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Pharmacological importance of *Pleurotus sajor-caju* (Fr.) Singer

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Abstract
Mushrooms are reported to be nutritionally as well therapeutically beneficial to humans. They contain a wide variety of biologically active components which are responsible for their significant antimicrobial, antitumor, immunological, antidiabetic, hypocholesterolemic activities. *Pleurotus* mushrooms have, since long, been a part of human diet and traditional medicine. *Pleurotus sajor-caju* is a mushroom with high nutritional and therapeutic value as reported in various studies. This review is a compilation of the scientific investigations on the pharmacological activities of *P. sajor-caju.* This mushroom contains polysaccharides, triterpenoids, fatty acids, enzymes and is reported to have antitumor, antimicrobial, antidiabetic, antiproliferative, antioxidant activities. Therefore, it shows great potential to be developed as a natural therapy for various diseases.

Keywords: Edible mushrooms; pharmacology; *Pleurotussajor-caju;* therapeutic value

1. Introduction
Exploring natural sources for new bioactive compounds has provided many compounds with considerable therapeutic potential. Mushrooms have a long history of use in traditional systems of medicine to prevent and treat various diseases and are therefore a rich source of novel bioactive compounds [1]. Many mushrooms are being investigated chemically and pharmacologically. Various chemical constituents have been reported in mushrooms such as polysaccharides, triterpenoids, flavonoids, phenols, sterols, polysaccharide-protein and polysaccharide-peptide complexes [2, 3, 4]. Mushroom extracts and pure compounds have shown diverse pharmacological activities such as antitumor, immunomodulatory, antioxidant, antiviral, antibacterial, antifungal, antihypercholesterolemic, antidiabetic, hepatoprotective, anti-inflammatory, anticholinesterase activities [5, 6, 7].
Mushrooms of the genus *Pleurotus* are a group of higher fungi (Basidiomycetes) consisting of about 40 species [8]. During morphogenesis, their fruiting bodies open up like oyster shell, so these are commonly known as oyster mushrooms [9]. These are one of the most widely consumed mushrooms and are the third largest commercially produced mushrooms in the world [10]. *Pleurotus* mushrooms have been used in traditional medicine for various ailments such as gastrointestinal disorders, nervous disorders, high cholesterol, cardiovascular disorders, diabetes, asthma, constipation, etc [11]. *Pleurotus sajor-caju* (Fr.) Singer was first found by Yan Dai Ke, an Indian scholar, at the foot of Himalayas [12]. It is a mushroom with high nutritional and therapeutic value. Studies have reported various kinds of glucans, enzymes, fatty acids and many other constituents from this species. This paper attempts to summarize the pharmacological investigations on this species.

2. Methods
Various databases such as Pubmed, Science Direct, Scifinder, Google Scholar have been used to analyse research papers and review articles for determining the pharmacological potential of *Pleurotus sajor-caju*.

3. Pharmacological activities
The summary of pharmacological activities of *P. sajor-caju* is presented in table 1.

Table 1: Pharmacological activities of *P. sajor-caju.*

Activity	Extract/ Fraction/ Constituent	Model	Dose, Route of Administration	Observations	References
Antibacterial	Aqueous, ethanol, methanol, ether, xylene, benzene, acetone extracts.	*In-vitro* (Zone of inhibition against bacteria)	5, 10, 20, 50 % aqueous extract	All the extracts had antibacterial activity, aqueous, ethanol, methanol and xylene extracts showed better action.	13
	Ribonuclease	*In-vitro* (against 12 bacterial species)	----	Inhibition of growth of only *Pseudomonas aeruginosa* and *Staphylococcus aureus*was observed.	14
	Ethyl acetate and n-butanol extracts	*In-vitro*	----	Both the extracts had good antibacterial activity. MIC for ethyl acetate extract ranged from 3.125 to 25.00 mg/mL and for n-butanol extract from 6.25 to 12.5 mg/mL	15
	Methanol extract	*In-vitro* (against various spp. Of Gram negative and Gram positive bacteria)	----	Extract showed antibacterial activity.	16
Anticoagulant	Extracellular polysaccharide (PN) and it's sulphated derivative (PS)	*In-vitro* (APTT test)	----	PN had no activity but PS prolonged the coagulation time in a concentration dependent manner.	17
Anti-complementary	Polysaccharides from basidiocarp, mycelium and culture broth	*In-vitro* (% inhibition of TCH_{50})	----	Inhibition of TCH_{50} was observed.	18
Antidiabetic	Glucan-rich polysaccharide (GE)	*In-vivo* (OGTT, blood glucose, serum insulin, adipokines- GLUT4, adiponectin, RBP4, inflammatory markers- IL-6, TNF-α, SAA2, CRP and MCP-1 levels in C57BL/6J ob/ob mice)	60, 120, 240 mg/kg with high fat diet	Animals receiving GE showed improved glucose tolerance, attenuated hyperglycemia, hyperinsulinemia, did not develop insulin resistance, downregulated expression of inflammatory markers, increased adiponectin, GLUT 4 expression, decreased RBP 4 expression.	19
Antifungal	Petroleum ether and acetone extracts	*In-vitro* (Cup-plate assay)	----	All the extracts inhibited *Aspergillusflavus*, *Aspergilluscandidus*, *Penicilliumpatulum*, *Rhizopusstolonifer*.	20
	Ribonuclease	*In-vitro* (against *Fusariumoxysporum* and *Mycosphaerellaarachidicola*)	----	Inhibitin of mycelia growth of *Fusariumoxysporum* and *Mycosphaerellaarachidicola* with IC_{50} of 95 and 72 µM, respectively.	14
	Ethyl acetate and n-butanol extracts	*In-vitro*	----	Both extracts inhibited mycelial growth and conidium germination.	15
Antimicrobial	Alcoholic extract	*In-vitro* (disc diffusion method)	100 µl	Extract showed activity against *S. aureus*and *C. glabrata.*	21
		In-vitro (disc diffusion method)	----	Ethanol extract was active against S. aureus (20.0 mm), S. mutans(18.0 mm), M. luteus (20.0 mm), B. subtilis (10.0 mm), E. coli (14.0 mm) and S. abony (14.0 mm)	22
		In-vitro (disc diffusion method)	----	Extract showed activity against the test microbes.	23
Antineoplastic	Polysaccharide fractions F-I, F-II, F-III-I and F-III-II	*In-vivo* (Ehrlich AsciticTumor in mice)	10mg/kg i.p. daily for 6 days.	F-I, F-II fractions showed decrease in number of neoplastic cells.	24
Antioxidant	Aqueous extract (Cold and hot water extracts)	*In-vitro* (DPPH, β-carotene linolenic acid, reducing power ability, phosphomolybdate assay)	50, 100, 250, 500 µl	Cold water extracts showed higher antioxidant activity in all the assays than hot water extracts.	25
	Aqueous extract	*In-vitro* (DPPH, Hydroxyl radical and superoxide anion radical scavenging activities)	----	Extract showed concentration dependent antioxidant activity in all the assays.	26
	Aqueous extract	*In-vitro* (DPPH, SOD, catalase assays)	----	Extract showed antioxidant activity in all the assays.	27
	Ethanol extract	*In-vitro* (β-carotene	0.5-10.0 mg/ml	Extract showed significant	28

		linolenic acid, reducing power, superoxide anion radical scavenging, DPPH, metal chelation assays)	(β-carotene linolenic acid), 1.0- 10.0 mg/ml (reducing power, superoxide anion radical scavenging, DPPH assay), 2.0-10.0 mg/ml (Metal chelation assay)	antioxidant activity in all the assays.	
		In-vitro (DPPH, FRAP, reducing power, ferrous ion chelation, hydrogen peroxide scavenging, superoxide scavenging activities)	0.5- 3 mg/ml (DPPH), 2-20 mg/ml (FRAP), 2-12 mg/ml (reducing power), 3-18 mg/ml (ferrous ion chelation), 1-6 mg/ml (H_2O_2 scavenging), 4-20 mg/ml (superoxide scavenging)	Extract showed significant antioxidant activity in all the assays.	29
		In-vitro (Ferric-reducing antioxidant power, DPPH assay)	2.5, 5.0, 7.5, 10, 15, 20 mg/ml	Water extract showed higher radical scavenging activity than ethanol extract.	30
	Ethanol and aqueous extracts	*In-vitro* (DPPH, CAT, SOD, POX assays, reducing power)	2, 4, 6 mg/ml (DPPH assay, reducing power)	Extract showed signofocant antioxidant activity in all the assays.	31
	Methanol extract	*In-vitro* (free radical scavenging potential)	----	Extract showed antioxidant activity.	16
		In-vitro (DPPH, reducing power, chelating ability)	2-10 mg/ml	Extract of fruiting bodies had higher activity in DPPH assay and reducing power, while mycelial extract showed higher chelating ability.	32
		In-vitro (β-carotene bleaching method, FRAP, TEAC, LPO assay)	0.2 ml (β-carotene bleaching method), 4- 20 mg/mL (FRAP assay), 10 µL (TEAC assay), 1 ml (LPO assay).	Aqueous and butanol extracts showed highest antioxidant activity, subfractions EP1, EP2, EP3, EP4 exhibited moderate antioxidant activity.	33
	Aqueous, aqueous-ethanol, butanol, ethyl acetate extracts, fractions of ethyl acetate extract EP1, EP2, EP3, EP4	*In-vitro* (total antioxidant capacity, superoxide radical scavenging, reducing power and ferric chelating)	100-600 µg/ml (DPPH assay), 50-300 µg/ml (Hydroxyl radical and superoxide anion radical scavenging activities)	Both exhibited promising antioxidant activities.	17
	Extracellular polysaccharide and its sulphated derivative	*In-vivo* (content of GSH, TBARS, activity of SOD, catalase, GPx in livers of hypercholesterolemic rats).	5% powder with 1% cholesterol and basal diet for 40 days.	Mushroom feeding significantly improved GPx activity (50%), but had no significant effect on TBARS, GSH, SOD and catalase in liver.	34
Anti-proliferative	Extracellular polysaccharide (PN) and it's sulphated derivative (PS)	*In-vitro* (against HeLa cells)	----	PN had no activity but PS demonstrated time dependent activity, inhibition rate being 60% after 72 hours.	17
Antitumor	Aqueous extract	*In-vitro* (laryngeal carcinoma (Hep-2) and cervical adenocarcinoma (HeLa) human tumor cell	----	Extract showed antitumor activity with MIC values 0.64% ± 0.02% for Hep-2 and 0.25% ± 0.02% for HeLa.	27

		lines)			
	Polysaccharides	*In-vivo* (Sarcoma 180 in mice)	----	Polysaccharides showed antitumor activity against Sarcoma 180 cells in mice.	35
	Exopolysaccharide (PE1) and mycelial polysaccharides (PM1, PM2)	*In-vivo* (Sarcoma 180 in mice)	3, 10, 30, 100 mg/kg i.p. for 10 days.	PE1 showed maximum inhibition of S180 cells (86%), followed by PM2 (82%). PM1 showed 80% inhibition at 100 mg/kg.	36
Antiviral	Methanol extract	*In-vivo* (Pox virus and IBDV)	500µl	Extract showed antiviral activity against both the viruses.	37
Cytotoxicity lethality assay	Methanol extract	*In-vivo* (Brine Shrimp Test)	----	Extract showed cytotoxicity activity.	37
Hepato-protective effect	Mushroom extract	*In-vivo* (serum proteins, ALT, AST, GPx, SOD levels, lipid peroxidation, histopathology in broilers fed aflatoxin)	1%, 2.5%, 5% levels	Mushroom produced improvement in all parameters in a dose dependent manner.	38
Hypolipidemic effect	Powder	*In-vitro* (hypercholesterolemic rats)	5% powder in diet	Reduced total cholesterol, triglycerides, LDL/HDL ratio, body weight and increased excretion of total lipids and cholesterol in faeces.	39
Hypotensive effect	Aqueous extract	*In-vivo* (effect on mean systemic BP in rats)	----	i.v. infusion of extract reduced mean systemic BP from 110 mm Hg to 70 mm Hg at the dose of 25mg.	40
Immunological activity	β-glucan	*In-vitro* (Murine macrophage cell line Raw 264.7, NO and cytokine levels determination)	0.1-300 µg/ml	β-glucan induced the production of NO and cytokines TNF-α, IL-1β.	41
		In-vitro (NO, TNF-α levels)	----	Functions of macrophages such as NO, TNF-α production were upregulated.	42
Lipo-mobilising and insulin-like effects	β-glucan in polysaccharide hot aqueous extract (GE)	*In-vitro* (in 3T3-L1 cells)	----	GE stimulated lipogenesis, lipolysis, reduced protein carbonyl and lipid hydroperoxide levels, increased expression of 5'-AMP-activated protein kinase subunit γ-2 and γ-3, induced expressions of hormone sensitive lipase, adipose triglyceride lipase enzymes, leptin, adinopectin, glucose transporter 4 in 3T3-L1 cells.	43
Lipid peroxidation	Methanol extract	*Ex-vivo* (LOOH, TBARS formation induced by AAPH and γ-radiation in rat liver mitochondria)	0.1%	Extract significantly inhibited lipid peroxidation, formation of LOOH and TBARS.	44
Macrophage activation	Glucan-protein complex	*In-vitro* (Cell viability of murine macrophage J774A cells, NO and TNF-α activation)	100 µg/ml	Increased NO and TNF-α production, no cytotoxicity.	42
Nematicidal activity	Culture filtrate	*In-vitro*	----	The mushroom showed toxic effect against *Meloidogynejavanica*.	45
Obesity and oxidative stress	*β*-glucan-rich extract	*In-vivo* (C57BL/6J mice)	60, 120, 240 mg/kg thrice a week for 16 weeks via epigastric route.	Extract treated groups showed reduction in body weight, serum lipids, liver enzyme levels, increased enzymatic antioxidant activities, induced lipolysis, expression of hormone sensitive lipase and adipose triglyceride lipase.	46
Protease inhibition tests	Methanol extract	*In-vitro* (Screen to Nature method)	2 drops of 10 µl extract (concentration 0.5 mg/ml)	No protease activity was observed.	37
Renal effects	Aqueous extract	*In-vivo* (in rats)	----	Extract caused decrease in glomerular filteration rate.	40
Translation inhibitory activity	Ubiquitin like peptide	*In-vitro*	----	It inhibited cell-free translation with an IC_{50} of 30 nM	47

Viability of tumor cells	Ribonuclease	*In-vitro* (against HepG2 and L1210 cells)	----	Viability of tumor cells was reduced with an IC_{50} of 0.22 and 0.1 µM for hepatoma and leukemia respectively.	14

MIC: Minimum inhibitory concentration; TCH_{50}: Total haemolytic complement; OGTT: Oral glucose tolerance test; GLUT4: Glucose transporter type 4; RBP4: Retinol binding protein 4; SAA2: Serum amyloid A2; CRP: C-reactive protein; MCP-1: Monocyte chemoattractant protein 1; POX: Peroxidase; FRAP: Ferric reducing antioxidant power; TEAC: Trolox equivalent antioxidant capacity; LPO: Lipid hydroperoxide; DPPH: 2,2-diphenyl-1-picrylhydrazyl; IBDV: Infectious Bursal Disease; ALT: Alanine transaminase; AST: Aspartate transaminase; GPx: Glutathione peroxidise; SOD: Superoxide dismutase; IL: Interleukin; LOOH: Lipid hydroperoxide; TBARS: Thiobarbituric acid reactive substances; AAPH: 2,2'-Azobis(2-amidinopropane) dihydrochloride; NO: Nitric oxide; TNF-α: Tumor necrosis factor α.

4. Conclusion

From the review of available literature, it is evident that *Pleurotus sajor-caju* is a mushroom of biomedical importance containing a variety of chemical constituents such as polysaccharides, triterpenoids, volatile compounds, ergosterol, vitamin C and enzymes. It has been used in traditional systems of medicine for treatment of various ailments. The traditional uses have been scientifically validated through various pharmacological studies and the results revealed that the mushroom has antitumor, hypotensive, hypolipidemic, immunological, hepatoprotective, antidiabetic, antimicrobial, anticoagulant activities. Many of these investigations are preliminary and only indicate activity of the mushroom, but do not show the mechanism or the safe doses of the bioactive extract/fraction. Detailed systematic investigations are required so that the constituent/s of *P.sajor-caju* responsible for a particular activity may be separated and characterised. For example, glucan rich polysaccharides isolated from the mushroom have shown antidiabetic and antineoplastic activity and ribonuclease has antibacterial and antifungal potential. In order to develop these as nutraceuticals or as medicines detailed safety and efficacy studies should be undertaken. It may be concluded that *P. sajor-caju* is a mushroom with high pharmacological potential and detailed mycochemical and pharmacological evaluation is required to develop it is a therapeutic agent for management of various diseases.

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