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Review

Pharmacological and therapeutic inventory of fungi in cancertherapy—A comprehensive review

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Abstract: Cancer remains one of the foremost causes of death worldwide. Despite advancements in pharmaceutical therapies, patients continue to experience adverse effects. Consequently, there is a considerable interest in exploring mushrooms as a supplemental cancer treatment. In Asian countries, edible and medicinal mushrooms have long been consumed in both culinary practices and herbal remedies. Their health and nutritional benefits have also garnered rising attention in Europe. Food-grade mushrooms have a variety of pharmacological properties, including soothing and immunomodulating effects, and are associated with abundant therapeutic benefits. The primary mechanisms behind their anticancer activity comprise immune system improvement, cell cycle arrest, regulation of apoptosis, prevention of metastasis, and inhibition of cancer cell growth. Here, we thoroughly review the anticancer activities of several culinary and medicinal mushrooms, as well as some endophytic fungi, with a particular focus on potential bioactive compounds and their molecular mechanisms.

Keywords: anticancer compound; antitumor; endophytic fungi; cytotoxicity; immunomodulatory; mushroom; nutraceuticals; secondary metabolites

Appendix

Table S1. List of bioactive compounds isolated from fungal species that exhibit anticancer or antitumor activities.

Chemical Class	Bioactive Compound	Fungal Source	Mechanism of Action	Type of cancer prevented	Experimental condition	Ref.
A. Polyketides	Fumagillin	*Aspergillus fumigates*	Strongly inhibiting degrees of expression of MMP-2, -9 in MCF-7, targets 14-3-3 protein	Breast carcinoma	***In vitro***: MCF-7 cell line; ***In vivo***: Mouse xenograft models (e.g., breast cancer models)	[29,30]
	Lovastatin	*Aspergillus terreus*	termination of the cell cycle at the G0/G1 stage and enhancement of p21 expression levels	Myeloid leukemia, fibrosarcoma, breast carcinoma, lymphoma, thyroid and prostate cancer, ovarian cancer, bowel cancer, and so forth.	***In vitro:*** Leukemia cell lines (e.g., HL-60), breast cancer cell lines (e.g., MCF-7)	[31,32]
	Citreoviridin	*Penicillium spp.*	arrest of the G0/G1 cell cycle, linked to higher transcription of p53 and p21 and lower levels of cyclin D1	Endothelial cell cancer	***In vitro:*** Endothelial cell lines (e.g., HUVEC)	[33]
	Radicicol	*Chaetomium spp., Monosporium*	Hsp90 inhibition	Breast cancer	***In vitro***: Breast cancer cell lines (e.g., MDA-MB-231); ***In vivo***: Mouse xenograft models	[34]
	Cryptocin	*Penicillium species*	Triggering cell cycle halt and cell death.		***In vitro***: Various cancer cell lines (e.g., HeLa, A549)	
	BE-40644	*Aspergillus sp., Actinoplanes mould.*	demonstrates cellular damage to many carcinoma cell lines and impairs the thioredoxin machinery.	Multiple human cancers	***In vitro***: Various carcinoma cell lines (e.g., HCT-116, A549)	[35]

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Chemical Class	Bioactive Compound	Fungal Source	Mechanism of Action	Type of cancer prevented	Experimental condition	Ref.
A. Polyketides	BE-14106	*Candida* strains	Inhibition of tubulin polymerization		***In vitro***: Cancer cell lines (e.g., HeLa, MCF-7)	[36]
	Nigrosporin B	*Nigrospora oryzae*	Promotes protective autophagy and apoptosis via blocking the signaling pathway of PI3K, AKT, and mTOR.	Human cervical cancer and several other cancers	***In vitro***: Cervical cancer cell lines (e.g., HeLa); ***In vivo:*** Mouse xenograft models	[37]
B. Alkaloids	Camptothecin	*Penicillium chrysogenum, Entrophosporain frequens*	Topoisomerase I inhibition, resulting in a breakdown of protein-DNA	Human colorectal carcinoma, ovarian cancer and laryngeal or squamous cell carcinoma	***In vitro***: Colorectal cancer cell lines (e.g., HCT-116); ***In vivo:*** Mouse models	[38,39]
	Vincristine, Vinblastine	*Talaromyces sp., Alternaria sp., and Cladosporium sp.*	Microtubule inhibition	Solid tumors, ALL (acute lymphocytic leukemia), and lymphomas.	***In vitro***: Leukemia cell lines (e.g., Jurkat); ***In vivo***: Mouse leukemia models	[40]
	Ergot alkaloids	*Claviceps purpurea*	Promotes apoptosis by activation of Caspase-3 showing secondary necrosis	Leukaemia, renal carcinoma, colon cancer, brain tumor, ovarian cancer, lung cancer, prostate cancer, and melanoma	***In vitro***: Leukemia cell lines (e.g., HL-60); ***In vivo:*** Mouse xenograft models	[41]
	Spirobrocazine C Brocazine G	*Penicillium brocae*MA-231		Ovarian cancer	***In vitro***: Ovarian cancer cell lines (e.g., SKOV-3)	[42]

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Chemical Class	Bioactive Compound	Fungal Source	Mechanism of Action	Type of cancer prevented	Experimental condition	Ref.
	Fumitremorgin C	*Aspergillus fumigates*	Reduced Bax expression that is pro-apoptotic and PI3K, Ras, Akt, Bcl-xL, and Bcl-2 protein upregulation deployed caspase-3, -8, and -9, resulting in PARP cleavage.	Prostate cancer	***In vitro***: Prostate cancer cell lines (e.g., PC-3); ***In vivo:*** Mouse xenograft models	[43]
	Indole alkaloids	*Aspergillus fumigates*	Diverse antiproliferative activities	Cervical, colon cancer, and leukemia, myelogenous leukemia	***In vitro***: Cervical cancer cell lines (e.g., HeLa); ***In vivo:*** Mouse xenograft models	[44]
	Verticillin A	*Clonostachys sp.*	reducing the activity of the SUV39H1 and SUV39H2 enzymes to prevent the trimethylation of histone H3 on lysine 9.	Pancreatic and ovarian cancer, Colon carcinoma	***In vitro***: Pancreatic cancer cell lines (e.g., PANC-1); ***In vivo***: Mouse xenograft models	[45,46]
	Secalonic acids	*Aspergillus spp., Pyrenochaeta spp., Claviceps spp.*	apoptosis induction and cell growth suppression	Hepatocellular carcinoma, colorectal adenocarcinoma, pancreatic cancer etc.	***In vitro***: Hepatocellular carcinoma cell lines (e.g., HepG2); ***In vivo***: Mouse models	[47]
	Stephacidin A	*Aspergillus ochraceus*	Inhibits Heat shock protein 60, a mitochondrial chaperone		***In vitro***: Cancer cell lines (e.g., MCF-7, A549)	[48]
C. Peptides	L-Asparaginase	*Aspergillus niger*	Depletion of asparagine in cancer cells, lessen the production of hazardous acrylamide	Acute lymphoblastic leukemia	***In vitro***: Leukemia cell lines (e.g., Jurkat); ***In vivo***: Mouse leukemia models	[49]
	Aureobasidin A	*Aureobasidium pullulans*	Interferes with ATP-binding cassette transporters, traps anticancer agents like vincristine in cancer cells with the help of P glycoproteins	Lung cancer	***In vitro***: Lung cancer cell lines (e.g., A549); ***In vivo:*** Mouse xenograft models	[50]

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Chemical Class	Bioactive Compound	Fungal Source	Mechanism of Action	Type of cancer prevented	Experimental condition	Ref.
D. Polysaccharide	Schizophyllan	*Schizophyllumra diatum*	Modulates immune response	Breast cancer	***In vitro***: Breast cancer cell lines (e.g., MCF-7); ***In vivo***: Mouse xenograft models	[51,52]
E. Terpenoids	Taxol (Paclitaxel)	*Taxomyces Andreanna, Phoma medicaginis*	Prevents the microtubule from depolymerizing. It does this by attaching to the β-tubulin subunit's N-terminus, forcing the G2/M-phase cell cycle to stop, which in turn triggers Cell death.		***In vitro***: Various cancer cell lines (e.g., HeLa, MCF-7); ***In vivo***: Mouse xenograft models	[53,54]
	Demethoxyviridin	*Nodulisporium*s p.	Inhibits PI3Kinase		***In vitro***: Cancer cell lines (e.g., MCF-7, A549)	[55]
	Ganoderic acids	*Ganoderma lucidum*	Blockage of the cell cycle at G1 phase, enforcement of natural killer cell activity	Lung cancer, breast cancer, melanoma	***In vitro***: Lung cancer cell lines (e.g., A549); ***In vivo:*** Mouse xenograft models	[56]
	Pleuromutilin	*Pleurotus passeckerianus, Omphalina mutila (P. mutilis, Saccharomyces cerevisiae* etc.	Inhibition of protein synthesis		***In vitro***: Cancer cell lines (e.g., HeLa, MCF-7)	[57]
	Ophiobolin A	*Bipolaris oryzae*	Induction of apoptosis through mitochondrial pathway	Glioblastoma of brain and several melanomas	***In vitro***: Glioblastoma cell lines (e.g., U87); ***In vivo:*** Mouse xenograft models	[58]

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Chemical Class	Bioactive Compound	Fungal Source	Mechanism of Action	Type of cancer prevented	Experimental condition	Ref.
F. Nucleoside derivative	Cordycepin	*Cordyceps militaris*	reduces the transcription of the apoptosis inhibiting Bcl-2 gene and enhances the expression of pro-apoptotic genes such as Bax, caspases nine, three, and twelve.	Liver, tongue, colon cancer etc.	***In vitro***: Liver cancer cell lines (e.g., HepG2); ***In vivo***: Mouse xenograft models	[59]
G. Quinones	Atovaquone	*Penicillium spp.*	Prevents STAT3 phosphorylation and the survival of cancer cells that are reliant on STAT3.	Haematological cancer	***In vitro***: Leukemia cell lines (e.g., HL-60); ***In vivo****:* Mouse leukemia models	[60]
H. Stilbenoids	Resveratrol	*Fusarium, Alternaria, Botryosphaeria, Penicillium, Aspergillus* etc.	decreases the level of transcription of NAF-1, which has anti-apoptotic action, and activates the Nrf2 signal.	Pancreatic and several other cancers	***In vitro***: Pancreatic cancer cell lines (e.g., PANC-1); ***In vivo***: Mouse xenograft models	[61]
I.Phenolic Compounds	Tannic acid		apoptotic activation and cancer cell growth retardation	Human Lung carcinoma	***In vitro***: Lung cancer cell lines (e.g., A549); ***In vivo***: Mouse xenograft models	[62]
J. Lactone derivative	Dehydrocurvularin	*Curvularin, Alternaria macrospora, A. tomato, Aspergillus aureofulgens, A. Terreus*	Targets Heat shock factor 1, induces the transcription and translation of HSP20, HSP70, and HSP90		***In vitro***: Cancer cell lines (e.g., MCF-7, A549)	[63]