation of cancer cells in the “S” phase | Cancer cell line: FTC238 [flow cytometry] | Ether extract | | Kaczor et al. (2004) |
| Inhibition of cancer cell growth | Mouse sarcoma S-37 [not given] | | | Blumenberg and Kessler (1963) |
resistance and therefore further increase the effectiveness of the active substances. Particularly noteworthy among the wide variety of biological activities of *F. betulina* extract, are properties proved in in vivo studies, e.g. the efficacy of water and ethanol extracts in treatment of the genital tract in dogs (Utzig and Samborski 1957; Wandokanty et al. 1954, 1955) or mice protection from lethal infection with the TBE virus by water, ethanol, and ether extracts (Kandefer-Szerszeń et al. 1981; Kandefer-Szerszeń and Kawecki 1974, 1979). The broad spectrum of antiviral and antimicrobial activity of *F. betulina* extracts proved by a number of research teams in different models based on different techniques deserves special attention as well (see references cited in Table 1).

Recently, Stamets (2011, 2014) has invented formulations prepared from different medicinal mushrooms including *F. betulina*, which are useful in preventing and treating viral and bacterial diseases, i.e. herpes, influenza, SARS, hepatitis, tuberculosis, and infections with *E. coli* and *S. aureus*.

Some pure compounds corresponding to the bioactivity of the birch polypore were also identified (Fig. 2). They belong to several chemical classes but the greatest attention was paid to small molecular weight secondary metabolites, especially triterpenoids. Kamo et al. (2003) isolated several triterpenoid carboxylic acids with a lanostane skeleton, e.g. polyporenic acids and their derivatives (Table 1). In in vivo tests, the substances suppressed TPA-induced mouse ear inflammation up to 49–86% at the dose of 0.4 µM/ear. Alresly et al. (2016) purified one previously unknown (identified as 3β-acetoxy-16α-hydroxyl-24-oxo-5α-lanosta-8-ene-21-oic acid) and ten known triterpenes from ethyl acetate extract of fruiting bodies of the fungus. The new compound showed anti-gram-positive bacteria activity. The medicinal activity of some triterpenoids tested was examined more accurately. It was shown that polyporenic acid C, just like another compound isolated from *F. betulina*, i.e. (E)-2-(4-hydroxy-3methyl-2-butenyl)-hydroquinone, had inhibitory activity against some matrix metalloproteinases (MMP), with IC₅₀ values (concentration causing inhibition by 50% compared to control) in the range from 23 to 128 µM (Kawagishi et al. 2002). Polyporenic acid C and three other *F. betulina* triterpenoids (Table 1) showed anti-inflammatory and antibacterial activity by strong inhibition of 3α-hydroxysteroid dehydrogenase and bacterial hyaluronate lyase activity, respectively (Wangun et al. 2004).

In their search for fungal antimicrobial substances, Schlegel et al. (2000) isolated another valuable compound—piptamine, N-benzyl-N-methylpentadecan-1-amine from submerged culture of *F. betulina* Lu 9-1. It showed activity against gram-positive bacteria (MIC,
Fig. 2 Chemical structures of bioactive compounds isolated from *F. betulina*
minimum inhibitory concentration, values in the range from 0.78 to 12.5 µg/ml) and yeasts including Candida albicans (MIC 6.25 µg/ml).

Polysaccharides from higher basidiomycota mushrooms have been usually considered to be the major contributors of their bioactivity. However, birch polypore polysaccharides have not yet been sufficiently explored, in terms of either the structure or pharmacological activity. It is known that the Fomitopsis cell wall contains (1→3)-β-d-glucans in an amount of ca. 52% dw (Jelsma and Kreger 1978; Grün 2003). They are built from β-d-glucopyranose units connected with (1→3)-linkages in the main chain, with (1→3)-β-d linked side branches. However, there are no reports about their biological activities. Another polysaccharide isolated from the birch polypore was water-insoluble, alkali-soluble (1→3)-α-d-glucan. Although α-glucans are believed to be biologically inactive, its carboxymethylated derivative showed moderate cytotoxic effects in vitro (Wiater et al. 2011).

Miscellaneous applications

With the knowledge of the mechanisms of action of brown rot decay, there are possibilities of new applications of these fungi in biotechnology. The enzymatic and non-enzymatic apparatus for lignocellulose degradation can be used for bioprocessing of biomass towards fuels and chemicals (Arantes et al. 2012; Giles and Parrow 2011; Ray et al. 2010). Brown rot fungi, including F. betulina, were tested for bioleaching of heavy metals (Cu, Cr, and As) from wood preservatives due to accumulation of metal-complexing oxalic acid (Sierra Alvarez 2007). Production of biomass degrading enzymes, for instance cellulases, hemicellulases, amylases, etc., was also studied (Krupodorova et al. 2014; Valašková and Baldrian 2006a, b).

The cell wall of F. betulina can be a source of useful polysaccharides, e.g. water-insoluble, alkali-soluble α-glucans (Grün 2003; Jelsma and Kreger 1979). (1→3)-α-d-glucans whose main chain contains 84.6% of (1→3)-linked α-d-glucopyranose in addition to 6% of (1→4)-linked units were purified and characterized by Wiater et al. (2011). Another polysaccharide, named piptoporane I, was extracted and purified by Olennikov et al. (2012). This α-glucan was built from residues of (1→3)-α-d-glucopyranose with occasional branching by single residues of β-d-glucopyranose at the C6 position (17.3%). It has been shown that fungal (1→3)-α-d-glucans, including that from F. betulina, effectively induce the production of microbial (1→3)-α-glucanases (mutanases), i.e. enzymes that have potential in dental caries prevention. (1→3),(1→6)-α-d-Glucan (mutans) synthesized by mutants streptococci are key structural and functional constituents of dental plaque matrix; therefore, they seem to be a good target for enzymatic anti-caries strategy (Pleszczyńska et al. 2015). However, streptococcal glucans are difficult to use as inducers of mutanases because of the low yield and structural variation. Birch polypore α-glucan, whose amount in the cell wall of F. betulina reaches even 44–53% dw (Grün 2003), can be used to replace streptococcal glucans (Wiater et al. 2008).

Conclusions and outlook

The F. betulina fungus has been widely used and appreciated in folk medicine, and modern pharmacological studies have confirmed its potential indicating significant anti-microbial, anticancer, anti-inflammatory, and neuroprotective activities. The possibility of successful cultivation thereof in artificial conditions additionally promotes the applicability of the fungus. However, compared with other polypore fungi, the research on F. betulina is less developed; for instance, little is known about its lifestyle, including the wood degradation strategy. Moreover, most of the bioactivity studies have been performed using crude extracts; hence, only a few of the effects have been associated with the active substances identified, e.g. antibacterial activities with piptamine or polyporen acids. With a few exceptions, we still do not know the mechanisms underlying the biological activities. Verification of biological activities in vivo and clinical studies is also required. The further research could contribute to better exploitation of the F. betulina application potential.

Compliance with ethical standards

Competing interests The authors have no conflict of interest to declare.

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