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Treasures from the forest: Evaluation of mushroom extracts as anti-cancer agents

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ABSTRACT

Mushrooms provide a reliable source of bioactive compounds and have numerous nutritional values, which is one of the reasons why they are widely used for culinary purposes. They may also be a remedy for several medical conditions, including cancer diseases. Given the constantly increasing number of cancer incidents, the great anticancer potential of mushrooms has unsurprisingly become an object of interest to researchers. Therefore, this review aimed to collect and summarize all the available scientific data on the anti-cancer activity of mushroom extracts. Our research showed that mushroom extracts from 92 species, prepared using 12 different solvents, could reduce the viability of 38 various cancers. Additionally, we evaluated different experimental models: *in vitro* (cell model), *in vivo* (mice and rat model, case studies and randomized controlled trials), and *in silico*. Breast cancer proved to be sensitive to the highest number of mushroom extracts. The curative mechanisms of the studied mushrooms consisted in: inhibition of cancer cell proliferation, unregulated proportion of cells in cell cycle phases, induction of autophagy and phagocytosis, improved response of the immune system, and induction of apoptotic death of cells via upregulation of pro-apoptotic factors and downregulation of anti-apoptotic genes. The processes mainly involved the expression of caspases -3, -8, -9, AKT, p27, p53, BAX, and BCL2. The quoted results could lead to the classification of mushrooms as nutraceuticals used to prevent a variety of disorders or to support treatment of cancer diseases.

1. Introduction

Thanks to their content of various nutritive and biologically active compounds, mushrooms are used as both a source of nourishment and a remedy for a number of diseases. Their nutritional value results from a relatively high amount of carbohydrates, proteins, dietary fiber, and low level of fat [1]. Mushrooms provide water-soluble vitamins, such as B1, B2, B12 and C, as well as fat-soluble vitamins like D and E [2,3]. They also contain bioactive phenolic compounds, carotenoids, and unsaturated fatty acids [4]. This composition might help overcome many medical conditions through antioxidant, antiviral, antifungal, antibacterial, anti-inflammatory, antihypertensive, immunostimulative, hepatoprotective, anti-allergic, antidiabetic, hypocholesterizing, and anti-cancer properties [5–9].

The anti-cancer activity is of particular interest in times of steadily growing numbers of patients suffering from cancer. Only in 2020, 19.3 million people were diagnosed with cancer and nearly 10 million died from the disease. If the rate of cancer prevalence continues increasing, 28.4 million cases of cancer are expected in 2040 [10]. Even though efforts to develop new anti-cancer drugs and methods of cancer detection are intense, the incidence of the disease and the number of deaths are constantly on the rise. The reason for that may be the ability of cancer to develop resistance to treatments through inactivation of drugs, alteration of drug targets, drug efflux, repair of DNA damage, inhibition of cell death, activity of epithelial-mesenchymal transition, and cancer cell heterogeneity [11]. It is no wonder thus that the search for new therapeutic agents is constantly ongoing. Mushrooms provide a good source of promising anti-cancer agents. Therefore, the aim of our work was to analyze all available literature on the subject and to identify mushroom extracts which showed promising antitumor activity. So far, numerous studies have been conducted on the antitumor activity of mushroom extracts, but no one has yet attempted to summarize their results. Our review is the first comprehensive meta-analysis of all the eligible results related to the anti-cancer potential of mushroom

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extracts, as well as the mechanisms of action, experimental models, and solvents used to obtain these extracts. The data collected in this paper may prove a useful tool for scientists as we present a broad spectrum of substances with anti-cancer efficacy and indicate the mechanisms of their action. Our comparison identifies gaps in current knowledge and shows the direction in which to develop mycological studies. The results of such research could lead to the classification of mushrooms as nutraceuticals supporting the treatment of cancer diseases. A diet rich in certain mushrooms is scientifically proven to help cure specific types of cancer.

2. Materials and methods

Prospective studies on using mushroom extracts against cancer were searched in scientific electronic databases, such as PubMed and Scopus. Studies from the last 40 years were taken into consideration. The search was performed using the following key terms: "mushroom", "extract", "cancer", and "tumor". The criteria for the selection of specific studies were as follows: (1) mushroom extract tested *in vitro* (cell model), *in vivo* (mice and rat model, case studies, randomized controlled trials), and *in silico* experimental models; (2) anti-cancer mechanisms of mushroom extracts. Only full versions of English-language articles were included. Articles that did not fulfill the above-mentioned requirements were excluded from the analysis. Due to a large number of variables, no systematic review was carried out. The research reviewed various species of mushroom extracts in terms of anti-tumor activity, considering different types of cancer and experimental models.

3. Results and discussion

3.1. Anticancer property of mushroom extracts

The anti-cancer mechanisms of selected mushroom extracts are summarized in Table 1. The data pointed to active fraction, type of cancer, experimental model, and anti-cancer mechanisms of reviewed mushroom extracts. Extracts from 92 various mushrooms were effective against the tested types of cancer. The evaluated mushroom extracts, prepared using 12 different solvents, showed promising anti-cancer effects against 38 various cancers. It needs to be highlighted that breast cancer was the most vulnerable kind because 61 extracts displayed strong antiproliferative potential against it. The predominant mechanisms of action were inhibition of cancer proliferation, arrest of the cell cycle, induction of cancer phagocytosis, inhibition of tumor angiogenesis, stimulation of the immune system, and induction of apoptotic cell death, mediated through regulation of the expression of caspases -3, -8, and -9, AKT, p27, p53, and BAX/BCL2 ratio. The studies cited were performed using *in vivo, in vitro*, and *in silico* experimental models (Table 1).

One of the described mechanisms is the arrest of the cell cycle, which can have antiproliferative effects. Anti-cancer agents can interfere at different phases of the cell cycle: G0 – state of depression, G1 – preparation of cell for DNA replication, S – synthesis of DNA, G2 – preparation for cell division, and M – mitosis. In phase G0, the metabolic function of proteins is inactivated. The role of these proteins is regulation of kinases and phosphatases, such as cyclin-dependent kinases (Cdks) and other cyclins. The most important protein is p53 – a transcription factor and tumor suppressor that determines which cells are repairable and which undergo apoptotic cell death [12].

Apoptosis is a form of controlled and energy-dependent programmed cell death, associated with no inflammation. Apoptosis causes shrinking of cells, packing of cell organelles, and condensation of chromatin [13]. Many proteins are involved in the apoptosis process, but the key role is played by caspases. These are divided into executioners (caspases -3, -6, and -7) and initiators (caspases -2, -8, -9, and -10 [14,15]. Tumor necrosis factor (TNF) conducts apoptosis death signal from the exterior of a cell to its interior [16]. All pathways lead to activation of executioner proteases and endonuclease caspases, which leading to cell fragmentation and degradation of the cystoskeleton. The proteins involved in the induction of apoptotic processes are caspase-activated DNase (CAD), apoptosis-inducing factor (AIF), and endonuclease C [17]. Important pro-apoptotic proteins include p53 and the related B-cell lymphoma 2 protein (BCL2). The latter regulates apoptosis through mitochondria-mediated pathways. This protein could also exert an anti-apoptotic effect – the estimated mechanism is related to antioxidant activity [18]. Apoptosis in cancer cells can be induced by blocking the unfolded protein response (UPR) pathway (through inhibiting pancreatic ER kinase (PERK) and reducing the expression of endoplasmic reticulum stress-related proteins) or induction of endoplasmic reticulum stress (ERS) [19]. ERS is associated with various types of cancer and relies on multipath UPR system, whose major aim is to maintain ER proteostasis, and which is regulated by inositol-requiring enzyme 1 (IRE1α), activating transcription. UPR is relevant for treatment of cancer because it causes inhibition of PERK and suppression of ERS-related proteins [20].

Reactive oxygen species (ROS) are relevant for cell signaling and also the regulation of apoptosis pathways via ER, mitochondria, and death receptors. ROS are produced a by mitochondria and the metabolic activity of other organs. For certain normal functions of the cell, it is important to maintain a low content of ROS because they take part in the regulation of caspases during apoptosis [21]. In specific states, ROS may damage DNA, RNA, lipids, and DNA related proteins which can mediate carcinogenesis [22].

Autophagocytosis is another way leading to the death of cancer cells and it is a tightly controlled and complex process that triggers cellular protein degradation to fueled metabolic pathways. Autophagy could be stimulated via induction of cellular stress or inhibition of mTOR (mechanistic target of rapamycin), but inhibition of autophagy can be accomplished by upregulation of Beclin 1, ULK1 (serine/threonine-protein kinase), and VPS34 (vacuolar protein sorting 34) inhibitors and downregulation of the fusion of lysosomes with autophagosomes. The biomarkers LC3-II (microtubule-associated protein 1A/1B-light chain 3) and ATG13 (autophagy-related protein 13) are used to monitor the process of autophagy and the number of autophagosomes in blood mononuclear cells. Also, BRAF mutations, RAS signaling, STAT3 (signal transducer and activator of transcription 3) activation, p53 status, and interleukins secretion are autophagy dependence markers. Numerous research studies have proven the efficacy of autophagic therapy against several types of cancer and its ability to reduce resistance to treatment [23]. Phagocytosis is related to autophagy; it is the process of ingestion of other cells or particles. The level of anti-phagocytosis factors in cancer cells is higher compared to normal cells due to the increased expression of pro-phagocytosis signals caused by oncogenic stress. Examples of pro-phagocytosis factors include tumor-associated neoantigens, calreticulin, and signaling lymphocytic activation molecule family member 7 (SLAMF7) [24].

Apoptosis and inhibition of growth, as well as induction of proliferation and promotion of cellular survival could be caused by growth factors and oncogenes. Mainly mitogens and activators of the mitogen pathway determine whether cells proliferate or die by increasing the level of proliferation agents such as cyclins and antiproliferation agents such as p21WAF1/ CIP1 – CDK inhibitors. The response to those signals may be the proliferation of cells. Also, pro-apoptotic oncoproteins, such as cyclin D, E2F, or c-myc from the downstream pathway, stimulate proliferation and activation of upstream mediators, such as RAS, cytoplasmic kinases, or growth factor receptors [25].

In order to gain a detailed knowledge of the dependencies between immune reactions and cancer, we must fully understand the crosstalk at the level of tumor microenvironment. The main element of this microenvironment is the immune/hematopoietic system, on which systemic tolerance depends. Several receptors, ligands, and signaling pathways with the ability to control the immune response are released in tumor environment. Disclosure of the immune reaction depends on the ratio of

Table 1
Comparison of anticancer effect as well mechanism, experimental models and solvent of extracts from different species of mushroom.

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Adenocarcinoma	*Taiwanofungus camphoratus*	Mycelia broth	*In vitro* (A549 cells)	The extracts increased the percentage of cells in the G0/G1 phases of the cycle. Apoptosis was induced by this fraction through caspase-3 and By-1 and could be correlated with ROS generation.	[35]
Astrocytoma	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (U373MG cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Bladder cancer	*Antrodia cinnamonea*	Crude ethanol extract	*In vitro* (RT4, TSGH-8301 and T24 cells)	Cell death was induced by suppression of cell migration by down-regulation of CDC2 and Cyclin B1. A secondary mechanism, replicative senescence, was mediated by the p53-independent overexpression of p21 with down alteration of retinoblastoma protein (pRb).	[37]
Bladder cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (T24 cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Breast cancer	*Agaricus blazei Murill*	Water extract	*In vitro* (MCF7 cells)	The extract induced proliferation of cells by enhanced expression of c-Jun/AP1 genes.	[39]
Breast cancer	*Agaricus brasiliensis*	Powdered basidiocarp and water, acid, and alkaline extracts	*In vivo* – rat model (W256 cells)	The extract reduced patients' loss of weight and tumor growth induced by cachexia and had antioxidant activity.	[40]
Breast cancer	*Antrodia cinnamonea*	Fermented culture broth	*In vitro* (MDA-MB-231 cells)	The extract decreased the activity of urokinase plasminogen activator (uPA), uPA receptor (uPAR), vascular endothelial growth factor (VEGF), and matrix metalloproteinase (MMP-9 and MMP-2). Further investigation showed that the extract suppressed the phosphorylation of ERK1/2, p38, and JNK1/2, leading to inhibition of NF-κB activation.	[41]
Breast cancer	*Antrodia cinnamonea*	Submerged fermentation culture	*In vitro* (MDA-MB-453 and BT-474 cells)	The treatment induced apoptosis mediated by cell cycle arrest at sub-G1, DNA fragmentation, dysfunction of mitochondrial caspase-3/-9 activation, cytochrome c release, degradation of PARP, and BCL2/BAX dysregulation.	[42]
Breast cancer	*Antrodia cinnamonea*	Ethanol extract	*In vivo* – mice model and *in vitro* (T47D cells)	The extract inhibited proliferation related to the arrest of cells at the G1 phase and induced autophagy. The stress of the endoplasmic reticulum was promoted by expression of inositol-requiring enzyme 1α (IRE1), glucose regulating protein 78 (GRP78/Bip), and C/EBP homologous protein (CHOP).	[43]
Breast cancer	*Antrodia cinnamonea*	Ethanol extract	*In vitro* (MCF-7 cells)	The treatment induced apoptosis, suppressed the mRNA expression of S-phase kinase-associated protein 2 (skp2) mediated by increasing miR-21-5p, miR-26-5p, and miR-30-5p expressions.	[44]
Breast cancer	*Antrodia salmonea*	Fermented culture broth	Mice model (MDA-MB-231 cells)	The extract caused inhibition of tumor growth and induction of autophagy and apoptosis via decreasing fragmentation of DNA and caspase-3.	[45]
Breast cancer	*Antrodia salmonea*	Fermented culture broth	Mice model (MDA-MB-231 cells)	The treatment arrested cells at the G2 cell-cycle phase by reducing the levels of cyclin B1, -A, -E, and CDC2 proteins. Moreover, it modulated the tumor progression mediated with induction of apoptosis and autophagy.	[46]
Breast cancer	*Boletus edulis*	Crude water and ethanol extracts	*In vitro* (MCF-7 cells)	An antiproliferative effect of the extracts was observed.	[47]
Breast cancer	*Clitocybe alexandri*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (MCF-7 cells)	An antiproliferative effect of the extracts was observed.	[48]
Breast cancer	*Coprinus comatus*	Ethyl acetate extract	*In vitro* (MCF7 cells)	The extract interfered with the NF-kappaB pathway induction together with H2O2 via inhibition of IkappaBalpha phosphorylation.	[49]
Breast cancer	*Cordyceps militaris*	Cordycepin-rich ethanol extract from brown rice-cultivated *Cordyceps militaris*	*In vitro* (MCF-7and MDA-MB-231 cells)	The extract showed antiproliferative activity through induction of apoptotic cell death caused by activation of p53. Moreover, it increased the level of Cu/Zn superoxide dismutase in cancer cells.	[50]
Breast cancer	*Cordyceps militaris*	Water extract			[51]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
			In vitro (MDA-MB-231 cells)	Apoptosis related to inhibition of AKT activation and PI3K/Akt inhibitor played a key role in the anticancer activity of the extract. Moreover, apoptosis was associated with caspase-3 activation and inactivation of AKT causing mitochondrial dysfunction.	
Breast cancer	*Coriolus versicolor*	Extract	*In vivo* – a meta-analysis of trials	The fraction exhibited antiproliferative activity against cancer.	[52]
Breast cancer	*Coriolus versicolor*	Water extract with metronomic zoledronic acid	*In vivo* – mice model (MDA-MB-231 cells)	The treatment suppressed the proliferation of cancer cells and tumor transmission. Also, it inhibited osteoclastogenesis and prevented bone osteolysis.	[53]
Breast cancer	*Coriolus versicolor*	Water extract	Mice model and *in vitro* (4T1 cells)	The extract exerted antitumor (reduction of tumor weight) and antimetastatic effect, simultaneously protecting bones against breast cancer-induced osteolysis. *In vitro* analysis revealed that the fraction inhibited migration and invasion of cancer cells.	[54]
Breast cancer	*Fomes fomentarius*	Ethanol extract	*In vitro* (MDA-MB-231 cells)	The treatment inhibited cell viability, cell growth and induced apoptosis via activation of caspase and inhibition of the phosphoinositide 3- kinase /AKT pathway.	[55]
Breast cancer	*Fuscoporia torulosa*	Hexane, chloroform, acetone, and methanol extracts	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer.	[56]
Breast cancer	*Ganoderma lucidum*	Ethanol extract (20:1) with spores, standardized to 13.5% polysaccharides and 6% triterpenes	*In vitro* (MDA-MB-231 cells)	The fraction showed an inhibitory effect against Akt phosphorylation on Ser473 and downregulation of Akt expression, which triggered inhibition of NF-kappaB, cyclin D1, and subsequently cdk4.	[57]
Breast cancer	*Ganoderma lucidum*	Extract containing 13.5% polysaccharides and 6% triterpenes	*In vitro* (MDA-MB-231 cells)	The extract suppressed adhesion, migration, and invasion of cancer cells, as well as down-regulated oncogene c-myc expression and secretion of uPA.	[58]
Breast cancer	*Ganoderma lucidum*	Water extract	*In vivo* – mice model (4T1 cells) and *in vitro* (MDA-MB-231 cells)	The extract inhibited tumor growth and migration via inhibition of Wnt/β-catenin signaling.	[59]
Breast cancer	*Ganoderma lucidum*	Water extract	*In vitro* (MCF-7 and MDA-MB-231 cells)	The extract suppressed proliferation activity related to estrogen receptors and NF-kappaB signaling.	[60]
Breast cancer	*Ganoderma lucidum*	Ethanol extract from spores	*In vitro* (MDA-MB-231 cells)	The extract had antiproliferative and anti-angiogenic properties.	[61]
Breast cancer	*Ganoderma lucidum*	Ether extract	*In vitro* (MCF-7 cells)	The telomerase activity was decreased by the extract, which upregulated hsa-miR-1285 miRNA and downregulated hsa-miR-27a miRNA.	[62]
Breast cancer	*Ganoderma lucidum*	Spore oil	*In vivo* – mice model and *in vitro* (MDA-MB-231 cells)	The therapy suppressed cancer cell growth-inducing apoptosis via a mitochondria-mediated pathway.	[63]
Breast cancer	*Ganoderma neojaponicum*	Ethanol extract	*In vitro* (MDA-MB-231 cells)	The extract showed suppression of cancer cells viability.	[64]
Breast cancer	*Gomphus clavatus*	Dichloromethane extract	*In vitro* (PC-3 cells)	The extract exerted a cytotoxic effect against the cancer cells.	[65]
Breast cancer	*Innotus obliquus*	Hot water extracts	*In vivo* – mice model (DMBA)	The anticancer effect of the extract was exerted via activation of innate immunity.	[66]
Breast cancer	*Kuehneromyces mutabilis*	Water and organic extracts	*In vitro* (MCF7 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Breast cancer	*Lactarius quietus*	Water and organic extracts	*In vitro* (MCF7 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Breast cancer	*Leccinum vulpinum Watling*	Phenolic extract	*In vitro* (MCF-7 cells)	The extract reduced cell viability, induced apoptosis and cellular damage of DNA.	[68]
Breast cancer	*Lentinellus cochleatus*	Water and organic extracts	*In vitro* (MCF7 cells)	The extract exerted antiproliferative property against cancer cells.	[67]
Breast cancer	*Lepista inversa*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer.	[48]
Breast cancer	*Lignosus rhinocerus*	Water sclerotial extract	*In vitro* (MCF-7 cells)	An antiproliferative property of the extract was detected.	[69]
Breast cancer	*Lignosus rhinocerus*	Cold water extract prepared from the sclerotia	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[70]
Breast cancer	*Lignosus tigris*	Cold water extract of the sclerotia	*In vivo* – mice model and *in vitro* (MCF-7 cells)	The extract had an antiproliferative and tumor growth inhibitory effect, causing cellular apoptosis via intrinsic and extrinsic signaling pathways. Apoptosis triggered the expression of proapoptotic protein BAX, caspase-8, and -9, simultaneously inhibiting the expression of BCL2.	[71]
Breast cancer	*Marasmius oreades*	Ethanol extract			[72]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
			In vitro (MCF-7 and MDA-MB-231 cells)	An antiproliferative property of extract was detected.	
Breast cancer	*Marasmius oreades*	Culture liquid ethyl acetate extract	*In vitro* (MCF7 cells)	The fraction disrupted the process of tumorigenesis via blockage of NF-kappaB activation.	[73]
Breast cancer	*Ophiocordyceps sobolifera*	Mycelial extract	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[74]
Breast cancer	*Phellinus igniarius*	Ethanol extract	*In vitro* (MCF-7 cells)	The anti-cancer property relied on the induction of apoptosis mediated by arresting the division of cells at the S-phase cycle.	[75]
Breast cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (MDA-MB-231 cells)	The extract caused autophagy of cancer cells via autophagic vacuolization, formation of acidic vesicular organelles, and association of autophagosome membrane of microtubule protein light chain 3.	[76]
Breast cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (MCF-7 cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Breast cancer	*Phellinus linteus*	Water extract	*In vitro* (MDA-MB-231 and MCF-7 cells)	Inhibition of proliferation was mediated by increasing p27Kip1 expression and arrest of the cell cycle at the S phase. Additionally, the extract inhibited cell adhesion, migration and invasion due to the suppression of uPA secretion. Downregulation of VEGF related to inhibition of capillary morphogenesis and suppression of serine-threonine kinase AKT signaling were also observed	[77]
Breast cancer	*Phellinus linteus*	Hot water extract	*In vivo* – mice model	The anti-cancer effect of the extract was achieved via activation of innate immunity.	[66]
Breast cancer	*Pleurotus cornucopiae*	Fermentation broth	*In vitro* (MCF-7 cells)	The broth exhibited antiproliferative activity against cancer cells	[78]
Breast cancer	*Pleurotus highking*	Purified fraction-III	*In vitro* (MCF-7 cells)	The fraction decreased the size and number of tumor spheres and promoted apoptosis by changes in the ratio of the expression of proapoptotic (p53 and BAX) and antiapoptotic (BCL2) genes.	[79]
Breast cancer	*Pleurotus highking*	Purified fraction-III	*In vitro* (MDA-MB-231 and HCC-1937 cells)	The treatment decreased the size and number of tumor spheres and suppressed the expression of Ki-67, matrix metallopeptidase-9, pAkt, and vimentin. The antiproliferative and anti-migratory properties were triggered by the suppression of Akt signaling.	[80]
Breast cancer	*Pleurotus ostreatus*	Methanol extract	*In vitro* (MCF-7 and MDA-MB-231 cells)	The extract exerted an antiproliferative effect associated with the arrest of the cell cycle at the G0/G1 phase. Furthermore, it induced p53-independent apoptosis via an increased level of p21 (cyclin-dependent kinase inhibitor) and p53 (tumor suppressor) with decreased activity of Rb phosphorylation.	[81]
Breast cancer	*Pleurotus ostreatus*	Methanol extract	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer cells	[82]
Breast cancer	*Polycephalomyces nipponicus*	Water and ethanol extract	*In vitro* (MCF-7 cells)	The fraction inhibited cell growth, colony formation and increased the percentage of cells at the G1 phase. The water extract induced arrest of the cell cycle at the G2/M phase. Moreover, it also caused downregulation in the CDK2, CDK4, and CDK6 genes, with upregulation of p21 after treatment.	[83]
Breast cancer	*Polycephalomyces nipponicus*	Ethyl acetate extract	*In vitro* (MCF-7 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[84]
Breast cancer	*Sarcodon imbricatus*	Water extract	*In vivo* – mice model (4T1 cells)	The therapy suppressed the growth, migration, and invasion capacity of the tumor. Also, it increased the levels of IL-2, IL-6, TNF-α, NK cell activity, and the proliferation of splenocytes and decreased the expression of programmed cell death-Ligand 1. Additionally, the extract had immunomodulatory activity.	[85]
Breast cancer	*Suillus collinitus*	Methanol extract	*In vitro* (MCF-7 cells)	An increase in the percentage of cells at the G1 phase of the cell cycle and induction of	[86]

(*continued on next page*)

Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
				apoptosis through enhanced p53 expression were observed after applying the extract.	
Breast cancer	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (MDA-MB-468 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Breast cancer	*Thelephora ganbajun*	Ethanol extract	*In vitro* (MCF-7 cells)	The extract showed an antiproliferative property against cancer cells.	[87]
Breast cancer	*Trametes versicolor*	Ethanol extract	*In vitro* (HepG2, Bcap37, ZR75-30, MCF-7 and T-47D cells)	An antiproliferative effect of the extracts was observed.	[88, 89]
Breast cancer	*Xylaria Hill*	Hexane, ethyl acetate, and methanol extracts	*In vitro* (MDA-MB-231 and MCF-7 cells)	An antiproliferative effect of the extracts was observed.	[90]
Breast cancer (estrogen-receptor positive and estrogen-receptor negative)	*Coprinellus* sp.	Water extracts	*In vitro* (MCF-7, MDA-MB-231, BT-20 cells)	The anticancer effect consisted in inhibition of breast cancer cell growth, apoptosis induction, and substantial inhibition of tumor formation.	[91]
Breast cancer (estrogen-receptor positive and estrogen-receptor negative)	*Coprinus comatus*	Water extracts	*In vitro* (MCF-7, MDA-MB-231, BT-20 cells)	The anticancer effect consisted in inhibition of breast cancer cell growth, apoptosis induction, and substantial inhibition of tumor formation.	[91]
Breast cancer (estrogen-receptor positive and estrogen-receptor negative)	*Flammulina velutipes*	Water extracts	*In vitro* (MCF-7, MDA-MB-231 and BT-20 cells)	The anti-cancer properties included: inhibition of breast cancer cell growth, induction of apoptosis and substantial inhibition of tumor formation.	[91]
Breast cancer (triple-negative)	*Lentinula edodes*	Cold water extract	*In vitro* (MDA-MB-231 cells)	The extract exerted an antiproliferative effect against cancer cells.	[92]
Bronchoalveolar	*Auricularia auricula-judae*	Dichloromethane extract	*In vitro* (NCI H358 cells)	The therapy promoted cytotoxicity and apoptosis of cancer cells. Apoptotic cell death was induced via overexpression of p53 and downregulation of BCL2 expression.	[93]
Bronchoalveolar	*Auricularia auricula-judae*	70% ethanol extract	*In vitro* (NCI H358 cells)	The extract inhibited the proliferation of cancer cells.	[94]
Carcinoma	*Lentinula edodes*	Hot water extract	*In vivo* – mice model (CT26 cells)	Oral administration of the extract inhibited inflammation in tumor-bearing mice and reduced levels of IL-6 in the serum.	[95]
Cervical cancer	*Agaricus blazei Murill*	Water extract	*In vivo* – clinical trial (test group n = 39, placebo n = 61/ duration – 3 weeks)	The extract significantly increased the natural killer cell activity compared with a control group.	[96]
Cervical cancer	*Coprinus disseminatus*	Mycelial culture broth extract	*In vitro* (HeLa, Caski and SiHa cells)	The therapy stimulated apoptosis of cancer cells through increased activity of caspase-3. The presence of Z-VAD-FMK (caspase-3 inhibitor) reversed the action of caspase-3.	[97]
Cervical cancer	*Fomitopsis pinicola*	Methanol extract	In vitro (HeLa cells)	The extract exerted a cytotoxic effect on cancer cells.	[98]
Cervical cancer	*Hexagonia glabra*	Ethanol, ethyl acetate, and water extracts	*In vitro* (HeLa, SiHa, and CaSki cells)	The fraction arrested division of cells at the G2/M check point of the cycle and induced apoptosis via enhancing the expression of caspase-3, caspase-9 and proapoptotic gene p53. Nevertheless, the expression of the BCL2 antiapoptotic gene was decreased.	[99]
Cervical cancer	*Phellinus igniarius*	Ethanol extract	*In vitro* (HeLa cells)	The anti-cancer property relied on the induction of apoptosis mediated by arresting the division of cells at the S-phase cycle.	[75]
Cervical cancer	*Pleurotus sajor-caju*	Water extracts	*In vitro* (HeLa cells)	The fraction inhibited cell proliferation and caused induction of apoptosis.	[100]
Cervical cancer	*Pleurotus eryngii* var. *ferulae*	Ethanol extract	*In vitro* (HeLa cells)	The extract inhibited cell viability through induction of apoptosis caused by the generation of ROS.	[101]
Cervical cancer	*Cordyceps sinensis*	Fermented mushroom, rich in selenium	*In vivo* – mice model	Administration of the extract to mice resulted in a reduction of tumor incidence, enhancement of the immune system, and restoration of the content of glutathione, glutathione reductase activity, glutathione S transferase activity, peroxidation of lipid, glutathione peroxidase activity, catalase activity, and activity of Na(+)/K(+)-ATPase.	[102]
Cervical cancer	*Hypsizigus marmoreus*	Water-soluble extracts	*In vitro* (HeLa cells)	The extract had an immunomodulating potential.	[103]
Cervical cancer	*Trametes gibbosa*	Ethanol extract	*In vitro* (HeLa cells)	The therapy exerted an antiproliferative activity against cancer cells.	[104]
Cervical cancer	*Trametes hirsuta*	Ethanol extract	*In vitro* (HeLa cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Cervical cancer	*Trametes versicolor*	Ethanol extract	*In vitro* (HeLa cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Cervix epithelial cancer		Water and organic extracts	*In vitro* (HeLa cells)		[67]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
	Kuehneromyces mutabilis			The extract showed antiproliferative activity against cancer cells.	
Cervix epithelial cancer	*Lactarius quietus*	Water and organic extracts	*In vitro* (HeLa cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Cervix epithelial cancer	*Lentinellus cochleatus*	Water and organic extracts	*In vitro* (HeLa cells)	The extract exerted antiproliferative property against cancer cells.	[67]
Colon cancer	*Agaricus blazei Murill*	Water extract	*In vivo* – mice model (HT-29 cells)	Oral administration of the extract decelerated the pace of tumor growth.	[105]
Colon cancer	*Antrodia cinnamonea*	Fermented culture broth	*In vitro* (SW620 and SW480 cells)	The mechanism is based on suppression of migration and invasion via inhibition of the PI3K/AKT/NFκB pathways.	[106]
Colon cancer	*Boletus edulis*	BE3 fraction	*In vitro* (LS180 cells)	The extract exerted an antiproliferative effect related to cell cycle G0/G1-phase arrest in cancer cells. It was linked with the p16/cyclin D1/CDK4-6/pRb pathway, an important component of cancer development.	[107]
Colon cancer	*Clitocybe alexandri*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (HCT-15 cells)	An antiproliferative effect of the extracts was observed.	[48]
Colon cancer	*Cordyceps sinensis*	Ethanol-soluble and ethanol-insoluble sub-fractions	*In vitro* (HT29 cells)	An antiproliferative effect of the extracts was observed.	[108]
Colon cancer	*Ganoderma lucidum*	Ethanol extract	*In vitro* (HT-29 cells)	Proapoptotic and anti-inflammatory activity of the extract was observed, along with inhibition of cytokine expression.	[109]
Colon cancer	*Ganoderma neojaponicum*	Hexane, chloroform, butanol, and water extracts	*In vitro* and *in silico* (CT 116 and HT29 cells)	The fractions had an antiproliferative effect via induction of apoptosis related to the regulation of BCL2 protein.	[110]
Colon cancer	*Hericium erinaceum*	Ethanol extract	*In vivo* – mice model and *in vitro*	The extract caused tumor growth arrest.	[111]
Colon cancer	*Hericium erinaceum*	Water extract	*In vivo* – mice model (CT-26 cells)	The therapy inhibited metalloproteinase-mediated migration, suppressed activation of ERK and JNK kinases, stimulated the activity of macrophages and NK cells along with inhibition of angiogenesis.	[112]
Colon cancer	*Hericium erinaceum*	Hot water extract and ethanol-water extract	*In vitro* (CT-26 cells)	The extract enhanced the activity of NK cells and macrophages. Moreover, it inhibited angiogenesis and consequently decreased tumor size.	[113]
Colon cancer	*Heterobasidion annosum*	Methanol extract	*In vivo* – mice model (DLD-1 cells)	The therapy suppressed cell proliferation and metabolic activity of cancer cells. Also, tumor growth was reduced by the extract.	[114]
Colon cancer	*Hypsizigus marmoreus*	Water-soluble extracts	*In vitro* (DLD-1 cells)	The extract had an immunomodulating potential.	[103]
Colon cancer	*Hypsizigus marmoreus*	Methanol extracts	*In vitro* (HepG2 cells)	The treatment showed antiproliferative and antimutagenic effects via reduction of phase I metabolic-activating enzymes and phase II enzyme activity.	[115]
Colon cancer	*Innotus obliquus*	Ethanol extract	*In vitro* (HT-29 cells)	The extract inhibited cell proliferation and synthesis of DNA by increasing the number of cells at the G1 phase. Moreover, it suppressed the expression of CDK2, CDK4, and cyclin D1 proteins, as well as enhanced expression of p21, p27, and p53. Also, inhibition of Rb phosphorylation Rb and expression of E2F1 were observed.	[116]
Colon cancer	*Innotus obliquus*	Water extracts	*In vitro* (HCT-116 cells)	The fraction exhibited cytotoxic activity against cancer cells.	[117, 118]
Colon cancer	*Innotus obliquus*	Water extract	*In vitro* (HT-29 cells)	The extract limited cancer cell growth and induced apoptosis via up-regulation of proapoptotic BAX and caspase-3 and down-regulation of antiapoptotic BCL2.	[119]
Colon cancer	*Innotus obliquus*	Hot water and ethanol extracts	*In vitro* (DLD-1 cells)	The ethanol extract exhibited antioxidant and antiproliferative activity causing induction of apoptosis. Although, no apoptosis was observed after hot water extracts exposure.	[120]
Colon cancer	*Innotus obliquus*	Hot water extracts	*In vivo* – mice model (AOM/DSS cells)	The anticancer effect of the extract was exerted via activation of innate immunity.	[66]
Colon cancer	*Lentinula edodes*	Hot water extract	*In vivo* – mice model (C26 cells)	Oral ingestion of the extract rebuilt antitumor T cell responses and decreased concentration of TGF-β and IL-6 in the plasma.	[121]
Colon cancer	*Lepista inversa*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (HCT-15 cells)	The fraction exhibited antiproliferative activity against cancer.	[48]
Colon cancer	*Marasmius oreades*	Ethanol extract	*In vitro* (HT-29 cells)	An antiproliferative property of extract was detected.	[72]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Colon cancer	*Phellinus linteus*	Ethyl acetate extract grown on germinated brown rice	*In vitro* (HT-29 cells)	The fraction exhibited antiproliferative activity against cancer cells	[122]
Colon cancer	*Phellinus linteus*	Hot water extract	*In vivo* – mice model	The anti-cancer effect of the extract was achieved via activation of innate immunity.	[66]
Colon cancer	*Pleurotus eryngii* var. *ferulae*	Cold water extracts	*In vitro* (HCT116 cells)	The therapy significantly inhibited the proliferation of cells and promoted apoptosis due to the increased ratio of BAX/BCL2. Moreover, it had the potential to inhibit the migration of cells and heterotypic cell-cell adhesion.	[123]
Colon cancer	*Pleurotus nebrodensis*	Cold water extract	*In vitro* (HCT116 cells)	The therapy significantly inhibited the proliferation of cells and promoted apoptosis, due to the increased ratio of BAX/BCL2. Moreover, it had the potential to inhibit the migration of cells and heterotypic cell-cell adhesion.	[123]
Colon cancer	*Pleurotus ostreatus*	Water extract	*In vitro* (COLO-205 cells)	The anticancer activity of the extract was caused by cell cycle arrest at the Go/G1 phase and induction of apoptosis due to increased expression of proapoptotic genes (caspase-3, caspase-9, BAX, cyclin-dependent kinases (CKIs), p16, and p21) and decreased expression of anti-apoptotic genes (BCL2).	[124]
Colon cancer	*Pleurotus ostreatus*	Methanol extract	*In vitro* (HT-29 and HCT-116 cells)	The extract exerted an antiproliferative effect associated with the arrest of the cell cycle at the G0/G1 phase. Furthermore, it induced p53-independent apoptosis via an increased level of p21 (cyclin-dependent kinase inhibitor) and p53 (tumor suppressor) with decreased activity of Rb phosphorylation.	[81]
Colon cancer	*Pleurotus ostreatus*	Ethanol extract	*In vivo* – mice model	The antitumor mechanism of action was related to the prevention of inflammation-associated carcinogenesis by inhibiting the expression of F4/80, Ki-67, COX-2, and cyclin D1 in mice.	[125]
Colon cancer	*Polyozellus multiplex*	Methanol extract	*In vitro* (HT29 cells)	The treatment reduced cell proliferation due to enhanced expression of the p53 tumor suppressor gene.	[126]
Colon cancer	*Thelephora ganbajun*	Ethanol extract	*In vitro* (HT-29 cells)	The extract showed an antiproliferative property against cancer cells.	[87]
Colon cancer	*Trametes gibbosa*	Ethanol extract	*In vitro* (LS174 cells)	The therapy exerted an antiproliferative activity against cancer cells.	[104]
Colon cancer	*Trametes hirsuta*	Ethanol extract	*In vitro* (LS174 cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Colon cancer	*Trametes versicolor*	Ethanol extract	*In vitro* (LS174 cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Colorectal cancer	*Ganoderma applanatum*	80% methanol extract	*In vitro* (Caco-2 cells)	The extract induced cell apoptosis via a p53-independent pathway, which was proved by an increased ratio of mRNA BAX/BCL2 with the regulation of p53 and caspase-3.	[127]
Colorectal cancer	*Agaricus blazei Murill*	Water extract	*In vitro* (Caco-2 cells)	The extract was investigated for antiproliferative activity and inhibition of P-glycoprotein (P-gp)-mediated transport in differentiated cells.	[128]
Colorectal cancer	*Cordyceps militaris*	Ethanol extract	*In vitro* and mice model (RKO cells)	The extract inhibited cell proliferation and tumor growth in the mice model. Also, it caused inhibition of apoptosis through a mitochondria-mediated pathway.	[129]
Colorectal cancer	*Coriolus versicolor*	Extract	*In vivo* – a meta-analysis of trials	The fraction exhibited antiproliferative activity against cancer.	[52]
Colorectal cancer	*Cynomorium coccineum* L.	Oil extract	*In vitro* (Caco-2 cells)	The fraction exhibited antiproliferative activity against cancer.	[130]
Colorectal cancer	*Fomitopsis pinicola*	Chloroform extract	*In vitro* (SW-480 cells)	The fraction induced ROS-mediated apoptosis and inhibited metalloproteinase-mediated migration.	[131]
Colorectal cancer	*Ganoderma lucidum*	Ethanol extracts of sporoderm-broken spores	*In vivo* – mice model and *in vitro* (HCT116 cells)	The therapy stimulated apoptosis and arrested cell cycle at the G0/G1 via deregulation of the expression of cyclins D1, p21, p16, PARP, BCL2, BAX, NAG-1, and caspase-3 protein, as well as the genes relevant in regulation of apoptosis. Additionally, it decreased cell migration via upregulation of the expression of E-cadherin and downregulation of MMP-1 and MMP-2.	[132]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Colorectal cancer	*Phellinus igniarius*	Ethanol extract	*In vitro* (HCT-116 cells)	The anti-cancer property relied on the induction of apoptosis mediated by arresting the division of cells at the S-phase cycle.	[75]
Colorectal cancer	*Piptoporus betulinus*	Ether and ethanol extracts	*In vitro* (LS180 cells)	The fraction exhibited antiproliferative activity against cancer cells	[133]
Colorectal cancer	*Pleurotus ostreatus*	Methanol extract	*In vitro* (Colo-205 cells)	The fraction exhibited antiproliferative activity against cancer cells	[82]
Colorectal cancer	*Pleurotus sajor-caju*	N-hexane extract	*In vitro* (HCT116 cells)	Increased expression of caspase-3, p53, and BAX, as well as a decreased level of BCL2 caused by the fraction proved to have a proapoptotic effect. Moreover, the extract arrested the cell cycle at the G2/M phase without a cytotoxic effect.	[134]
Cystadenocarcinoma	*Ganoderma lucidum*	Fruit body water extract and spores in a salvage setting	*In vivo* – case study	The treatment stabilized the disease and may facilitate disease control.	[135]
Dalton lymphoma ascites	*Phellinus rimosus*	Ethyl acetate, methanol, and water extracts	*In vitro* (EAC cells)	The fraction exhibited antiproliferative activity against cancer cells	[136]
Ehrlich ascites carcinoma	*Agaricus brasiliensis*	Beta-glucan-rich extract	*In vivo* – mice model	The extract treatment inhibited proliferation associated with decrease in IL-10 production and induction of migration of immunocompetent cells to the tumor to create a more effective immune-responsive environment.	[137]
Ehrlich ascites carcinoma	*Hohenbuehelia geogenius*	Culture filtrate	*In vivo* – mice model (EAC cells)	The fraction exhibited antiproliferative activity against cancer cells.	[138]
Ehrlich ascites carcinoma	*Phellinus rimosus*	Ethyl acetate, methanol, and water extracts	*In vitro* (DLA cells)	The fraction exhibited antiproliferative activity against cancer cells	[136]
Ehrlich ascites carcinoma	*Termitomyces clypeatus*	Water-soluble extract	*In vivo* – mice model (EAC cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Ehrlich ascites carcinoma	*Tricholoma giganteum*	Ethanol fraction	*In vitro* (EAC cells)	Cell cycle arrest at sub-G0/G1 and decrease in the number of cells at G2/M after the therapy implied apoptosis. It was related to enhancing the expression of proapoptotic p53 protein causing upregulation of the BAX gene.	[139]
Endocervical adenocarcinoma (papillomavirus related)	*Phellinus igniarius*	Ethanol extract	*In vitro* (BEL-7402 cells)	The anti-cancer property relied on the induction of apoptosis mediated by arresting the division of cells at the S-phase cycle.	[75]
Endometrial cancer	*Agaricus blazei Murill*	Water extract	*In vivo* – clinical trial (test group n = 39, placebo n = 61/ duration – 3 weeks)	The extract significantly increased the natural killer cell activity compared with a control group.	[96]
Endometrial cancer	*Cordyceps sinensis*	Water extract	*In vitro* (Ishikawa, Hec-1A and AN3-CA cells)	The therapy inhibited phosphorylation of AKT and simultaneously reduced the level of pAKT, causing autophagic cell death.	[140]
Endometrial cancer	*Ganoderma lucidum*	Fruit body water extract and spores in a salvage setting	*In vivo* – case study	The treatment stabilized the disease and may facilitate disease control.	[135]
Endometrial cancer	*Ganoderma tsugae*	Ethanol extract	*In vitro* (AN3 CA, HEC-1-A and KLE cells)	The extract inhibited cell proliferation, induced cell cycle arrest at the G1/S phase, mitochondria-mediated apoptosis, and caused inhibition of the Akt signaling pathway.	[141]
Esophageal cancer	*Pleurotus eryngii* var. *ferulae*	Ethanol extract	*In vitro* (Eca-109 cells)	The extract inhibited cell viability through induction of apoptosis caused by the generation of ROS.	[101]
Fibrosarcoma	*Agaricus blazei Murill*	Intratumoral injection of extract and a protein-bound (17%) alpha-glucan and beta-glucan	*In vivo* – mice model (MCA-205 cells)	The extract induced production of immunosuppressive acidic protein, causing inhibition of the growth of a metastatic tumor.	[142]
Fibrosarcoma	*Coliolus versicolor*	Intratumoral injection of hot water extract of cultured mycelia from and a protein-bound beta-glucan	*In vivo* – mice model (MCA-205 cells)	The extract inhibited tumor growth of primary and metastatic tumors via induction of immunosuppressive acidic protein production.	[142]
Fibrosarcoma	*Hypsizigus marmoreus*	Water and methanol extracts	Mice model (Meth A cells)	The fraction exhibited antiproliferative activity against cancer cells.	[143]
Fibrosarcoma	*Tricholoma matsutake*	Intratumoral injection of extract (protein-bound (38%) a-glucan)	*In vivo* – mice model	The extract induced production of immunosuppressive acidic protein, causing inhibition of the growth of metastatic tumors.	[142]
Gastric cancer	*Agaricus blazei Murill*	Water extract	*In vitro* (AGS cells)	Inhibition of cell growth caused by the extract was associated with the arrest of the cell cycle at the G2/M phase and the induction of apoptosis (upregulation of BAX and the activation of caspases with down-regulation of XIAP and cIAP-1 related with decreasing levels of cyclin B1 and CDC2.	[144]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Gastric cancer	*Auricularia auricula-judae*	Dichloromethane extract	*In vitro* (SNU1 cells)	The therapy promoted cytotoxicity and apoptosis of cancer cells. Apoptotic cell death was induced via overexpression of p53 and downregulation of BCL2 expression.	[93]
Gastric cancer	*Auricularia auricula-judae*	70% ethanol extract	*In vitro* (SNU 1 cells)	The extract inhibited the proliferation of cancer cells.	[94]
Gastric cancer	*Clitocybe alexandri*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (AGS cells)	An antiproliferative effect of the extracts was observed.	[48]
Gastric cancer	*Cordyceps taii*	Chloroform extract	*In vitro* (SGC-7901 cells)	The extract exhibited an antiproliferative effect via inhibition of tumor growth in the mice model. Furthermore, it induced necrosis of tumor tissue and enhanced the activity of the GSH-Px of various cancer tissues.	[145]
Gastric cancer	*Coriolus versicolor*	Extract	*In vivo* – a meta-analysis of trials	The fraction exhibited antiproliferative activity against cancer.	[52]
Gastric cancer	*Ganoderma lucidum*	Methanol extract	*In vitro* (AGS cells)	The therapy enhanced autophagosome formation, increased the level of LC3-II, and decreased p62concentration, which proved the anti-cancer potential of the extract based on cellular autophagy of cancer cells.	[146]
Gastric cancer	*Ganoderma lucidum*	Ethanol extracts	*In vitro* (AGS cells)	The fraction prompted apoptosis of cancer cells mediated through the death receptor-mediated extrinsic signaling pathway and mitochondria-mediated caspase pathways linked with Akt signal pathway inactivation.	[147]
Gastric cancer	*Ganoderma lucidum*	Methanol extract	*In vitro* (AGS cells)	Inhibition of cancer cell growth caused by the extract was caused by cell cycle arrest and cellular autophagy.	[148]
Gastric cancer	Grifola frondosa	Water-soluble extract	*In vitro* (TMK-1, MKN28, MKN45 and MKN74 cells)	The results showed that the extract induced cancer cell apoptosis via caspase-3 pathways.	[149]
Gastric cancer	*Hericium erinaceum*	Ethanol extract	*In vivo* – mice model and *in vitro*	The extract caused tumor growth arrest.	[111]
Gastric cancer	*Hypsizigus marmoreus*	Water-soluble extracts	*In vitro* (AGS cells)	The extract had an immunomodulating potential.	[103]
Gastric cancer	*Lepista inversa*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (AGS cells)	The fraction exhibited antiproliferative activity against cancer.	[48]
Gastric cancer	*Phellinus igniarius*	Ethanol extract	*In vitro* (SGC-7901 cells)	The therapy arrested the cell cycle at G0/G1 phase and induced mitochondrial-dependent apoptosis by suppressing the expression of cyclin D1. Apoptosis was promoted by an imbalance of mitochondrial membrane potential, activation of caspase-9, -3, PARP cleavage, and increased proportion of BAX/BCL2.	[150]
Gastric cancer	*Phellinus igniarius*	Ethanol extract	*In vitro* (MGC-803 cells)	The anti-cancer property relied on the induction of apoptosis mediated by arresting the division of cells at the S-phase cycle.	[75]
Gastric cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (AGS cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Gastric cancer	*Pleurotus eryngii* var. *ferulae*	Ethanol extract enriched with terpenoids	*In vitro* (BGC 823 and GES-1 cells)	The fraction inhibited tumor cell viability, arrested cells at G0/G1 phases of the cell cycle and promoted apoptosis by enhancing the expression of caspase-3 and genes relevant to apoptotic cell death. Moreover, it induced necrosis of cancer cells, suppressed the activity of MMP, and limited cell invasion.	[151]
Gastric cancer	*Pleurotus eryngii* var. *ferulae*	Ethanol extract	*In vitro* (BGC823 cells)	The extract inhibited cell viability through induction of apoptosis caused by the generation of ROS.	[101]
Gastric cancer	*Polyozellus multiplex*	Methanol extract	*In vitro* (SNU668 cells)	The treatment reduced cell proliferation due to enhanced expression of the p53 tumor suppressor gene.	[126]
Glioblastoma	*Agrocybe cylindracea*	Hot water extracts	*In vitro* (C6 cells)	The mechanism of the extract is based on the induction of necrosis and cell apoptosis.	[152]
Glioblastoma	*Cantharellus cibarius*	Water and ethanol extracts	*In vitro* (U87MG and LN-18 cells)	Inhibition of proliferation, cell cycle at subG1 or G2/M phase, and matrix metalloproteinase activity were observed after therapy with extracts.	[153]
Glioblastoma	*Coprinus comatus*	Water and ethanol extracts	*In vitro* (U87MG and LN-18 cells)	Inhibition of proliferation, cell cycle arrest at subG1 or G2/M phase, and matrix	[153]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
				metalloproteinase activity were observed after therapy with the extracts.	
Glioblastoma	*Ganoderma lucidum*	Water extract	*In vitro* (U87MG and GBM8901 cells)	The extract suppressed cancer cell proliferation, arrested cell cycle at the S phase, mediated by the cyclin-CDK2 pathway, and induced mitochondria-mediated cell apoptosis.	[154]
Glioblastoma	*Lactarius deliciosus*	Water and ethanol extracts	*In vitro* (U87MG and LN-18 cells)	Inhibition of proliferation, cell cycle arrest at subG1 or G2/M phase, and matrix metalloproteinase activity were observed after therapy with the extracts.	[153]
Glioblastoma	*Lycoperdon perlatum*	Water and ethanol extracts	*In vitro* (U87MG and LN-18 cells)	Inhibition of proliferation, cell cycle arrest at subG1 or G2/M phase, and matrix metalloproteinase activity were observed after therapy with the extracts.	[153]
Glioblastoma	*Phellinus linteus*	Ethanol extract	*In vitro* (U-87 cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Hepatocarcinoma	*Anthodia camphorata*	Extract from fruiting bodies (AC-FB), the mycelium of solid-state cultures (AC-SS), liquid-state cultures (AC-LS), and polysaccharide extracts from liquid-state cultures (AC-PS)	*In vitro* (HepG2 cells)	The extracts (AC-FB and AC-SS) exerted antiproliferative effects by immunomodulatory property of the macrophages. Moreover, the extract increased mRNA expression of TNF-α and protein related to apoptosis on activation of MC-CMs. Polysaccharide extracts induced macrophage-derived antitumor property by Akt and IL-1β activation.	[155]
Hepatocarcinoma	*Antrodia cinnamonea*	Ethyl acetate fraction of an ethanol extract of mycelia	*In vivo* – rat/mice model and *in vitro* (HepG2 and SMMC-7721 cells)	The extract reduced viability, induced apoptosis, and inhibited migration/invasion of cells. Also, the therapy decreased the level of mRNA and downregulated protein expression of STAT3 and JAK2, involving proteins related to apoptosis inhibition BCL-xL and BCL2 and anti-invasion proteins MMP-2 and -9.	[156]
Hepatocarcinoma	*Coprinus comatus*	Chloroform and acetone extracts	*In vitro* (HepG2 cells)	An antiproliferative effect of the extracts was observed.	[157]
Hepatocarcinoma	*Ganoderma colossum*	Ethanol extract	*In vitro* (HepG2 cells)	The treatment reduced PMA-induced invasion and the activity of matrix metalloproteinase-9. Additionally, it suppressed PMA-induced phosphorylation of ERK1/2 (extracellular signal-regulated kinase), AKT, activator protein-1 (AP-1), and concentration of NF-kappaB.	[158]
Hepatocarcinoma	Grifola frondosa	Water extracts	*In vitro* (Hep3B cells)	The extract caused the arrest of the cell cycle at the S phase, induced apoptosis using caspase-3 and caspase-9, as well as decreased the expression of extracellular signal-regulated kinase and kinase B.	[159]
Hepatocarcinoma	*Hericium erinaceum*	Crude water-soluble polysaccharide	*In vitro* (HepG2 cells)	Dox-mediated apoptotic death cell induced by the extract was mediated by a decreased expression of c-FLIP with activation of JNK through NF-κB inhibition.	[160]
Hepatocarcinoma	*Hypsizigus marmoreus*	Methanol extracts	*In vitro* (HepG2 cells)	The treatment showed antiproliferative and antimutagenic effects via reduction of phase I metabolic-activating enzymes and phase II enzyme activity.	[115]
Hepatocarcinoma	*Inonotus baumii*	Ethanol extract	*In vitro* (SMMC-7721 cells)	The fraction enhanced autophagy through increased expression of autophagy-related LC3-II protein with reduced expression of AMPK/mTOR/ULK1 pathway and p62.	[161]
Hepatocarcinoma	*Innotus obliquus*	Water extracts	*In vitro* (HepG2 cells)	The fraction exhibited cytotoxic activity against cancer cells.	[117, 118]
Hepatocarcinoma	*Lentinula edodes*	Water-soluble and alcohol-insoluble fractions	*In vivo* – rat model (AH414 cells)	The extract inhibited hepatocarcinogenesis and proliferation of cancer cells.	[162]
Hepatocarcinoma	*Phellinus linteus*	Ethanol extract	*In vitro* (HepG2 cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Hepatocarcinoma	*Pleurotus cornucopiae*	Fermentation broth	*In vitro* (HepG2 cells)	The broth exhibited antiproliferative activity against cancer cells	[78]
Hepatocarcinoma	*Pleurotus eryngii* var. *ferulae*	Cultivated and wild *Pleurotus ferulae* ethanol extracts	*In vivo* – mice model (H22 and HepG2 cells)	Inhibition of hepatocellular carcinoma cell growth was achieved through induction of	[163]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
				apoptosis related to ER stress-dependent and mitochondria-dependent pathways. The extract also caused endoplasmic reticulum stress due to enhanced JNK phosphorylation, cleavage of HSP70 and caspase-12, as well as a drop in membrane mitochondrial potential associated with cytochrome c release and cleavage of caspases -3, -7, and -9 and PARP. It was found that the fraction might induce the generation of ROS and reduction of matrix metalloproteinases 2 and 9.	
Hepatocarcinoma	*Pleurotus pulmonarius*	Water extract	*In vivo* – mice model (Huh7 cells)	The treatment suppressed the proliferation of cancer cells via inhibiting the phosphoinositide 3-kinase (PI3K)/Akt signaling pathway.	[164]
Hepatocarcinoma	*Polyozellus multiplex*	Methanol extract	*In vitro* (HepG2 cells)	The treatment reduced cell proliferation due to enhanced expression of the p53 tumor suppressor gene.	[126]
Hepatocarcinoma	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (HepG2 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Hepatocarcinoma	*Thelephora ganbajun*	Ethanol extract	*In vitro* (HepG2 cells)	The extract showed an antiproliferative property against cancer cells.	[87]
Hepatocarcinoma	*Trametes versicolor*	Ethanol extract	*In vitro* (7703, 7721 and PLC cells)	An antiproliferative effect of the extracts was observed.	[88, 89]
Hepatocarcinoma	*Tricholoma matsutake*	Water extract	*In vivo* – Mice model and *in vitro (*HepG2 and SMMC-7721 cells)	Caspase-dependent mitochondrial apoptosis of extract-treated cells was induced due to reduction of BCL2 expressions and stimulation of PARP, BAD, and BAX expression in tumor and cancer cells.	[165]
Hepatocarcinoma	*Fomitopsis pinicola*	Methanol extract	In vitro (SNU-354/185, SK-Hep 3B, Hep3B and PLC/RF/5 cells)	The extract exerted a cytotoxic effect on cancer cells.	[98]
Hepatocarcinoma	*Agaricus blazei Murill*	Water extract	Mice model (Smmu 7721 cells)	The extract reduced formation of tumor metastasis.	[166]
Hepatocarcinoma	*Agrocybe cylindracea*	Hot water extracts	*In vitro* (Hep 3B cells)	The mechanism of the extract is based on the induction of necrosis and cell apoptosis.	[152]
Hepatocarcinoma	*Ganoderma lucidum*	Ethanol reflux extract	*In vivo* – mice model and *in vitro* (QGY7703 and SK-Hep1 cells)	The anti-cancer activity relied on inhibition of the RAS/RAF/MEK/ERK signaling pathway.	[167]
Hepatocarcinoma	*Hericium erinaceum*	Ethanol extract	*In vivo* – mice model and *in vitro*	The extract caused tumor growth arrest.	[111]
Kidney cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (ACHN cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Large intestine cancer	*Coriolus versicolor*	Hot water extract	*In vivo* – mice model	The fraction exhibited antiproliferative activity against cancer.	[168]
Laryngeal cancer	*Pleurotus sajor-caju*	Water extracts	*In vitro* (Hep-2 cells)	The fraction inhibited cell proliferation and caused induction of apoptosis.	[100]
Laryngeal cancer	*Lentinula edodes*	Water extract	*In vitro* (HEP-2 cells)	The extract showed a chemopreventive activity by regulation of mitotic apoptosis. Additionally, it arrested division of cells at the sub-G1 phase of the cycle, stimulated mitochondrial depolarization, and generated intracellular ROS.	[169]
Leukemia	*Agaricus blazei Murill*	Water extract	*In vitro* (THP-1 cells)	The mechanism of the extract was based on induction of ROS-dependent JNK activation apoptosis through mitochondrial pathway and NF-κB suppression.	[170]
Leukemia	*Antrodia Cinnamonea*	Ethanol extract	*In vivo* – mice model (WEHI-3 cells)	The extract decreased the level of protein p-Akt and p-ERK1/2, and increased the expression of p21 and p27. Furthermore, the therapy reduced tumor growth through decreasing the expression of MMP-9, cyclin E, cyclin D1 and increasing the expression of p21 and p27.	[171]
Leukemia	*Ganoderma lucidum*	Crude extract	*In vivo* – mice model (WEHI-3 cells)	The extract promoted macrophage phagocytosis by enhancing the activity of natural killer cells. Also, it upregulated CD3 and CD19 and downregulated Mac-3 and CD11b markers.	[172]
Leukemia	*Hericium erinaceum*	Water extract	*In vitro* (U937 cells)	The extract caused apoptosis via the downregulation of antiapoptotic proteins.	[173]
Leukemia		Culture filtrate			[138]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
	Hohenbuehelia geogenius		*In vivo* – mice model (L1210 cells)	The fraction exhibited antiproliferative activity against cancer cells.	
Leukemia	*Meripilus giganteus*	Methanol extracts	*In vitro* (L1210 cells)	An antiproliferative property of extract was detected.	[174]
Leukemia	*Pleurotus ostreatus*	Extract	*In vitro* (Jurkat and KG-1 cells)	The fraction inhibited cell proliferation, migration, expression of matrix metallopeptidase-9 and promoted apoptosis due to enhanced expression of the BAX gene.	[175]
Leukemia	*Pleurotus pulmonarius*	Water extract	*In vivo* – rat model	The extract enhanced leukopoiesis and demonstrated phagocytic properties.	[176]
Leukemia	*Pleurotus* sp.	Hot water extract	*In vitro* (NB4 cells)	The therapy inhibited cell viability and arrested the cell cycle at the G2/M phase.	[177]
Leukemia	*Pyropolyporus fomentarius*	Ethanol extract	*In vivo* – mice model (L1210 cells)	The therapy-induced apoptosis due to lowered mitochondrial membrane potential and enhanced level of caspase-3, caspase-9, and BAX, proving that the effect of the extract involved a mitochondria-related pathway. Additionally, the extract boosted the proliferation and splenic lymphocytes activation.	[178]
Leukemia	*Suillus granulatus*	Methanol extracts	*In vitro* (L1210 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[174]
Leukemia	*Suillus luteus*	Methanol extracts	*In vitro* (L1210 cells)	The extract showed antiproliferative activity against cancer cells.	[174]
Leukemia	*Ganoderma lucidum*	Methanol extracts	*In vitro* (L1210 cells)	The fraction exhibited antiproliferative activity against cancer.	[174]
Leukemia benzene-induced	*Pleurotus ostreatus*	Water extract	*In vivo* – rat model	The extract enhanced leukopoiesis and demonstrated phagocytic properties.	[176]
Leukemia myelogenous	*Agaricus blazei Murill*	Water, 50% ethanol, 70% ethanol and 100% absolute ethanol extracts	*In vitro* (NB-4 and K-562 cells) and mice model	The effect of the extract was based on antiproliferation and, in part, on the induction of apoptosis.	[179]
Leukemia myelogenous	*Daedalea gibbosa*	Mycelium organic extracts	*In vivo* – mice model and *in vitro* (K562 cells)	The therapy led to induction of apoptosis and inhibited proliferation, enhanced the activity of kinase recombinant ABL, autophosphorylation of BCR-ABL, and formation of the cell colonies.	[180]
Leukemia myelogenous	*Ganoderma lucidum*	Ethanol extract	*In vitro* (U937 cells)	The fraction exerted antiproliferative, proapoptotic, genotoxic, and antioxidant effects.	[181]
Leukemia myelogenous	*Agaricus blazei Murill*	Water extract	*In vitro* (INA-6, RPMI-8226, U226, KG1a, and Meg 01 cells)	The extract caused a cytotoxic and immunomodulatory effect in myeloma cells.	[182]
Leukemia promyelocytic	*Agaricus blazei Murill*	Water extract	*In vitro* (HL-60 cells)	The extract caused a cytotoxic and immunomodulatory effect in myeloma cells.	[182]
Leukemia promyelocytic	*Agrocybe cylindracea*	Hot water extracts	*In vitro* (HL-60 cells)	The mechanism of the extract is based on the induction of necrosis and cell apoptosis.	[152]
Leukemia promyelocytic	*Antrodia cinnamonea*	Fermented culture	*In vitro* and *in vivo* – mice model (HL-60 cells)	The therapy induced arrest of cells at the G1 phase via reducing the concentrations of cyclins -A, -E, -D1, CDK4, CDK2 and phosphorylation of p-Rb. Moreover, the extract induced ROS generation and mitochondrial dysfunction and also increased the expression of CDK proteins, including p21 and p15. Additionally, an *in vivo* study revealed that treatment reduced the tumor burden.	[183]
Leukemia promyelocytic	*Antrodia salmonea*	Fermented culture broth	Mice model and *in vitro* (HL-60 cells)	The extract induced apoptosis by mitochondrial and death receptor pathways. *In vivo* studies showed reduction in the size of tumors and delays in their growth.	[184]
Leukemia promyelocytic	*Cordyceps militaris*	Hot water extracts of cultured mycelia and cultivated fruiting bodies	*In vitro* (HL-60 cells)	The treatment possessed antiproliferative properties caused by apoptotic activity mediated by activation of caspase-3, induction of PARP protein, and laddering of DNA.	[185]
Leukemia promyelocytic	*Coriolus versicolor*	Water I'm-Yunity® extract	*In vitro* (HL-60 and U-937 cells)	Water extract suppressed proliferation of cells, arrested the cell cycle, induced apoptosis and caused modifications in the expression of extracellular signaling regulatory proteins.	[186]
Leukemia promyelocytic	*Meripilus giganteus*	Ethanol extract	*In vitro* (Jurkat and HL-60 cells)	The extract promoted apoptotic cell death by reducing ROS concentration, increasing the BAX/BCL2 ratio, and inducing the expression of the FAS gene. The reduction of ROS was linked with apoptosis induced by death receptors.	[187]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Leukemia promyelocytic	*Polyozellus multiplex*	Methanol extract	*In vitro* (Jurkat T, HL60 and U937 cells)	The treatment reduced cell proliferation due to enhanced expression of the p53 tumor suppressor gene.	[126]
Leukemia promyelocytic	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (HL-60 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Lewis lung carcinoma	*Hypsizigus marmoreus*	Water extract	*In vivo* – mice model (LLC cells)	The extract had an antiproliferative effect against cancer cells.	[188]
Lewis lung carcinoma	*Innotus obliquus*	Water extract	*In vivo* – mice model (3LL cells)	The extract inhibited tumor growth and caused tumor reduction, as well as inhibited vascularization and increased agglomeration of the tumor.	[189]
Lewis lung carcinoma	*Meripilus giganteus*	Methanol extracts	*In vitro* (3LL cells)	An antiproliferative property of extract was detected.	[174]
Lung cancer	*Agaricus lanipes*	Methanol extract	*In vitro* (A549 cells)	The extract showed antiproliferative potency and strong pro-apoptotic activity.	[190]
Lung cancer	*Antrodia cinnamonea*	Ethanol extract	*In vivo* – mice model (LLC and CL1-5 cells)	The therapy inhibited tumor growth and induced cell apoptosis via inhibition of the STAT3 signaling pathway.	[191]
Lung cancer	*Antrodia cinnamonea*	Ethanol extract	*In vitro* (CL1-0 cells)	The extract inhibited migration and cell motility, suppressed the activity of matrix metalloproteinase (MMP)-2 and -9, increased the level of tissue inhibitors of MMP (TIMP-1 and TIMP-2), and inhibited the phosphorylation of p38, AKT, and JNK1/2.	[192]
Lung cancer	*Calvatia gigantea*	Methanol extract	*In vitro* (A549 cells)	The extract caused the arrest of the cell cycle and induction of apoptosis mediated by decreased expression of Akt, BCL2, CCND1, CCND2, and CDK4 and increased expression of caspase-3, caspase-9, BAX, and p53.	[193, 194]
Lung cancer	*Clitocybe alexandri*	Ethanol extract	*In vitro* (NCI-H460 cells)	The extract arrested cells at the S-phase and caused accumulation of apoptotic cells.	[195]
Lung cancer	*Clitocybe alexandri*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (NCI-H460 cells)	An antiproliferative effect of the extracts was observed.	[48]
Lung cancer	*Clitocybe alexandri*	Ethanol extract	*In vitro* (NCI-H460 cells)	The fraction induced apoptosis by relating p53 and caspase-3 pathway and accumulation of cells at cell cycle.	[196]
Lung cancer	*Cordyceps militaris*	Water extract	*In vitro* (A549 cells)	Apoptotic cancer cell death was induced by a mitochondria-mediated caspase pathway and signaling cascade of receptor-mediated death. Additionally, the extract inhibited hTERT transcriptional activity triggered by the action of diminished telomerase causing apoptosis.	[197]
Lung cancer	*Cordyceps taii*	Chloroform extract	*In vitro* (A549 cells)	The extract exhibited an antiproliferative effect via inhibition of tumor growth in the mice model. Furthermore, it induced necrosis of tumor tissue and enhanced the activity of the GSH-Px of various cancer tissues.	[145]
Lung cancer	*Ganoderma lucidum*	Standardized ethanol extract containing 6% triterpenes and 13.5% polysaccharides	*In vivo* – mice model (MDA-MB-231 cells)	Oral administration of the extract inhibited tumor growth and cancer metastases. Moreover, it decreased the expression of genes related to invasive capacity (MCAM, I2PP2A, HRAS, VIL2, S100A4, and FN1) and inhibited cell migration.	[198]
Lung cancer	*Ganoderma lucidum*	Methanol extracts	*In vitro* (3LL cells)	The fraction exhibited antiproliferative activity against cancer.	[174]
Lung cancer	*Lentinula edodes*	Cold water extract	*In vitro* (A549 cells)	The extract exerted an antiproliferative effect against cancer cells.	[92]
Lung cancer	*Lepista inversa*	Phenolic (methanol and ethanol) and polysaccharidic (boiling water) extracts	*In vitro* (NCI-H460 cells)	The fraction exhibited antiproliferative activity against cancer.	[48]
Lung cancer	*Lignosus rhinocerus*	Cold water extract prepared from the sclerotia	*In vitro* (A549 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[70]
Lung cancer	*Lignosus tigris*	Cold water extract of the sclerotia	*In vivo* – mice model and *in vitro* (A549 cells)	The extract had an antiproliferative and tumor growth inhibitory effect, causing cellular apoptosis via intrinsic and extrinsic signaling pathways. Apoptosis triggered the expression of proapoptotic protein BAX, caspase-8, and -9, simultaneously inhibiting the expression of BCL2.	[71]
Lung cancer	*Macrolepiota procera*	Mycelial extract	*In vitro* (A549 cells)	Antiproliferative and proapoptotic effects were the main mechanisms of action and were caused by an enhanced expression of caspase-3, -9, PTEN, PUMA, p21, and p53, as well as suppressed expression of BCL2, Akt,	[199]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
				cyclin Dl, CDK4, CDK6, and NOXA genes. The extract also reduced invasion.	
Lung cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (A549 cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase-3 and -9.	[38]
Lung cancer	*Phellinus linteus*	Ethanol extract	Mice model (LKR cells) and *in vitro* (H5800 cells)	The extract exerted mainly apoptotic activity via fragmentation of DNA, activation of proapoptotic caspases and loss of clonogenicity.	[200]
Lung cancer	*Pleurotus eryngii* var. *ferulae*	Water extract	*In vivo* – mice model (TC-1 cells)	The antitumor activity consisted in enhancing the immune system.	[201]
Lung cancer	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (A549 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Lung cancer	*Thelephora ganbajun*	Ethanol extract	*In vitro* (A549 cells)	The extract showed an antiproliferative property against cancer cells.	[87]
Lung cancer	*Trametes gibbosa*	Ethanol extract	*In vitro* (A549 cells)	The therapy exerted an antiproliferative activity against cancer cells.	[104]
Lung cancer	*Trametes hirsuta*	Ethanol extract	*In vitro* (A549 cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Lung cancer	*Trametes versicolor*	Ethanol extract	*In vitro* (A549 cells)	The extract showed an antiproliferative property against cancer cells.	[104]
Lung cancer	*Xylaria Hill*	Hexane, ethyl acetate, and methanol extracts	*In vitro (*A-549 cells)	An antiproliferative effect of the extracts was observed.	[90]
Lung cancer	*Suillus luteus*	Methanol extracts	*In vitro* (3LL cells)	The extract showed antiproliferative activity against cancer cells.	[174]
Lung caner	*Suillus granulatus*	Methanol extracts	*In vitro* (3LL cells)	The fraction exhibited antiproliferative activity against cancer cells.	[174]
Lymphoma	*Agaricus blazei Murill*	Methanol, dichloromethane, and n-hexane extracts	*In vivo* – mice model (Yac-1 cells)	The extract normalized the natural killer activity and induced the mitogen-induced proliferative function of spleen cells.	[202]
Lymphoma	*Hericium erinaceum*	Water extracts	*In vitro* (Yac-1 cells)	The fraction boosted the cytolytic ability of NK cells and induced IL-12 in splenocytes.	[203]
Lymphoma	*Hypsizygus ulmarius*	Ethanol extracts	*In vitro* (DLA cells)	The treatment exhibited antiproliferative activity against cancer cells.	[204]
Lymphoma	*Termitomyces clypeatus*	Water-soluble extract	In *in vitro* (U937 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Melanoma	*Agaricus blazei Murill*	Water extract	Mice model (B16F10 cells)	The extract reduced formation of tumor metastasis.	[166]
Melanoma	*Antrodia cinnamonea*	Ethanol extract	*In vitro* (B16-F0 cells)	The extract exhibited antiproliferative effects that inhibited the ability of the cells to migrate. Also, the treatment arrested cells at the sub-G1 phase and caused an increase in early apoptotic cells and chromatin condensation.	[205]
Melanoma	*Cambodian Phellinus*	Water extract	*In vivo* – mice model (B16BL6 cells)	The fraction inhibited metastasis by modification of uPA connected with tumor cell-induced platelet aggregation (TCIPA).	[206]
Melanoma	*Coriolus versicolor*	Methanol extract	*In vivo* – mice model (B16 cells)	The fraction showed inhibition of cell proliferation and arrested cells at the G0/G1 phase of the cell cycle, causing apoptotic and necrotic cell death and also promoting macrophages.	[207]
Melanoma	*Cynomorium coccineum* L.	Oil extract	*In vitro* (B16F10 cells)	The fraction exhibited antiproliferative activity against cancer.	[130]
Melanoma	*Fomitopsis pinicola*	Methanol extract	In vitro (HO-1 cells)	The extract exerted a cytotoxic effect on cancer cells.	[98]
Melanoma	*Innotus obliquus*	Water extracts	*In vivo* – mice model	Tumor growth inhibition was observed after exposure to the extract.	[208]
Melanoma	*Lentinula edodes*	Hot water extract	*In vivo* – mice model (B16 cells)	The treatment increased the percentage of regulatory T cells in mice.	[209]
Melanoma	*Pleurotus eryngii* var. *ferulae*	Ethanol extract enriched with terpenoids	*In vitro* (B16F10 cells)	The fraction inhibited tumor cell viability, arrested cells at G0/G1 phases of the cell cycle and promoted apoptosis by enhancing the expression of caspase-3 and genes relevant to apoptotic cell death. Moreover, it induced necrosis of cancer cells, suppressed the activity of MMP, and limited cell invasion.	[151]
Melanoma	*Pleurotus ostreatus*	Water extract	*In vivo* – mice model (B-16 cells)	The antitumor activity relied on stimulation of the immune system.	[210]
Melanoma	*Cordyceps taii*	Chloroform extract	*In vivo* – mice model (B16F10 cells)	The extract exhibited an antiproliferative effect via inhibition of tumor growth in the mice model. Furthermore, it induced necrosis of tumor tissue and enhanced the	[145]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
				activity of the GSH-Px of various cancer tissues.	
Melanoma	*Pleurotus eryngii* var. *ferulae*	Ethanol extract	*In vitro* (B16 cells)	The extract inhibited cell viability through induction of apoptosis caused by the generation of ROS.	[101]
Neuroblastoma	*Phellinus linteus*	Mycelium extracts	*In vitro* (SK-N-MC cells)	The fraction induced apoptosis mediated with activation of caspase-3 and enhanced the expression of BAX rather than suppressing BCL2.	[211]
Neurogliocytoma	*Innotus obliquus*	Polysaccharide extract	*In vitro* (U251 cells)	The anti-cancer activity was associated with apoptosis via a decreased level of BCL2 and an increased expression of caspase-3.	[212]
Oral cancer	*Agaricus brasiliensis*	50% ethanol extracts and hot water extracts	*In vitro* (CAL 27 cells)	The extracts induced apoptosis related to cytochrome c release from mitochondria and activation of caspase-3.	[213]
Ovarian cancer	*Agaricus blazei Murill*	Water extract	*In vivo* – clinical trial (test group n = 39, placebo n = 61/ duration – 3 weeks)	The extract significantly increased the natural killer cell activity compared with a control group.	[96]
Ovarian cancer	*Antrodia Cinnamonea*	Fermentation culture	*In vitro* (SKOV-3 cells)	The treatment significantly decreased the number of cells in G2/M related to down-regulation of cyclin D1, A, B1, and Cdk1, increased p27 expression, and inhibited the activation of PI3K/Akt. Moreover, it induced apoptosis mediated by DNA fragmentation, release of cytochrome c, activation of caspase-3/-9, PARP degradation, and dysregulation of BCL2/BAX. The extract also induced ROS-dependent cell death.	[214]
Ovarian cancer	*Antrodia salmonea*	Fermented culture broth	*In vitro* (SKOV-3 and A2780 cells)	The extract induced ROS-dependent autophagic death of cells. The treatment modulated PI3K/AKT and HER-2/NEU signaling pathways triggered by 3-MA and CQ autophagy inhibitors.	[215]
Ovarian cancer	*Coprinus comatus*	Ethyl acetate extract	*In vitro* (ES-2 cells)	The extract induced apoptosis via extrinsic and intrinsic pathways through reduction in the concentrations of procaspases -3, -8, and -9.	[216]
Ovarian cancer	*Ganoderma lucidum*	Fruit body water extract and spores in a salvage setting	*In vivo* – case study	The treatment stabilized the disease and may facilitate disease control.	[135]
Ovarian cancer	*Ganoderma lucidum*	Ethanol extract containing 6% triterpenes and 13.5% polysaccharides	*In vitro* (HO 8910 cells)	The treatment caused downregulation of the VEGF expression and upregulation of the Cx43 expression downstream.	[217]
Ovarian cancer	*Ganoderma lucidum*	Water and ethanol extracts	*In vivo* – mice model and *in vitro* (OVCAR-3 cells)	Suppression of tumorigenesis was achieved through stimulation by phase II detoxification enzymes and activity of antioxidants. Moreover, the extract activated NRF2-mediated cytoprotective genes.	[218]
Ovarian cancer	*Kuehneromyces mutabilis*	Water and organic extracts	*In vitro* (A2780 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Ovarian cancer	*Lactarius quietus*	Water and organic extracts	*In vitro* (A2780 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Ovarian cancer	*Lentinellus cochleatus*	Water and organic extracts	*In vitro* (A2780 cells)	The extract exerted antiproliferative property against cancer cells.	[67]
Ovarian cancer	*Termitomyces clypeatus*	Water-soluble extract	*in vitro* (OAW-42 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Pancreatic cancer	*Agaricus blazei Murill*	Hot water extract	*In vitro* (MIAPaCa-2, PCI-35, and PK-8 cells)	The extract inhibited cell proliferation through the arrest of cells at the G0/G1 phase and caspase-dependent apoptosis. Moreover, proapoptotic genes were upregulated.	[219]
Pancreatic cancer	*Calocybe indica*	Ethanol extract	*In vitro* (PANC-1 and MIAPaCa2 cells)	The fraction showed cell growth inhibition and apoptosis induction in cancer cells via modulation of caspase-3 and caspase-9, and p53 protein levels. Moreover, it decreased BCL2 protein and migration of cancer cells.	[220]
Prostate cancer	*Agaricus bisporus*	Ethanol extract	*In vitro* (PC3 cells)	The extracts decreased the proliferation of cells by modulation of IL-8 secretion and decreasing the level of VEGF. Mushroom extracts also decreased nuclear and NFκB activity.	[221]
Prostate cancer	*Antrodia Cinnamonea*	Water extract	*In vitro* (PC3 cells)	The extract exerted several effects on cell viability, e.g. inducing apoptosis via phosphorylation of JNK, ERK, and p38 MAPKs.	[222]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Prostate cancer	*Antrodia Cinnamonea*	Crude extract	*In vitro* (PC-3 and LNCaP cells)	The treatment induced apoptosis of cells related to Akt, p53, p21, and CDK4/cyclin D1. The extract arrested cells at the G1/S phase, leading to inhibiting cyclin D1 activity apoptosis. In PC-3 cells, it caused a G2/M-phase arrest through p21 and cyclin B1/Cdc2.	[223]
Prostate cancer	*Coprinus comatus*	Ethanol and ethyl acetate extracts	*In vitro* (LNCaP cells)	The treatment inhibited dihydrotestosterone-induced cell proliferation and secretion of prostate-specific antigen and triggered the arrest of cancer cells at the G1 phase.	[224]
Prostate cancer	*Coprinus comatus*	Hexane extract	*In vitro* (LNCaP cells)	The fraction suppressed cell proliferation, formation of tumor colonies, and activity of AR-mediated reporter.	[225]
Prostate cancer	*Fomitopsis pinicola*	Ethanol extract	*In vivo* – mice model (PCa cells)	The therapy reduced tumor growth.	[226]
Prostate cancer	*Fuscoporia torulosa*	Hexane, chloroform, acetone, and methanol extracts	*In vitro* (PC-3 cells)	The fraction exhibited antiproliferative activity against cancer.	[56]
Prostate cancer	*Ganoderma lucidum*	Ethanol and ethyl acetate extracts	*In vitro* (LNCaP cells)	The treatment inhibited dihydrotestosterone-induced cell proliferation and secretion of prostate-specific antigen. It also triggered cancer cell cycle arrest at the G1 phase.	[224]
Prostate cancer	*Ganoderma lucidum*	Water extract	*In vitro* (PC-3 cells)	The extract inhibited the proliferation of cancer cells via decreasing the expression of CDC2 and cyclin B, as well as increasing the expression of p21. Moreover, the treatment arrested cancer cell cycle at the G2/M phase and promoted apoptosis via suppression of the expression of NF-kappaB-regulated BCL2 and BCL-xl. The ratio of BAX/BCL2 and BAX/BCL-xl was enhanced through the upregulation of the pro-apoptotic protein BAX.	[227]
Prostate cancer	*Gomphus clavatus*	Dichloromethane extract	*In vitro* (MCF-7 cells)	The extract exerted a cytotoxic effect against the cancer cells.	
Prostate cancer	*Lentinula edodes*	Ethanol extracts	*In vitro* (PC3 cells)	The extracts decreased the proliferation of cells by modulation of IL-8 secretion and decreasing the level of VEGF. Mushroom extracts also decreased nuclear and NFκB activity.	[221]
Prostate cancer	*Lignosus tigris*	Cold water extract of the sclerotia	*In vivo* – mice model and *in vitro* (PC3 cells)	The extract had an antiproliferative and tumor growth inhibitory effect, causing cellular apoptosis via intrinsic and extrinsic signaling pathways. Apoptosis triggered the expression of proapoptotic protein BAX, caspase -8, and -9, simultaneously inhibiting the expression of BCL2.	[71]
Prostate cancer	*Phellinus linteus*	Extract	*In vivo* – case study	Remission of refractory prostate cancer hormone was observed.	[228]
Prostate cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (PC-3 and LNCaP cells)	The growth of cancer cells was reduced via induction of oxidative stress and its cytotoxic effect. Moreover, the extract induced apoptotic cell death due to increased expression of caspase -3 and -9.	[38]
Prostate cancer	*Phellinus linteus*	Water extract	*In vivo* – mice model (PC3 and DU145 cells)	The treatment inhibited tumor proliferation and induced apoptosis due to activation of proapoptotic caspases.	[229]
Prostate cancer	*Phellinus linteus*	Ethanol extract	*In vitro* (LNCaP and PC3 cells)	The major antic-cancer activity of the extract involved an induction of apoptotic cell death linked with enhanced activity of proapoptotic caspase 2.	[230]
Prostate cancer	*Pleurotus ostreatus*	Water extract	*In vitro* (PC-3 cells)	The extract induced apoptotic death of cancer cells.	[231]
Prostate cancer	*Trametes versicolor*	Ethanol extract	*In vitro* (LNCaP, JCA-1, PC-3, and DU-145 cells)	The extract caused upregulation of signal transducer and activator of transcription factors STAT 1 and STAT. Moreover, it exerted a chemopreventive effect, as well as inhibited the progression of tumor from hormone-dependent to hormone-refractory form.	[232]
Prostate cancer	*Tremella fuciformis Berk*	Water extract	*In vitro* (PC-3 cells)	The extract promoted apoptotic cell death due to activation of caspase -3, increased proportion between BAX and BCL2, and suppressed expressions of MMP -9.	[233]

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Table 1 (*continued*)

Type of Cancer	Species	Solvent/Fraction	Experimental Model	Mechanism/Results	Ref.
Retinoblastoma	*Termitomyces clypeatus*	Water-soluble extract	*In vitro* (Y-79 cells)	The treatment exhibited an antitumor effect related to its antioxidant property.	[36]
Sarcoma	*Agaricus blazei Murill*	Water-insoluble residue	*In vivo* – mice model (S180 cells)	The extract exerted an antiproliferative effect.	[234]
Sarcoma	*Agaricus blazei Murill*	Hot-water extract	*In vivo* – mice model (S180 cell)	The extract had an antiproliferative effect.	[235]
Sarcoma	*Agaricus blazei Murill*	Ethanol-soluble, water-ethanol-soluble, ammonium oxalate-soluble, and ammonium oxalate-insoluble fraction	*In vivo* – mice model (Meth-A cells)	The cell cytotoxic effect of the extracts was inducted by the production of immunosuppressive acidic protein and macrophage chemotactic factor activity through activated macrophages and neutrophils.	[236]
Sarcoma	*Agaricus blazei Murill*	Hot water extract	*In vivo* – mice model (S180 cells)	Secretion of tumor necrosis factor-α and interleukin-6 and decreased ability to remove endotoxin were caused by the extract.	[237]
Sarcoma	*Agaricus brasiliensis*	Mycelia extract obtained from solid-state fermentation	*In vivo* – mice model (S180 cells)	The tumor growth decrease was achieved by normalizing the balance between cellular and humoral immunity and also by increasing CD4+ and CD8+ and decreasing CD19+ cell populations.	[238]
Sarcoma	*Agaricus brazei*	Hot water extracts	*In vivo* – mice model (Meth A cells)	Treatment with the extracts increased activity of natural killer cells and enhanced the induction of antigen-specific cytotoxic T lymphocytes and production of interferon-gamma.	[239]
Sarcoma	*Anthracophyllum lateritium*	Crude extract	*In vitro* (RD cells)	The extract induced cell apoptosis mediated by both nitric oxide and nitrite ions.	[240]
Sarcoma	*Auricularia auricula-judae*	70% ethanol extract	*In vitro* (S180 cells)	The extract inhibited the proliferation of cancer cells.	[94]
Sarcoma	*Cordyceps taii*	Chloroform extract	*In vivo* – mice model (S180 cells)	The extract exhibited an antiproliferative effect via inhibition of tumor growth in the mice model. Furthermore, it induced necrosis of tumor tissue and enhanced the activity of the GSH-Px of various cancer tissues.	[145]
Sarcoma	*Elfvingia applanata*	Hot water extract	*In vivo* – mice model (S180 cells)	The anti-cancer activity consisted in the immunostimulant activity of the extract.	[241]
Sarcoma	*Fomitopsis pinicola*	Ethanol extract	*In vivo* – mice model (S180 cells)	The therapy reduced tumor growth.	[242]
Sarcoma	*Ganoderma lucidum*	Mycelia obtained from solid-state fermentation	*In vivo* – mice model (S180 cells)	The anti-cancer mechanism was based on restoring the correct balance between humoral and cellular immunity by increasing the levels of CD4+ and CD8+ and decreasing CD19+.	[238]
Sarcoma	*Ganoderma lucidum*	Methanol and water extracts	*In vivo* – mice model (S180 cells)	The fraction exhibited antiproliferative activity against cancer.	[243]
Sarcoma	*Hypsizigus marmoreus*	Water and methanol extracts	Mice model (S180 cells)	The fraction exhibited antiproliferative activity against cancer cells.	[143]
Sarcoma	*Pyropolyporus fomentarius*	Petroleum ether extract	*In vivo* – mice model and *in vitro* (S180 cells)	The extract inhibited tumor growth, decreased immune organ toxicity, and promoted mitochondria-dependent or ROS-dependent apoptosis.	[244]
Sarcoma	*Sarcodon aspratus*	Methanol and water extracts	*In vivo* – mice model (S180 cells)	An antiproliferative effect of the extracts was observed.	[243]
Skin epidermoid cancer	*Kuehneromyces mutabilis*	Water and organic extracts	*In vitro* (A431 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Skin epidermoid cancer	*Lactarius quietus*	Water and organic extracts	*In vitro* (A431 cells)	The extract showed antiproliferative activity against cancer cells.	[67]
Skin epidermoid cancer	*Lentinellus cochleatus*	Water and organic extracts	*In vitro* (A431 cells)	The extract exerted antiproliferative property against cancer cells.	[67]

inhibitory and stimulation signals. The immune system plays a key role in response to cancer diseases, e.g. T cells and antibodies can detect and kill cancer cells. Secretion of FOX3 (canonical transcription factor) dependent on regulatory T cells takes part in controlling the response to pathogens and tolerance to cancer antigens, and the opportunity for immune-mediated elimination. Suppression of the immune reaction via the activity of regulatory T cells is based on an increased level of inhibitory cytokines, such as transforming growth factor (TGF-β) and interleukin (IL-10). Besides tolerance mechanisms related to tumor-specific T cells, cancer microenvironment is full of mechanisms that dampen anti-cancer responses locally. These signals are the main targets for immunotherapy [26].

The results of the studies which we analyzed indicate that various mushroom extracts, including water, ethanol, methanol, hexane, ethyl acetate, acetone, chloroform, petroleum ether, oil fraction, dichloromethane, and fermented broth, may exhibit anti-cancer activity. Our review summarizes all published scientific results regarding mushroom ammonium oxalate-soluble and ammonium oxalate-insoluble fractions of 92 species of mushrooms with anti-cancer and antitumor potential.

The market of nutraceuticals, including mushrooms, is constantly growing. It is estimated that by 2025, it will have grown to USD 373 billion (from USD 241 billion in 2019). Increased demand for functional

food and the ever-increasing awareness of the nutritional and health-promoting properties of mushrooms are likely to drive the growth of this market [27]. Forecasts also indicate a steady rise in the value of the edible mushroom market, which is predicted to reach USD 62.19 billion in 2023 and USD 72.50 billion in 2027 [28]. Increased use of compounds from fungi in cosmetology, nutrition and medicine is also forecast: a good example of this being polysaccharides, e.g. glucans [29]. Numerous medications already use chemical compounds of fungal origin with proven healing properties. These include, among others, schizophyllan, krestin, coriolan, lentinan, and many others [30,31]. Lovastatin – a drug used in hypercholesterolemia, derived from *Pleurotus ostreatus* – is in increasing demand, predicted to grow even more [32]. Many clinical trials of the use of mushrooms in cancer therapy or prevention are currently underway. The literature provides evidence of the influence of: the White Button Mushroom on inflammation in obese women at high risk of breast cancer and on the reduction of PSA in prostate cancer, Yunzhi extract on breast cancer, MICODIGEST (nutraceutical which contains extracts *from Ganoderma lucidum, Agaricus blazei, Grifola frondosa, Hericium erinaceus, Cordyceps sinensis, Inonotus obliquus, Pleurotus ostreatus, Polyporus umbellatus*, and *Lentinula edodes*) on colorectal cancer, and many others. A large group of completed clinical trials has brought promising results, which may lead to the development of new anti-cancer drugs in the future [33].

3.2. Combination therapy of mushroom extracts

Cancer therapies using a combination of two or more anti-cancer agents are widely applied as they are beneficial for patients. They make it possible to significantly increase the efficiency and safety of treatment [34]. The mechanisms of synergistic anti-cancer effects and experimental models are presented in Table 2. A blend of several mushroom species with polysaccharides (β-1,3-glucan or chitosan) or a mushroom extract with vitamin C have been shown to cause an increase in the anti-tumor activity of cancers therapies. Also, a combination of mushroom extracts with chemotherapy has a positive effect.

Table 2
Synergistic anticancer effect of mushroom extracts combined with biological active natural ingredients and chemotherapeutics.

Species	Compound	Type of cancer	Experimental model	Mechanism/Results	Ref.
Agaricus blazei Murill	Extract combination with chitosan	Hepatocarcinoma	*In vivo* – mice model (SK-Hep 1 cells)	Therapy with the blend reduced secretion of vascular endothelial growth factor and the masses of the tumors.	[245]
Agaricus blazei, Cordyceps sinensis, Coriolus versicolor, Ganoderma lucidum, Grifola frondosa and Polyporus umbellatus and β-1,3-glucan	Dietary supplement MycoPhyto® Complex (MC)	Breast carcinoma	*In vitro* (MDA-MB-231 cells)	MC inhibited cell proliferation arrested the cell cycle at the G2/M phase, inhibited cell adhesion, cell migration, and cell invasion. MC inhibited the expression of genes that regulate the cell cycle, such as ANAPC2, ANAPC2, BIRC5, Cyclin B1, Cyclin H, CDC20, CDK2, CKS1B, Cullin 1, E2F1, KPNA2, PKMYT1, and TFDP1. Moreover, the decreased invasiveness was correlated to the suppression of urokinase plasminogen activator secretion from cancer cells.	[246]
Antrodia cinnamomea	Mushroom combined with chemotherapy: cisplatin, carboplatin, oxaliplatin, adriamycin, taxane, vinorelbine, and 5-fluorouracil	Gastric, lung, liver, breast, and colorectal cancer	*In vivo* – randomized controlled trial (test group n = 17, placebo n = 20/duration – 4 weeks)	The combination only slightly increased the survival rate compared to control. The treatment significantly decreased the platelet counts and improved patient sleep quality.	[247]
Coriolus versicolor and *Ganoderma lucidum*	Water and ethanol extracts	Promyelocytic leukemia	*In vitro* (HL-60 cells)	Ethanol extracts of the blend were more active in inducing cell death (expression of caspase-3 and BAX) compared to water extracts. Also, ethanol extracts exhibited a stronger effect compared to water extracts. The blend caused growth suppression and apoptosis induction, downregulation of phosphorylation of Rb, and increased cleavage of poly(ADP-ribose) polymerase to an inactive form.	[248]
Ganoderma colossum	Colossolactone H plus gefitinib	Bronchoalveolar carcinoma	*In vivo* – mice model (H1650 cells)	The blend effectively inhibited the progression of tumors in mice.	[249]
Ganoderma lucidum	Extract blended with quercetin	Gastric cancer	*In vitro* (SNU719 and MKN1-EBV cells)	The combination induced lytic reactivation of the Epstein-Barr virus, the main risk factor of gastric cancer, and induced cancer cell apoptosis.	[250]
Grifola frondosa	D-fraction polysaccharide blended with vitamin C	Hepatocarcinoma	*In vitro* (SMMC-7721 cells)	The mechanism of anti-cancer activity is related to induction of cell apoptosis by the downregulation of BCL2, upregulation of BAX, activation of poly-(ADP-ribose)-polymerase, and the secretion of cytochrome c.	[251]
Taiwanofungus salmoneus	Ethanol extract blended with cisplatin	Hepatocarcinoma	*In vitro* (SK-Hep-1 cells)	The blend inhibited proliferation of cancer cells by extending the sub-G1 phase, causing damage to DNA, activation of caspases -3, -8, and -9 and prompting apoptosis.	[252]
Pleurotus ostreatus	Methanol extract plus doxorubicin hydrochloride	Erythroleukemia	*In vitro* (KG-1 cells)	The fraction induced apoptosis and significantly increased its anti-cancer effects in combination with doxorubicin hydrochloride.	[253]

4. Conclusions

Mushrooms are a food which is appreciated for its culinary values with many pro-health properties. Mushroom extracts have an anti-cancer effect and their activity against certain types of cancers and experimental models has been investigated by many researchers. The majority of extracts (61) showed cytotoxicity against breast cancer in a variety of experimental models: *in vitro* (cell model), *in vivo* (rat model, mice model, case study, and randomized controlled trials), and *in silico*. The fractions triggered cell viability inhibition, increased the number of cells at specific cell cycle phases, induced phagocytosis and autophagy, promoted the immune response, and induced apoptosis related to the expression of caspases -3, -8, and -9, AKT, p27, p53, BAX, and BCL2. Moreover, therapy based on combination of mushroom extracts with different anti-cancer agents, such as biologically active natural compounds and chemotherapy, upregulated the efficacy of treatment, improving the safety and comfort of patients. Our work is the first comprehensive review of all available research related to the anti-cancer properties of mushroom extracts, as well as anti-cancer mechanisms, accounting for the above-mentioned experimental models. It has the potential to become a compendium of comprehensive knowledge for researchers, physicians, and companies. It provides a solid foundation for further development of presented studies and identifies gaps in mycological knowledge. In the future, it may contribute to the classification of mushrooms as nutraceuticals or to creation of dietary supplements supporting cancer therapy.

CRediT authorship contribution statement

Patryk Nowakowski: Conceptualization, Writing – original draft, Project administration. **Renata Markiewicz-Żukowska:** Validation, Methodology. **Joanna Bielecka:** Formal analysis, Visualization. **Konrad Mielcarek:** Data curation, Software. **Monika Grabia:** Resources, Writing – review & editing. **Katarzyna Socha:** Supervision, Writing – review & editing.

Conflicts of interest statement

None.

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