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Bioactive compounds with special references to anticancer property of oyster mushroom *Pleurotus ostreatus*

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Abstract
Pleurotus ostreatus is a macro fungus belongs to the class Basidiomycetes and family Agaricaceae, known as the oyster mushroom. Globally the mushroom is the second most cultivated for food purposes. It is reputed for its nutritional and pharmacological uses and a number of pure bioactive compounds have been isolated from its different solvent extract of the fruiting body and mycelium. Several research papers reported that those bioactive compounds exhibit many health beneficial activities such as tumour chemopreventive, antiviral, immunomodulatory, anti-inflammatory, hypocholesterolemic activity etc. The short review embraces updated information about the bioactive compound of anticancer activity of *P. ostreatus*. A total number of 13 reported anticancer activities, students was consulted in this review and a critical analysis revealed that different solvent extract and polysaccharide extract of *Pleurotus ostreatus* showed significant anticancer activity on animal cell line and human cell lines compared with control.

Keywords: *Pleurotus ostreatus*, antileukemic, immunomodulatory, polysaccharide extracts, *in vitro*

Introduction
Mushrooms are considered as a source of nutrition and provide pharmacologically important bioactive compounds useful in medicine [1]. Consumption of edible fungi to fulfill human nutritional needs has been a common denominator in the history of mankind. The increased nutritional importance is due to the nutritive value of high-grade mushrooms, which almost equals that of milk [2]. Mushrooms constitute an integral part of the normal human diet mostly for its unique flavour, meaty taste and medicinal value [3] and are considered as valuable health foods because of low in calories, fats and essential fatty acids, and high in vegetable proteins, vitamins and minerals [4-7]. The different substrates used in cultivating these mushrooms, obviously have a significant effect on the nutritional and functional properties of oyster mushroom [8].

Pleurotus ostreatus (Jacq. ex Fr.) P. Kumm., known as oyster mushroom is a macro fungus of the family Agaricaceae under the class Basidiomycetes [9] which mainly grows on dead and hardwood trees [10], capable of degrading lignin and cellulose [11, 12]. It is the second most important cultivated mushroom for food purposes throughout the globe [13]. *Pleurotus ostreatus* are reported for its several pharmacological activities which are associated with various health promoting activities e.g. prebiotic, tumor chemopreventive, antiviral, immunomodulatory and anti-inflammatory properties [14-18].

Now a days, Cancer is one of the major leading causes of human death which is currently estimated at 8.2 million and will likely rise to 13 million worldwide per year till 2030 [19]. Current treatments for cancer include chemotherapy, radiotherapy and chemically derived drugs. Treatments such as chemotherapy and radiotherapy can put patients under a lot of strain and further damage of their health. Therefore, recently there is a focus on using alternative treatments and therapies against cancer [42].

From the very earlier civilization phytoresources are used in health beneficiary purposes in human life or traditional medicines from generation to generation. It is reported that over 60% of currently used anti-cancer agents are come from natural sources [20]. Thus, research has developed into investigating the potential properties and uses of terrestrial phytoresources for the preparation of potential drugs for curing diseases including cancer. In this review various important types of anticancer application and available potent bioactive compounds are recorded from oyster mushroom and to exploit by the pharmaceutical industry to generate green medicine for treatment of cancer and ailments.

Bioactive composition of *Pleurotus ostreatus:* Bioactive compounds with their bioactivity of *Pleurotus ostreatus* had been reported by several researchers. Different solvent extracts contained large number of structurally diverse compounds and near about 200 structurally diverse chemical compounds were estimated. The major bioactive compounds are listed in Table No. 1.

Table 1: Bioactivities and active compound of *P. ostreatus*

Sl. No.	Bioactivity	Bioactive Compounds	References
1	Antimicrobial activity	3-(2-aminopheny1thio)-3-hydroxypropanoic acid, p-Hydroxybenzoic acid, Protocatechuic acid, Syringic acid, Vanillic acid, Caffeic acid, Cinnamic acid, Ferulic acid, Syringaldazine, O-dianisidine, 2,6-dimethoxyphenol, 1-octen-3-ol, Benzoic acid , 3-octanone, 3-octanol; 4-hydroxy-benzoic Acid, 14, 17- Octadecadienoic acid, methyl ester (E,E); N-8-Guanidino-spermidine; 9,12-Octadecadienoic acid, methyl ester (E,E); p-anisaldehyde (4-methoxybenzaldehyde); Protocatechuic acid; Chlorogenic acid.	[21, 22, 23]
2	Anticancer activity	Resveratrol, Cibacron blue affinity purified protein; *Pleurotus ostreatus* mycelium polysaccharides 2 (POMP2), *Pleurotus ostreatus* polysaccharides -1(POPS-1).	[24, 25, 26]
3	Antitumor and immunomodulating effects	Concanavalin A, Cibacron blue affinity purified protein.	[24,27]
4	Anti-inflammatory activity	Concanavalin A.	[28]
5	Nematicidal activity	As*trans*-2-decenedioic acid	[29]
6	Antioxidant activity	Pleuran, Ergosta-7,22-dienol; α-tocopherol; Ergosta-5,7-dienol; Ergosta-7-enol; Ergosterol.	[4,30,31]
7	Antirespiratory tract infections	Pleuran	[32]
8	Hypocholesterolemic Effect	Linoleic acid, Lovastatin, Ergosterol	[33]
9	Prebiotic activity	β-(1,3/1,6)-D-glucan, 1,3-α-glucan	[34]

Anti-cancer activity

Cytotoxic bioassay of Ethyl acetate, hexane and chloroform extract of *Pleurotus ostreatus* in different concentrations on brine shrimp lethality bioassay was resulted the LC_{50} values of 10 µg/ml, 40µg/ml and 75µg/ml for hexane, ethyl acetate and chloroform, respectively. Results revealed that *Pleurotus ostreatus* has potent anticancer activity [35]. A recent experiment showed that polysaccharides extracted from *Pleurotus ostreatus* mycelium component, *Pleurotus ostreatus* mycelium polysaccharides 2 ($POMP_2$) had a significant inhibitory effect on the BGC-823 human gastric cancer cell line *in vitro* and MTT assay resulted that $POMP_2$ when administered at a concentration of 400 mg/l for the time 72 h, the rate of inhibition was 35.6%. Male BALB/c (nu/nu) nude mice were inoculated with injections of 2×10^6 BGC-823 cells per mouse and tumor bearing were treated by orally administered $POMP_2$ at the doses 50 mg/kg, 100 mg/kg and 200 mg/kg in which 100 mg/l $POMP_2$ resulted significant reduction in colony formation in BGC-823 cells ($P<0.05$) [25].

The different polysaccharide fraction extracted from mycelium biomass of *Pleurotus ostreatus* inhibited the development of Ehrlich Tumor (ET) and Sarcoma 180 (S180) but a fraction 30mg/kg apparently had no toxic effect on healthy animals.[18] A gemmotherapic extract in different concentrations from young parts of *Pleurotus ostreatus* exhibited a significant inhibitory effect in HCT- 116 cell line (colorectal carcinoma cell line) by MTT assay (3-[4,5-dimethylthizol-2-yl]-2,5-diphenyltetrazolium bromide) and results suggested that the extract had a significant inhibitory activity in HCT-116 cells [36].

Furthermost investigation revealed that, water soluble *P. ostreatus* polysaccharide extract on human Caco-2 cells reduced the secretion of MMP-2 and MMP-9 and inhibited the invasion of Caco-2 cells (colon cancer cells) through the basement membrane but did not induce apoptosis in Caco-2 cell line [37]. The Anti-leukemic and immunomodulatory effects of *P. ostreatus* metabolites was reported using on benzene-induced leukemia in Wister rats model. *P. ostreatus* metabolites enhanced leukopoiesis and showed phagocytic actions. This experiments exhibited profound anti-leukemic potential by suppressing leukemia ($P<0.05$) and demonstrated immunotherapeutic activities on Wister rats models after oral administration in various experimental groups [38]. In the *In-vitro* study and in-vivo study showed that Cibacron blue affinity purified protein (CBAEP) extracted from *P. ostreatus*, has been shown to have potent anticancer, immunomodulatory and antitumor activity against Dalton lymphoma (DL)-bearing mice, Sarcoma-180, and B16F0 melanoma tumor-bearing mice. The results showed that CBAEP reduced about 35.68 and 51.43% Dalton lymphoma (DL) cell growth in 5 mg/kg and 10 mg/kg body weight, respectively and activated immunosuppression condition in DL tumor-bearing mice. [24]

A polysaccharide POPS-1 isolated from *P. ostreatus* showed *in vitro* antitumor activity against Hela tumor cell and compared with 5-fluorouracil, exhibits significantly lower cytotoxicity to human embryo kidney 293T cells than Hela tumor cells . As a result it may be considered as a potential drug for developing a novel low toxicity antitumor agent [26].

The polysaccharide extract from *Pleurotus ostreatus* exhibited the inhibitory results to the development of Ehrlich ascitic tumor cells and reduced the neoplasic cells at the level 76% in the female Swiss albino mice [40]. *Pleurotus ostreatus* showed the potential therapeutic or preventive action on human breast and colon cancer cells [41]. Water-soluble proteoglycan fractions from *P. ostreatus* mycelia showed the *in vitro* and *in vivo* immunomodulatory and anticancer effects on Sarcoma180 bearing mouse model. In vivo injection of proteoglycans to Sarcoma 180 bearing mice decreased the number of tumor cells. Thus the proteoglycans derived from *P. ostreatus* mycelia may be used as immune-modulators and anti-cancer agents [27]. Another experiments showed that DNA isolated from fruit bodies of *P. ostreatus* possessed immunomodulatory activity and biotherapeutic potential. *In vitro* administration of the mushroom DNA resulted in extends of NK cytotoxic activity and significant increase of the life span of mice treated with solid Ehrlich carcinoma [39].

Table 2: Summary of reports of anticancer activity of *Pleurotus ostreatus*:

Sl. No	Experimental model	Supplementation	Outcome/ Result	References
1.	HCT- 116 cell line (colorectal carcinoma cell line)	Gemmotherapic extract of young parts of *P. ostreatus*	Exhibit antitumor activity.	[36]
2.	Ehrlich Tumor (ET) and Sarcoma 180 (S180)	Polysaccharide fraction extracted from mycelium biomass of *Pleurotus ostreatus*	Inhibited the development of Ehrlich Tumor (ET) and Sarcoma 180 (S180)	[18]
3.	Brine shrimp lethality bioassay	Ethyl acetate, hexane and chloroform extract of *Pleurotus ostreatus*	Potent anticancer activity	[35]
4.	BGC 823 human gastric cancer cell line *in vitro/in vivo*	Polysaccharides extracted from *Pleurotus ostreatus* mycelium and a compound *Pleurotus ostreatus* mycelium polysaccharides 2 (POMP2)	POMP2 inhibited the proliferation of BGC-823 cells in vitro/ in vivo	[25]
5.	Male BALB/c (nu/nu) nude mice	Polysaccharides extracted from *Pleurotus ostreatus* mycelium and a compound *Pleurotus ostreatus* mycelium polysaccharides 2 (POMP2)	POMP2 significantly decreases the tumor weight compared with control *in vivo*	[25]
6.	Human Caco-2 cell line in vitro	*Pleurotus ostreatus* polysaccharide extract	Down-Regulates the Expression of MMP-2 and MMP-9 on human Caco-2 cells.	[37]
7.	Benzene-induced leukemia in Wister rats	Fungal metabolites of *Pleurotus ostreatus*	Enhanced leukopoiesis, showed phagocytic actions and exhibits significant therapeutic potential to suppress leukemia ($P<0.05$)	[38]
8.	Dalton lymphoma (DL)-bearing mice, Sarcoma-180, and B16F0 melanoma tumor-bearing mice	Cibacron blue affinity purified protein (CBAEP)	CBAEP reduced Dalton lymphoma (DL) cell growth and activated immunosuppression condition in DL tumor-bearing mice.	[24]
9.	Hela tumor cell and human embryo kidney 293T cells in vitro	Aqueous polysaccharide POPS-1 of fruiting bodies of *Pleurotus ostreatus*	Significantly higher antitumor activity against Hela tumor cell in vitro and lower cytotoxicity to human embryo kidney 293T cells.	[10]
10.	The Ehrlich ascitic tumor bearing female Swiss albino mice	Polysaccharide extract from *Pleurotus ostreatus*	Inhibit the development of Ehrlich ascitic tumor cells and reduced the neoplasic cells.	[40]
11.	Breast cancer (MCF-7, MDA-MB-231) and colon cancer (HT-29, HCT-116) cells	P. ostreatus extracts	P. ostreatus prevents the proliferation of breast and colon cancer cells	[41]
12.	Sarcoma 180 bearing mouse *in vitro/ in vivo*	Water-soluble proteoglycan fractions from P. ostreatus mycelia	Sarcoma 180 bearing mice decreased the number of tumor cells in vivo.	[27]
13.	Mice with solid Ehrlich carcinoma	DNA isolated from the fruit body of P. ostreatus	Increase of the life span of mice with solid Ehrlich carcinoma.	[39]

Conclusion: Oyster mushroom composed of several bioactive compounds which showed profound anticancer activity against various cancer cell lines *in vitro* and *in vivo* animal models. The multiple activities exhibited by this mushroom can be attributed due to possession of large number of active principles. There is still need to carry out further research to identify other more active principles involved in different activities. This documentation will help pharmaceutical industry to formulate novel drugs from *P. ostreatus* for treatment of various types of cancer, targeted diseases and ailments.

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