POLISH SOCIETY FOR HORTICULTURAL SCIENCE

Folia Hort. 30(2), 2018, 191-201

DOI: 10.2478/fhort-2018-0012

FOLIA HORTICULTURAE

Published by the Polish Society
for Horticultural Science since 1989

REVIEW | Open access | www.foliahort.ogr.ur.krakow.pl

Bioactive compounds and medicinal properties of Oyster mushrooms (*Pleurotus* sp.)

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ABSTRACT

There are about 40 species in the *Pleurotus* genus, including those with high economic significance, i.e. *P. ostreatus* and *P. pulmonarius*. The fruiting bodies of oyster mushrooms are of high nutritional and health-promoting value. In addition, many species belonging to the *Pleurotus* genus have been used as sources of substances with documented medicinal properties, such as high-molecular weight bioactive compounds (polysaccharides, peptides and proteins) and low-molecular weight compounds (terpenoids, fatty acid esters and polyphenols). The bioactive substances contained in the mycelium and fruiting bodies of *Pleurotus* species exhibit immunostimulatory, anti-neoplastic, anti-diabetic, anti-atherosclerotic, anti-inflammatory, antibacterial and anti-oxidative properties. Their multidirectional positive influence on the human organism is the result of interaction of bioactive substances. Extracts from individual *Pleurotus* species can be used for the production of dietary supplements increasing the organism's immunity. They are also used for the production of cosmetics. They can be added to functional foods as probiotics, or used as natural preservatives or ingredients of special foodstuffs for patients with specific diseases.

Keywords: fruiting bodies, functional food, health-promoting activities, oyster mushrooms

INTRODUCTION

Mushrooms have been used in folk medicine all over the world since ancient times (Wasser and Weis, 1999). They have been chiefly used in traditional medicine in China and other Asian countries. Mushrooms have antineoplastic, antibacterial, antiviral, hypoglycaemic, hypocholesterolemic, anti-inflammatory and anti-oxidative properties (Guillamon et al., 2010; Wasser, 2011, 2014). *Ganoderma lucidum* and *Lentinula edodes* are the best-known species with therapeutic properties. An increasing number of studies from different centres confirm the fact that mushroom species of the *Pleurotus* genus exhibit multidirectional health-promoting effects (Khan and Tania, 2012; Stachowiak and Reguła, 2012; Deepalakshmi and Mirunalini, 2014; Correa et al., 2016). Many authors indicate that oyster mushrooms could be classified as functional food due to their positive effect on the human organism (Synytsya et al., 2008; Patel et al., 2012).

There are about 40 species in the *Pleurotus* genus (Kues and Liu, 2000). These mushrooms grow on various lignocellulosic substrates and form shell-shaped fruiting bodies of high nutritional value as they are rich in proteins, vitamins and minerals.

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At present, oyster mushrooms are the world's third most common species of cultivated mushrooms after button mushrooms and shiitake mushrooms (Fernandes et al., 2015). Poland is a leading producer of oyster mushrooms in Europe – the yearly volume of production exceeds 80,000 tonnes. *P. ostreatus* and *P. pulmonarius* are the most economically significant species of oyster mushrooms (dos Santos Bazanella et al., 2013).

Research on the therapeutic properties of oyster mushrooms started in the late 20th century. First, their hypotensive properties were confirmed (Bajaj et al., 1997). Next, studies proved the anti-neoplastic properties of the mushrooms (Wang et al., 2000). Research became intensified in the early 21st century (Cohen et al., 2002; Lavi et al., 2006; Lee et al., 2007; Li et al., 2008; Jedinak and Sliva, 2008). Studies confirmed the health-promoting and therapeutic properties of various oyster mushroom species, such as *P. ostreatus* (Fr.) Kumm., *P. pulmonarius* (Fr.) Quel., *P. ostreatus* f. *florida* Cetto, *P. cornucopiae* (Pers.) Roland, *P. eryngii* (Fr.) Kumm., *P. sajor-caju* (Fr.) Sing., *P. citrinopileatus* Sing. and *P. tuber-regium* (Fr.) Sing.

The multidirectional health-promoting and therapeutic effects of mushrooms of the *Pleurotus* genus result from the presence of secondary metabolites, which have been isolated from both oyster mushroom fruiting bodies and mycelia (Morris et al., 2017). The bioactive compounds identified in *Pleurotus* mushrooms can be divided into those with a high and those with a low molecular weight. High-molecular weight bioactive compounds chiefly encompass polysaccharides, including *β*-glucans, peptides and proteins. Low-molecular weight bioactive compounds include terpenes, fatty acid esters and polyphenols (Patel and Goyal, 2012). Bioactive substances exhibit immunostimulatory, anti-neoplastic, anti-diabetic, anti-atherosclerotic, anti-inflammatory, hepatoprotective and anti-oxidative properties (Lindequist et al., 2005; Alam et al., 2009; Jayakumar et al., 2011; Wasser, 2014).

BIOACTIVE COMPOUNDS AND THEIR ACTIVITY

Polysaccharides

The polysaccharides contained in the mushroom cell wall include *β*-glucans and *α*-glucans. These compounds are composed of glucopyranose molecules linked with glycosidic bonds of the type (1→3)-*β*, (1→6)-*β*- or (1→3)-*α*. *β*-glucans are a group of polysaccharides which has been researched well. β-glucans acquired from mushrooms differ in their structure, water solubility, size of the molecule and molecular weight. They exhibit a very wide spectrum of health-promoting effects (Zhu et al., 2015; Friedman, 2016). *β*-glucans of higher molecular weight are more effective (Wasser, 2002). The effectiveness of *β*-glucans also depends on their solubility (Wasser, 2011). The physicochemical modification of polysaccharides by changing the degree of their branching or by adding substituent groups (sulphates, selenates) influences their bioactivity (Li and Shah, 2014; Witkowska, 2014).

According to Rop et al. (2009), oyster mushrooms are one of the most important sources of *β*-glucans. Individual oyster mushroom species differ in the concentration of total glucans, *α*- and *β*-glucans. According to Sari et al. (2017), total glucans range from 18.260 g 100 g^{-1} D.M. (dry mass) in *P. citrinopileatus* to 25.636 g 100 g^{-1} D.M. in *P. ostreatus*. The concentration of *β*-glucans ranges from 15.321 g 100 g^{-1} D.M. in *P. eryngii* to 24.230 g 100 g^{-1} D.M. in *P. ostreatus*. *β*-glucans can also be found in the mycelium of oyster mushrooms. The total concentration of *β*-glucans in *P. ostreatus* fruiting bodies reaches 9 g 100 g^{-1} D.M. The concentration of *β*-glucans in the oyster mushroom mycelium ranges from 2.5 g 100 g^{-1} D.M. in *P. pulmonarius* to 4.6 g 100 g^{-1} D.M. in *P. ostreatus* (Nitschke et al., 2011). According to Synytsya et al. (2009), the concentration of *β*-glucans in the stem of *P. ostreatus* fruiting bodies amounts to 32.5-50% D.M. and is higher than in the cap (27.4-39.2% D.M.). The concentration of *β*-glucans in the fruiting bodies of *P. eryngii* amounts to 39.1 D.M. in the stem and 20.4% D.M. in the cap.

Pleuran is the best-known *β*-glucan extracted from oyster mushrooms. It is composed of D-glucose molecules linked with bonds of the type (13)-*β*- and (1→6)-*β*-. Extraction with hot water is the most common method of acquiring pleuran from fruiting bodies. It can also be obtained from liquid cultures (Maftoun et al., 2013). The compound exhibits anti-neoplastic properties against various cells, including colorectal cancer cells HT-29 (Lavi et al., 2006), prostate cancer cells PC-3 (Gu and Sivan, 2006) and breast cancer cells MCF-7 (Martin and Brophy, 2010). In addition, it has anti-oxidative and antiviral properties (Selegean et al., 2009).

A group of polysaccharides which has not been investigated so well is that of *α*-(1→3) -glucans. They can be found in the deepest layer of the mushroom cell wall. They have structural and supportive functions, and serve as a reserve material. α-glucans have been found to exhibit anti-neoplastic, immunostimulatory and anti-oxidative properties (Wiater et al., 2012). The total concentration of *α*-(1→3)-glucans in the fruiting bodies of various oyster mushroom species ranges from 2.0% D.M. in *P. eryngii* to 4.0% D.M. in *P. citrinopileatus* (Sari et al., 2017). Investigations have proved that the fraction of -glucans from *P. ostreatus* fruiting bodies exhibit an anti-neoplastic effect against colorectal cancer cell lines (Augustin et al., 2007).

The bioactivity of *α*-(1→3)-glucans depends on their solubility, structure and concentration. The activity of linear insoluble α-glucans can be increased by chemical modification. Investigations have proved that the derivatives produced by carboxymethylation of *α*-(1→3)-glucans from *P. ostreatus* exhibit high cytotoxic activity towards HeLa cell lines. The carboxymethylated *α*-(1→3) -glucan isolated from *P. citrinopileatus* exhibits cytotoxic activity to cervical cancer cells but it is not toxic to normal cells (Wiater et al., 2011, 2015).

The fruiting bodies and mycelia of different oyster mushroom species have provided a wide range of polysaccharides of diversified activity. Zhang et al. (2012) isolated two fractions of polysaccharides from *P. ostreatus* and proved their strong anti-oxidative properties. Facchini et al. (2014) proved that polysaccharides extracted from the *P. ostreatus* mycelium successfully inhibited the development of neoplastic cells of Ehrlich tumour and sarcoma 180. Two substances with anti-inflammatory properties have been isolated from the *P. sajor-caju* species: (1→3)-*β*-D-glucan and mannogalactan (Silveira et al., 2014, 2015). Cui et al. (2015) isolated the PN-S polysaccharide from *P. nebrodensis* and proved that it was capable of stimulating the activity of macrophages. Another fraction of polysaccharides (PNPA) has also been acquired from the same species. The fraction has been proved to prevent myocardial ischaemia (Yan et al., 2015). Another polysaccharide (PAP) has been acquired from *P. abalonus*. It exhibits anti-proliferative properties against human colorectal cancer cells LoVo (Ren et al., 2015). Li and Shah (2014) conducted sulphatation of polysaccharides obtained from *P. eryngii* cells. The researchers proved that this fraction of polysaccharides had stronger anti-oxidative and antibacterial properties (Li and Shah, 2015). The polysaccharides isolated from the *P. ostreatus, P. ostreatoroseus* and *P. florida* species exhibit anti-inflammatory effects (Ghazanfari et al., 2010; Gunawardana et al., 2014; Correa et al., 2015). Investigations have proved the anti-oxidative properties of polysaccharides obtained from *P. tuber-regium* (Wu et al., 2014). A *β*-glucan obtained from *P. pulmonarius* has been found to exhibit analgesic and anti-inflammatory effects (Baggio et al., 2012).

Proteins, peptides and lectins

Proteins, peptides and lectins are other high-molecular weight substances acquired from mushrooms of the *Pleurotus* genus which exhibit medicinal properties. Nebrodeolysin is a haemolytic protein isolated from *P. nebrodensis*, which induces apoptosis of neoplastic cells L929 and HeLa (Lv et al., 2009). The substance also exhibits an antiviral effect against HIV-1. A protein derived from *P. ostreatus* has a structure similar to ubiquitin and inhibits HIV-1 reverse transcriptase (Wang and Ng, 2000). A protein extract obtained from *P. ostreatus* exhibited a therapeutic effect towards the colorectal cancer cell line SW 480 and monocytic leukaemia THP-1 by inducing their apoptosis (Wu et al., 2011). In addition, eryngin and pleurostrin – the proteins isolated from the *P. eryngii* and *P. ostreatus* species exhibit antifungal and antibacterial properties (Erjavec et al., 2012). The *P. cornucopiae* species has provided two oligopeptides which exhibit antihypertensive properties (Jang et al., 2011). Moreover, the mycelium and fruiting bodies of *P. citrinopileatus* contain large amounts of ergothioneine, a water-soluble amino acid, which is considered an excellent antioxidant (Lin et al., 2016).

Enzymes isolated from oyster mushrooms also exhibit health-promoting effects. Ribonuclease from *P. djamor* inhibits the proliferation of hepatic cancer and breast cancer cells (Wu et al., 2010). Research has also confirmed the antiviral effect of laccase isolated from *P. ostreatus* against the hepatitis C virus (El-Fakharana et al., 2010).

Lectins are another group of mushroom compounds with multidirectional health-promoting effects (Wang and Ng, 2000; Hassan et al., 2015). Lectins include polysaccharide-protein and polysaccharide-peptide complexes. Research has proved that the polysaccharide-peptide complex from *P. abalonus* reduces the blood glucose level in mice (Chen et al., 2015). Lectins from *Pleurotus citrinopileatus* exhibit antineoplastic and antiviral effects (Li et al., 2008).

Other compounds

Mono- and sesquiterpenoids, ergosterol and fatty acid esters are low-molecular weight bioactive compounds identified in oyster mushrooms. Terpenoids exhibiting cytotoxicity towards HeLa and HepG2 cancer cells have been isolated from the *P. cornucopiae* mycelium (Wang et al., 2013). Menikpurage et al. (2009) researched the antifungal activity of different fractions isolated from *P. cystidiosus*. They found that the fraction containing ergosterol – 3*β*,5*α*,6*β*-trihydoxyergosta-7,22-diene was the most effective against *Colletotrichum gloeosporioides* fungi that cause anthracnose. Fatty acid esters in an extract from *P. eous* have been found to exhibit a strong antibacterial effect – they inhibit the growth of Gram-positive and Gram-negative bacteria (Suseem and Saral, 2013).

The fruiting bodies of mushrooms of the *Pleurotus* genus contain lovastatin, which belongs to the group of statins affecting the metabolism of cholesterol. These compounds inhibit LDL cholesterol oxidation and positively affect the coagulation system and fibrinolysis. They have anti-inflammatory, anticoagulation and anti-oxidative properties. According to Alarcon et al. (2003), the average lovastatin content in the dry matter of oyster mushrooms amounts to 0.7-2.8%. The concentration of lovastatin in oyster mushroom species varies, ranging from 101 mg kg^{-1} D.M. in *P. cystidiosus* to 216 mg kg^{-1} D.M. in *P. ostreatus* fruiting bodies (Chen et al., 2012). Alam et al. (2009) conducted a study on animals and proved that the lovastatin contained in powdered fruiting bodies of *P. osteratus* and *P. sajor-caju* positively affected the lipid profile as well as the hepatic and renal functions. The total cholesterol and triglyceride levels in the rats' blood decreased.

Many authors have indicated that oyster mushrooms contain phenolic compounds with anti-oxidative effects (Palacios et al., 2011; Muszyńska et al., 2013; Piska et al., 2017). Aqueous and ethanol extracts exhibiting high anti-oxidative activity have been isolated from *P. citrinopileatus* fruiting bodies and mycelium. The highest activity has been shown by ethanol extracts from the fruiting bodies of this species due to the high total concentration of phenolic compounds (Lee et al., 2007). Investigations conducted by Jaworska et al. (2015) found that the total phenolic content in *P. ostreatus* fruiting bodies amounted to 708 mg 100 g^{-1} D.M., in which the flavonoid content amounted to 170 mg 100 g^{-1} D.M. According to Gąsecka et al. (2016), ferulic acid and *p*-coumaric acid are the chief phenolic acids in oyster mushrooms. Their concentrations in the fruiting bodies amount to, respectively, 30.00 and 10.54 µg g^{-1} D.M. in *P. ostreatus* and to 29.00 and 13.49 µg g^{-1} D.M. in *P. eryngii*.

Medicinal activities and the bioactive substances found in some *Pleurotus* species are presented in Table 1.

APPLICATION OF *PLEUROTUS* MUSHROOMS IN THE PHARMACEUTICAL, FOOD AND COSMETICS INDUSTRIES

According to studies conducted so far, mushrooms of the *Pleurotus* genus exhibit numerous potentially therapeutic properties. Medicinal substances can be found in the mycelium, the fruiting bodies, and extracts from them. A therapeutic effect can be achieved by consuming fresh oyster mushroom fruiting bodies, foodstuffs containing dried oyster mushrooms or supplements with such content. The market offers a preparation based on -glucan from the fruiting bodies of *P. ostreatus*. It is used for immunotherapy when the immunity of the organism is low and there are frequent infections and allergies. Research has proved the positive influence of pleuran, which exhibits immunomodulatory properties in children with respiratory infections and allergies (Jesenak et al., 2013, 2014; Pasnik et al., 2017). Studies have also proved the positive effect of pleuran on the function of the immune system in people doing intense physical exercises (Bergendiova et al., 2011). Pleuran can be applied in antibiotic therapy and can be used in chemotherapy and radiotherapy as an adjunctive therapeutic. It also positively affects people exposed to long-lasting stress.

Oyster mushrooms can be used for the production of functional food with significant influence on human health (Wakchaure et al., 2010; Carrasco-Gonzalez et al., 2017; Piska et al., 2017). *Pleurotus* meal is used as an additive to products made from cereals, such as: breads, pastries, noodles, tortillas, etc., because it increases the protein and fibre content (Aishah and Wan Rosli, 2013). Research has proved that when the oyster mushroom additive did not exceed 10%, it did not have a negative effect on the sensory evaluation of products (Adebayo-Oyetoro et al., 2010). Researchers have conducted studies on dried oyster mushrooms used as an additive to cereal products to increase their health-promoting value. Their investigations showed that dried oyster mushrooms added to maize bread and wheat bread reduced the glycaemic index of these products (Reguła and Gramza-Michałowska, 2013). The lipid profile of patients with hypercholesterolemia

Table 1. Medicinal effects of *Pleurotus* mushrooms

Activity	Bioactive compounds	Species	References
Anti-cancer	*β*-glucans	*P. ostreatus*	Jedinak et al., 2010 Jedinak and Sliva, 2008
	α-glucan	*P. ostreatus*	Lavi et al., 2006 Wu et al., 2011
	proteins	*P. ostreatus*	Wang and Ng, 2000
		P. nebrodensis	Lv et al., 2009
Antitumour	polysaccharides	*P. ostreatus*	Tong et al., 2009
	proteoglycans	*P. ostreatus*	Sarangi et al., 2006
	lectin	*P. citrinopileatus*	Li et al., 2008
		P. ostreatus	Wang et al., 2000
Immunomodulatory	polysaccharides	*P. ostreatus* *P. cornucopiae*	Shamtsyan et al., 2004
	heteroglycan	*P. ostreatus*	Devi et al., 2013
Antihypercholesterolemic	lovastatin	*P. ostreatus*	Alam et al., 2009
		P. sajor-caju *P. florida*	Khan et al., 2011
	ergosterol	*P. ostreatus*	Dissanayake et al., 2009
Antihypertensive	D-mannitol	*P. cornucopiae*	Hagiwara et al., 2005
	peptides	*P. cornucopiae*	Jang et al., 2011
Anti-atherogenic	angiotensin converting enzyme inhibitor peptide	*P. cornucopiae*	Abidin et al., 2017
	ergothioneine	*P. eryngii*	
	chrysin	*P. ostreatus*	
	lovastatin	*P. ostreatus*	
Antiviral	proteins	*P. ostreatus*	Wang and Ng, 2000
		P. nebrodensis	Lv et al., 2009
	polysaccharides	*P. abalonus*	Wang et al., 2011
	lectins	*P. citrinopileatus*	Hassan et al., 2015
Antibacterial	*β*-glucans	*P. ostreatus*	Iwalokun et al., 2007 Karaman et al., 2010 Mirunalini et al., 2012
	fatty acids esters	*P. eous*	Suseem and Saral, 2013
Antifungal	ergosterol	*P. cystidiosus*	Menikpurage et al., 2009
	proteins	*P. ostreatus* *P. eryngii*	Erjavec et al., 2012
Anti-oxidative	phenols	*P. citrinopileatus*	Lee et al., 2007
	lectins	*P. florida*	Bera et al., 2011
	polysaccharides	*P. ostreatus*	Mitra et al., 2013 Jayakumar et al., 2011
		P. tuber-regium	Wu et al., 2014
Hypoglycemic	unspecified	*P. ostreatus*	Ravi et al., 2013
	β-glucans	*P. sajor-caju*	Kanagasabapathy et al., 2012
	polysaccharide-peptide	*P. abalonus*	Chen et al., 2015
Anti-inflammatory	polysaccharides	*P. ostreatus*	Gunawardena et al., 2014
		P. ostreatoroseus	Correa et al., 2015
		P. florida	Ghazanfari et al., 2010
Anti-arthritic	*β*-glucans	*P. sajor-caju*	Patel et al., 2012
		P. ostreatus	Rovensky et al., 2011
Anti-atopic dermatitis	pleuran	*P. ostreatus*	Park et al., 2016
Anticataractogenic	unspecified	*P. ostreatus*	Isai et al., 2009
Antinociceptive	*β*-glucans	*P. eous*	Suseem et al., 2011
		P. pulmonarius	Baggio et al., 2010, 2012

improved when they consumed bread with dried oyster mushrooms rather than traditional wheat bread. The level of total cholesterol and its LDL fraction in the plasma of all the patients decreased. The people who consumed soup with dried oyster mushrooms every day for 21 days had a lower level of triglycerides and a lower total blood cholesterol level (Schneider et al., 2011).

Oyster mushrooms can also be used for the production of fermented milk beverages. Extracts from *Pleurotus* are a good source of prebiotics due to the high soluble fibre content (Aida et al., 2009; Synytsya et al., 2009). Research has proved that when an aqueous extract from *P. ostreatus* is added to yoghurt, it stimulates the growth of useful microorganisms *Streptococcus thermophilus* and *Lactobacillus bulgaricus* (Pelaes Vital et al., 2015). Studies have also proved that an extract from *P. eous* can be added to foodstuffs as a natural source of antibacterial substances (Suseem and Saral, 2013). The study by Li and Shah (2015) proved that an extract from *P. eryngii* (PEPS) could be added to fermented milk beverages as a natural preservative.

The use of oyster mushrooms in cosmetology and dermatology is another issue. Due to the presence of antioxidants, anti-ageing, anti-wrinkle, whitening and moisturising components oyster mushroom extracts can be used for the production of various cosmetics and cosmeceuticals. A line of cosmetics containing β-glucans has been produced from a few mushroom species, including *P. nebrodensis* (Hyde et al., 2010). Extracts from *P. cornucopiae* var. *citrinopileatus* applied to mice have given positive effects against atopic dermatitis (Tomiyama et al., 2008). Research has confirmed the usefulness of *P. citrinopileatus* as a source of ingredients for the production of skin care cosmetics (Meng et al., 2011). A *P. nebrodensis* extract has proven to be a very effective skin whitener and it could be used for the production of preparations against skin discoloration (Dangre et al., 2012).

Cosmetics containing mushroom extracts are very popular in Asia. They have appeared in Europe only recently. Some countries sell hand-made soap with a *P. ostreatus* extract, which regenerates the skin. Application of a pleuran-based cream as an adjunctive therapeutic to patients with atopic dermatitis has produced good results. The latest scientific reports confirm the usefulness of different oyster mushroom species as a raw material for the cosmetics industry (Taofiq et al., 2016; Wu et al., 2016; Morris et al., 2017).

CONCLUSIONS

According to the current state of knowledge, *Pleurotus* mushrooms are a good source of bioactive substances. Although in recent years the number of studies on the health-promoting effects of *Pleurotus* mushrooms has increased rapidly, most of them have involved *in vitro* or *in vivo* experiments on animals. So far, there have been relatively few clinical trials on humans. At the same time, it is necessary to stress the fact that not all mechanisms of action of bioactive substances in oyster mushrooms have been fully investigated. At present, state-of-the-art techniques are being applied in intense research to extract new metabolites from oyster mushrooms. It will be necessary to verify their pharmacological effects *in vitro* and in clinical trials. The identification of the synergic effect of these substances in the human organism would give a possibility to take full advantage of the health-promoting and therapeutic potential of oyster mushrooms.

AUTHOR CONTRIBUTIONS

I.G.S – reviewed the relevant literature and wrote the manuscript; A.K – co-wrote the manuscript and prepared it for submission; M.S. – revised the text; T.S. and K.S. – contributed to such aspects of this manuscript as development of the idea, review of available literature and writing. All the authors are equally responsible for the content.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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Received November 4, 2017; accepted February 19, 2018