Review Narrative Review: Bioactive Potential of Various Mushrooms as the Treasure of Versatile Therapeutic Natural Product

Hitesh Chopra 1,†, Awdhesh Kumar Mishra 2,†, Atif Amin Baig 3, Tapan Kumar Mohanta 4,*, Yugal Kishore Mohanta 5,*, and Kwang-Hyun Baek 2, *

1 Chitkara College of Pharmacy, Chitkara University, Punjab 140401, India; chopraontheride@gmail.com
2 Department of Biotechnology, Yeungnam University, Gyeongsan 38541, Gyeongsangbuk-do, Korea; awadhesh.biotech07@gmail.com
3 Unit of Biochemistry, Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu 20400, Malaysia; atifamin@unisz.a.edu.my
4 Natural and Medical Sciences Research Centre, University of Nizwa, Nizwa 616, Oman; tapan.mohanta@unizwa.edu.om
5 Department of Botany, Maharaja Siriram Chandra Bhanj Deo University, Baripada 757003, India
* Correspondence: ykmohanta@gmail.com (Y.K.M.); khbaek@ynu.ac.kr (K.-H.B.)
† These authors contributed equally.

Abstract: Mushrooms have remained an eternal part of traditional cuisines due to their beneficial health potential and have long been recognized as a folk medicine for their broad spectrum of nutraceuticals, as well as therapeutic and prophylactic uses. Nowadays, they have been extensively investigated to explain the chemical nature and mechanisms of action of their biomedicine and nutraceuticals capacity. Mushrooms belong to the astounding dominion of Fungi and are known as a macrofungus. Significant health benefits of mushrooms, including antiviral, antibacterial, anti-parasitic, antifungal, wound healing, anticancer, immunomodulating, antioxidant, radical scavenging, detoxification, hepatoprotective cardiovascular, anti-hypercholesterolemia, and anti-diabetic effects, etc., have been reported around the globe and have attracted significant interests of its further exploration in commercial sectors. They can function as functional foods, help in the treatment and therapeutic interventions of sub-optimal health states, and prevent some consequences of life-threatening diseases. Mushrooms mainly contained low and high molecular weight polysaccharides, fatty acids, lectins, and glucans responsible for their therapeutic action. Due to the large varieties of mushrooms present, it becomes challenging to identify chemical components present in them and their beneficial action. This article highlights such therapeutic activities with their active ingredients for mushrooms.

Keywords: anti-HIV; immunomodulatory; antioxidant; hepatoprotective; anti-inflammatory

1. Introduction

Mushrooms have been present on earth for ages and are an important, indispensable part of global cuisine. Along with this, mushrooms are exploited for their beneficial health properties. There are about 2000 mushroom species worldwide, but just a handful are edible or nutraceutical. Agaricus bisporus is the most widely grown mushroom, followed by Lentinus edodes and Flammulina velutipes. Mushrooms contain various metabolites, such as terpenes, steroids, anthraquinone, phenolic acid, and benzoic acid, while primary metabolites contain proteins, oxalic acid, and peptides. Mushrooms have been reported to have an action against both Gram-positive and Gram-negative bacteria [1].

Nutritionally, they are rich in protein and amino acids but lack fatty acid content [2]. However, they contain a significant amount of vitamins such as B1, B2, B12, C, D, and E [3–8]. Thus, they act as the perfect source of present nutrition and promote the health for synergistic effects of present bioactive compounds. Structurally, mushrooms comprise...
the pileus, lamella, stipe, mycelium, and roots. The roots are mainly responsible for absorbing and gathering nutrients [9]. Earlier, there was a misconception regarding the classification of mushrooms as plants. Later, with advancement in science, they were added under the independent kingdom known as Mycota, mainly characterized by chitin inside the cell walls. Globally, various regulatory agencies have approved their use as dietary supplements such as the National Institute of Health, Food for Specific Health Use, National Health Service, etc. The purpose of this article is to curate and review the tremendous benefits and varieties of various mushrooms, unveiling their use at a broad scale to be resource-able for future therapeutic usage. These mushrooms include edible though they can be medicinal.

2. Pharmacological Actions of Mushroom

2.1. Mushrooms and Wound Healing

For ages, mushrooms have been shown to have the potential for wound healing application. Wound healing is a complex phenomenon, requiring nutrition and a moist environment for speeding up wound healing. The *Auricularia auricula*-judge, a type of medicinal mushroom, has been beneficial for wound healing [10]. The mushroom acts via the promotion of fibroblasts and keratinocytes and acts as a catalyst for collagen synthesis during wound healing. The extract could show dose-dependent wound healing activity. The extract reduces the expression of E-cadherin, causing the down-regulation. The down-regulation handles the wound healing effect, as suggested by other researchers as well.

Many other mushrooms have been shown to possess the wound healing action via the formation of ROS. The level of ROS decides the speed of the wound healing process. The low levels of ROS activate the wound healing process; however, higher levels of ROS handle the detoxification, causing cellular damage [11]. The wound healing activity is regulated via the balance between the pro-inflammatory and pro-regenerative signals regulated via cytokines. The polysaccharides derived from the *Gracilaria lemaneiformis* also speed up the wound closure rate, thus improving the epithelial layer thickness and collagen deposition [12]. As figured out through the Edu assay, the polysaccharide fraction significantly increased the DNA content during the S-phase. It was also found that the EdU positive was observed near the woundless area and the wound area [12]. Regulating the wound healing activity by increasing the cell proliferation causes accelerated wound healing [13]. The fraction could also activate the PI3K/PKC (Phosphatidylinositol 3-Kinase/Protein kinase) signaling pathway. Jesus et al. evaluated the wound healing effect of a β-D-glucan from the edible mushroom *Piptoporus betulinus* [14]. They found that the β-D-glucan derived showed promotion of viability of caco-2 cells confirmed by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) assay. It was also seen that the polysaccharide derived from mushrooms sped up the in vitro wound healing process via migration of epithelial intestinal cell migration.

Rao et al. coupled the zinc nanoparticles with the chitosan derived from the mushroom *Agaricus Bisporus, Aspergillus Niger* [15]. The chitosan acted as a capping material at zinc nanoparticles. The 500 µg of nanoparticles could cause an 83% and 81% reduction in skin fibroblasts and keratinocyte cell viability and showed excellent biocompatibility towards the skin cells. Because of zinc nanoparticles, the complex showed antibacterial action on *Staphylococcus aureus*. The Beta-glucan content derived from mushroom *Sparassis crispa* showed wound healing action on diabetic wounds [16]. Researchers evaluated the effect of medicinal mushroom *Sparassis crispa* on the diabetes-induced animal model. The administration of mushrooms resulted in a faster mechanism of wound healing compared to the standard control group. The population of infiltrating neutrophils increased as the mushroom was administered. The immuno-histochemical staining confirmed the migration of macrophages. The presence of mushroom extract also resulted in the expression of TGF-1 in the subcutaneous dermal layer. Moreover, the results of the Azan Mallory staining confirmed the collagen regeneration in the wound area. Many researchers have also reported the wound healing potential of mushrooms, as presented in Table 1.
Table 1. Medicinal mushrooms have wound-healing properties.

| Name of Mushroom | In-Vivo | In-Vitro | Outcome of Study | References |
|------------------|---------|----------|------------------|------------|
| *Coriolus versicolor* and *Boletus edulis* | - | Cell lines: MCF-7, breast cancer cell lines; HT-29, human colorectal cancer cell line; HUH-7, human hepatoila cell lines; Antibacterial: (Pseudomonas aeruginosa, Klebsiella pneumonia, Staphylococcus aureus, and Enterococcus faecalis) and Antifungal (Candida albicans and Candida utilis). L929, murine fibroblast cell line. | The silver nanoparticles synthesized from mushrooms showed anticancer properties. The silver nanoparticles synthesized from mushrooms showed antifungal properties. | [17] |
| *Agaricus bisporus* | - | Human ocular fibroblasts | Use of *Agaricus bisporus* results in wound healing in a dose-dependent manner. | [18] |
| *Agaricus blazei* | Induced burn-wound-treated rats | - | The use of *Agaricus blazei* in the treatment of burns wounds induces the expression of IL-1 mRNA and increases the accumulation of macrophages in the wound area. | [19] |
| *Agaricus Sylvaticus* | Rats with wound | - | Phenolic component of mushroom was found associated to the wound healing properties. | [20] |
| *Phanerochaete chrysosporium* | - | NIH 3T3, Murine Embryonic Fibroblast cell lines | Prepared curcumin loaded mycelium-based film capable of curing the injured tissue | [21] |
| *Ganoderma lucidum* | Indomethacin induced gastric mucosal lesions in rats | - | Polysaccharide fraction causes the healing of peptic ulcers in rats | [22] |
| *Ganoderma lucidum* | Sprague-Dawley rats induced with wound | - | Accelerated wound healing in rat liver tissues after Monopolar Electrosurgery | [23] |
| *Sparassis crispa* | Streptozotocin induced diabetic mice | - | Wound healing activity was observed on topical application of *Sparassis crispa* extract on wound | [24] |
| *Hericium erinaceus* | Male Sprague-Dawley rats induced with wound | - | Topical application of an aqueous extract of *Hericium erinaceus* showed wound healing action in rats | [25] |
| *Phellinus gilvus* | Streptozotocin induced diabetic rats | - | Isolated polysaccharides showed wound healing action | [26] |
| *Dioscorea batatas Decne* | - | INT-407 cells | The phytyglucoprotein isolated showed wound healing action at the intestinal epithelial wound | [27] |
| *Flammulina velutipes* | Female Sprague-Dawley rat | - | *Flammulina velutipes* polysaccharides scaffold showed skin wound healing and hair follicle regenerative action | [28] |
**Table 1. Cont.**

| Name of Mushroom          | In-Vivo | In-Vitro            | Outcome of Study                                                                 | References |
|---------------------------|---------|---------------------|---------------------------------------------------------------------------------|------------|
| *Schizophyllum commune*   | NA      | L929 fibroblasts cells | Electrospun fiber with polyvinyl alcohol showed improved wound healing and promoted the migration of cells at the wound site | [29]       |
| *Lignosus rhinocerotis*   | NA      | Human dermal cells   | Gold nanoparticles synthesized with the mushroom extract and chitosan showed wound healing capability though non-cytotoxic | [30]       |

### 2.2. Mushrooms in Anti-HIV Action

Mushrooms have also been reported to target HIV. Mushrooms such as *Agaricus sylvaticus* reduce the oxidative stress in HIV-infected patients [31]. Administration with the supplementation containing the mushroom extract showed improved antioxidant defense in the infected individual. A reduction in TBARS (Thiobarbituric acid reactive substance; a method used to detect lipid peroxidation) and an increase by NN values in DPPH (2,2-Diphenyl-1-picrylhydrazyl) and Trolox equivalent capacity were reported in HIV-positive patients. The supplementation causes reversed oxidative alterations and improvement in antioxidant defense and can be used as a complementary strategy for the patients. Researchers administered the patients with the nutrients derived from the *Alternanthera pungens* to the asymptomatic HIV-positive patients. It was seen that there was a significant decrease in the marker TBARS, and a rise in the number of CD4+ and CD8+ T cells was observed [32]. Many other mushrooms, such as *P. abalonus*, *Coriolus versicolor*, *A. bisporus*, *P. citrinopileatus*, *L. edodes*, have been reported to possess anti-HIV action [33–37].

A marketed formulation known as Immune Assist 24/7 has constituents derived from mushrooms [38]. It has components that have immunomodulating and antiviral properties. In clinical trials conducted in Ghana, it was found that administering 800 mg of tablets of Immune Assist 24/7, once daily, increased CD4+T lymphocytes. In one of the cases, the increase in CD4+ T cells showed a 4000% increase in 60 days. The laccase enzyme produced by the *Ganoderma* spp. and *Lentinus* spp. have been reported to possess the property to inhibit the reverse transcriptase of HIV [39]. Flow cytometry results showed that the extracts of mushrooms showed over 50% inhibition for viral replication. The enzymatic extract from the *Lentinus* spp. showed an 86.4% inhibition rate at a concentration of 2466 U/L. The inhibition efficiency was higher, but it was lower than the antiretroviral therapy drug AZT (98%). The efficiency was compared with two batches taken from the same species, but variation was observed. The laccases are derived from the *Coprinus comatus* mushroom. The derived component of mushroom showed anti-HIV-1 RT activity against the IC$_{50}$ values of 5.85 µM [40]. The lectins derived from the *Agaricus bitorquis* also showed to possess the anti-HIV nature [41]. The lectins showed anti-HIV-1 reverse transcriptase activity at a IC$_{50}$ value of 4.69 µM, which was more effective than *A. bisporus* with an IC$_{50}$ value of 8 µM [35].

Sillapachaiyaporn et al. studied the effect of *Auricularia polytricha* on HIV-1 [42]. Anti-HIV-1 protease activity of the isolated compounds from hexane crude extracts of *Auricularia polytricha* (APH) [(Linoleoyl oleoyl palmitoylglycerol, Linoleoyl oleoyl stearoylglycerol, Distearoyl palmitoylglycerol, Linoleic acid, Ergosterol) Table S1]. These compounds, such as Ergosterol, Linoleic acid, Distearoylpalmitoylglycerol, acted unitedly for the inhibition. They made this evidenced by the low solubility of ergosterol in water. When combined with all other components, their activity increased (for chemical structures, refer to Figure 1). El-Mekkawy et al. reported the role of Ganoderiol F, ganodermanontriol as anti-HIV agents [43]. Moreover, other compounds such as ganoderic acid B, ganoderiol B, ganoderic acid C1, 3 β-5 α-dihydroxy-6 β-methoxyergosta-7,22-diene, ganoderic acid α, ganoderic
acid H, and ganoderiol A showed mild inhibition activity towards the HIV-1 PR. Similarly, El-Dine et al. reported isolating new triterpenes, such as colorssolactone V, Colossolactone VI, Colossolactone VII, and Colossolactone VIII, from the Ganoderma colossum, showing anti-HIV activity [44]. Hui et al. reported the isolation of hemolysin from the edible mushroom Pleurotus nebrodensis, using chromatography techniques [45]. The molecule Nebrodeolysin has a molecular weight of 27 kDa. In vivo studies showed hemolytic activity against the rabbit erythrocytes and caused the efflux of potassium ions. The compound could induce cytotoxicity against the L929 and HeLa cells, as evidenced by microscopic observations and DNA ladder, respectively.

Figure 1. Active phytochemicals derived from mushrooms having the anticancer effect.

Edible mushroom Pholiota adiposa showed constituents with antioxidant and anti-HIV activities [46]. The compound HEB showed antioxidant potency, DPPH radical activity. The compound could show the inhibition of HIV-1 replication in the TZM-BL cells infected by the pseudovirus. The compound showed the inhibition of the viral entry process and enzymes required to enter the HIV-1 life cycle. The HEB showed inhibition of reverse transcriptase and integrase activities, which was high compared to pepstatin A. Many other researchers also reported anti-HIV action of mushrooms and their constituents, as shown in Table 2.
Table 2. Mushrooms and their active constituents for the anti-HIV.

| Name of Mushroom | Active Constituent | Anti-HIV Activity against | References |
|------------------|--------------------|---------------------------|------------|
| Russula paludosa | Fraction SU2       | HIV-1 RT                  | [47]       |
| Agaricus bitorquis | Agaricus bitorquis Lectin | HIV-1 RT and leukemic cells | [41] |
| Lignosus rhinocerus | heliantriol F and 6 α-fluoroprogesterone | HIV-1 protease inhibitor; inhibition of HIV-1 induced syncytial formation and p24 production in the infected MOLT-4 cells. | [48] |
| Ganobera colossum | Ganomycin I, Ganomycin B | HIV-1 protease | [49] |
| Cordyceps sobolifera | Cordysobin | HIV-1 RT | [50] |
| Fomes fomentarius | Water-soluble melanin-glucan complex; insoluble chitin-glucan-melanin complex | HIV-1 protease | [51] |
| A. subrufescens | β-glucan | HIV-1 RT | [52] |
| A. subrufescens | Laccase | HIV-1 RT | [53] |
| A. subrufescens | Lectin | HIV-1 RT | [54] |
| Inonotus obliquus | Terpenes | HIV-1 RT | [55] |
| I. obliquus | Polysaccharides | HIV-1 RT | [56] |
| I. obliquus | Terpenes | HIV-1 RT | [57] |
| I. obliquus | Polyphenols | HIV-1 RT | [58] |
| I. obliquus | Terpenes | HIV-1 RT | [59] |
| Phellinus igniarius | Terpenes | HIV-1 RT | [60] |
| Pleurotus abalonus | Polysaccharide–peptide complex LB-1b | HIV-1 RT | [36] |
| Flammulina velutipes | Velutin | HIV-1 RT | [61] |
| Hypsizigus marmoreus | Marmarin | HIV-1 RT | [62] |
| Pleurotus citrinopileatus | Lectin | HIV-1 RT | [33] |
| Russula delica | Dimeric lectin | HIV-1 RT | [34] |
| Pleurotus ostreatus | Glycoprotein | HIV-1 RT | [63] |
| Pholiota adiposa | Lectin | HIV-1 RT | [64] |
| Agrocybe cylindracea | Agrocybin | HIV-1 RT | [65] |
| Pleurotus cornucopiae | Laccase | HIV-1 RT | [66] |
| Schizophyllum commune | 20-kDa ribonuclease | HIV-1 RT | [67] |
| Lentinus edodes | Lentin | HIV-1 RT | [68] |
| Hericium erinaceum | Lentin | HIV-1 RT | [69] |
| Pleurotus abalonus | 120-kDa Polysaccharide | HIV-1 RT | [70] |

2.3. Mushrooms and Anticancer Potentials

Cancer is one of the leading causes of death worldwide. The uncontrolled growth of cells can characterize as cancer and may be present in blood and body parts. Mushrooms have been reported to control the cell division, and, used in cancer therapy [71], such as the chaga mushroom (Inonotus obliquus), possess anti-cancerous compounds [72,73]. The main chemical constituents include lanosterol, 7,9(11),24-lanostatriene-3β-21-diol, ergosterol, inotodiol, ergosterol peroxide, and trametenolic acid (mentioned in Figure 1); they showed anticancer activity counter to the prostatic carcinoma cell lines PC3 and breast cancer cell line MDA-MB-231. The compounds that showed IC50 values against PC3 were calculated to be 9.82 ± 0.98 µg/mL for ergosterol, 38.19 ± 1.67 µg/mL for ergosterol...
peroxide, 63.71 ± 3.31 µg/mL for trametenolic acid, and 73.46 ± 0.64 µg/mL for 7,9(11),24-lanostatriene-3β-21-diol. However, inotodiol and lanosterol were non-efficient with IC₅₀ values above 100 µg/mL, while Nakata et al. successfully isolated the inonotsuoxides A, inotodiol, trametenolic acid, and lanosterol from the same mushrooms and showed anti-tumor activity in vivo [74]. Park and his coworkers reported the isolation of proteins from the Cordyceps militaris (CMP). The isolated proteins showed trypsin-like serine protease activity. The protein could inhibit F. oxysporum and cytotoxicity towards the human breast and bladder cancer cells [75]. Kosanic et al. studied the effect of metal concentration on anticancer activity of Lactarius deliciosus and Macrolepiota procera [76]. The anticancer activity was determined on the HeLa cells, human lung carcinoma A545 cells, and human colon carcinoma LS174 cells. The study showed that the M. procera showed comprehensively better anticancer effects on the A549 and LS174 cell lines, while the HeLa cell lines were more prone to Lactarius deliciosus. Similarly, Kim et al. isolated the hetero polysaccharides from the L. deliciosus with anticancer activity [77].

Boobalan et al. prepared carbon dots derived from the oyster mushroom [78]. These can be used as colorimetric sensors for the quantification of Pb²⁺ ions. These dots can also be used as a fluorescent probe for DNA recognition through electrostatic interaction between the ctDNA and C-dots. These dots also showed anticancer activity against the MDA-MB-231 breast cancer cells. The presence of C-dots caused morphological changes in the cell blebbing and chromatin condensation. The Hoechst 33,342 staining of cancer cells confirmed the fragmentation of the nuclear region. The nanoparticles of selenium decorated with the water-soluble polysaccharides were extracted from the mushroom [79]. The nanoparticles were stable for 13 weeks and with a particle size of 91–102 nm. The gastric adenocarcinoma cells were found to be more sensitive to nanoparticles. Nanoparticles induced the caspase and mitochondria-mediated apoptosis.

Similarly, the polysaccharides (HLP-1-1 and HLP-2-1) derived from Helvella leucopus showed anticancer activity against the HepG2 cells [80]. The secondary metabolites of Ganoderma applanatum were effective against the human colon cancer cell lines (Caco-2) [81]. The metabolites caused morphological alterations and an increase in levels of glutathione. Moreover, the levels of the Bax/Bcl-2 ratio increased significantly with the treatment of metabolites. The in vivo study showed a reduction in solid Ehrlich tumor mass after 5 days of exposure to metabolites. Researchers studied the ethanol extract of Marasmius oreades on the HT-29, MCF-7, and MDA-MB-231 cells by using MTT assay [82]. Anticancer activities of mushroom extract of other researchers have been cited in Table 3.

Table 3. Mushrooms have anticancer properties.

| Sl. No. | Name of Mushroom | Tested Chemical Constituent | Cell Lines Studied | References |
|--------|-----------------|-----------------------------|--------------------|------------|
| 1      | *Flammulina velutipes* | Water extract | BT-20, MCF-7 and MDA-MB-231 | [83] |
| 2      | *F. velutipes* | Flammulinolide A, B, C, and F | Hela, HepG2 and KB cells | [84] |
| 3      | *F. velutipes* | Enokipodin B, D, and J, 2,5-cuparadiene-1,4-dione | HepG2, MCF-7, A549, and SGC7901 | [85] |
| 4      | *F. velutipes* | Alkaline-soluble polysaccharide | SC-180 mouse model | [86] |
| 5      | *F. velutipes* | Polysaccharides | S-180 mice tumor model and SMMC-7721 human hepatoma cells | [87] |
| 6      | *F. velutipes* | Polysaccharide | BEL-7402 cell | [88] |
| 7      | *F. velutipes* | Ergosterol, and 22, 23-dihydroergosterol | SGC, HepG2, A549, and U251 | [89] |
| 8      | *F. velutipes* | Proflamin | B-16 melanoma and Ca755 adenocarcinoma | [90] |
Table 3. Cont.

| Sl. No. | Name of Mushroom          | Tested Chemical Constituent | Cell Lines Studied                        | References |
|---------|---------------------------|-----------------------------|------------------------------------------|------------------|
| 9       | *Ganoderma neo-japonicum* | Ethanolic extract           | Human colonic carcinoma cells            | [91]             |
| 10      | *Astraceus hygrometricus* | Astrakurkurone               | Hep 3B and Hep G2                        | [92]             |
| 11      | *Cantharellus cibarius*   | Polysaccharides             | NK92 cells                               | [93]             |
| 12      | *Agrocybe aegerita*       | Antitumor lectin            | HeLa, SW480, SGC-7901, MGC80-3, BGC-823, HL-60, and mouse sarcoma S-180 | [94]             |
| 13      | *A. aegerita*             | *A. aegerita* galectin      | 4T1 cells                                | [95]             |
| 14      | *Agaricus bisporus*       | Gal β-1,3-GalNAc-binding lectin | HT29 colon cancer cells                  | [96]             |
| 15      | *Armillaria luteo-virens* | dimeric lectin              | MBL2 cells, HeLa cells, and L1210 cells  | [97]             |
| 16      | *Boletus speciosus*       | *B. speciosus* hemagglutinin | Hep G2 cells and L1210                  | [98]             |
| 17      | *Clitocybe nebularis*     | Lectin                      | Human leukemic T cells                   | [99]             |
| 18      | *Flammulina velutipes*    | Hemagglutinin               | Leukemia L1210 cells                     | [100]            |
| 19      | *Ganoderma capense*       | Lectin                      | L1210 and M1 cells and HepG2 cells       | [101]            |
| 20      | *Grifola frondosa*        | N-acetylglactosamine-specific lectin | HeLa cells                             | [102]            |
| 21      | *Hericium erinaceum*      | *H. erinaceum* agglutinin  | HepG2 and MCF7                           | [69]             |
| 22      | *A. bisporus*             | Mannogalactoglucon          | HepG2 cells                              | [103]            |
| 23      | *Ganoderma lucidum*       | *G. lucidum* polysaccharides | HT29 cells                              | [104]            |
| 24      | *G. lucidum*              | *G. lucidum* polysaccharides | LNCaP human prostate cancer cells        | [105]            |
| 25      | *G. lucidum*              | *G. lucidum* polysaccharides | K562 and RG2 cells                       | [106]            |
| 26      | *Grifola frondosa*        | *G. frondose* polysaccharides | MCF-7 and MDA-MB-231                     | [107]            |
| 27      | *Hericium erinaceus*      | HEFP-2b polysaccharide      | HCT-116 cancer cells                     | [108]            |
| 28      | *Lentinus edodes*         | Mannogalactoglucon-type polysaccharides | Sarcoma 180 solid tumor                | [109]            |
| 29      | *L. edodes*               | Homogeneous polysaccharide  | Human cervical carcinoma HeLa cells      | [110]            |
| 30      | *Cordyceps sinensis*      | *C. sinensis* polysaccharide | HCT116 cancer cell line                  | [111]            |
| 31      | *Pleurotus eryngii*       | *P. eryngii* polysaccharides | HepG-2                                  | [112]            |
| 32      | *Pleurotus ostreatus*     | *P. ostreatus* polysaccharide | Murine lymphoid cancer cell line         | [113]            |

2.4. Mushrooms as Immunomodulators

The immune system is a combination of specialized cells and protein networks that protects the body against infection. The level of immunity decides how healthy a person is. The active part of mushrooms acts along with the human body’s immune system and fights against diseases. The mushroom acts via modulating the innate and adaptive immune system (Figure 2). The host pattern recognition receptors and pathogen-associated molecular patterns decide the response after invasion by foreign bodies. The pattern recognition receptors activate the innate immunity after pathogen recognition, while Toll-like receptors activate the pathways coordinating with the innate immunity and trigger the immunity response [114].
Figure 2. The schematic diagram for the mechanism of innate and adaptive immunity; activity of mushroom extracts on cyclic pathways, adapted from [115].

Velde et al. studied the immunomodulatory potential of the Agaricus subrufescens and Coprinus conatus species of mushroom using the THP-1 cells [116]. Various other researchers also evaluated the upregulation of genes using the extracts of Ganoderma lucidum, L. edodes, Agaricus bisporus, and A. subrufescens [117–120]. Velde et al. isolated the polysaccharide fraction of two mushrooms as curdlan and zymosan. They observed that the polysaccharides could induce cytokine secretion as a better response on THP-1 macrophages than THP-1 monocytes, showing polysaccharides' immunomodulatory potential, while cell differentiation results showed that the zymosan and A. subrufescens polysaccharide showed limited potency compared to standard compounds. In another study, researchers studied the immunomodulatory effect of Pleurotus albidus, as basidiome with cold water, hot water, hot alkali and Exo, and endopolysaccharide. The basidiome extracts were able to stimulate the production of TNF-α and nitric oxide, but no IL-6 was generated. Moreover, the phagocytosis activity of zymosan particles decreased [121].

Lin et al. studied the response of Maitake MD-fraction from the Grifola frondosa (active component β-glucan), showing an increase in the response of granulocytes, macrophages (CFU-GM) to bone marrow cells progenitors [122]. Moreover, the recovery pattern showed a rise for CFU-GM after administration of doxorubicin (DOX) induced hematopoietic suppression. PG101, a water-soluble extract derived from L. lepideus, activates the selective cytokines by controlling the cellular transcription factor, Nuclear factor-kB [123]. Administration to mice increased GCF-GM. In addition, PG101 increased the number of granulocytes and myeloid progenitors. The morphological studies showed the PG101 induced the differentiation of progenitor cells to granulocytes. The levels of GM-CSF, IL-6, and IL-1β also showed a spike after per se administration of PG101. The fruiting bodies from the G. lucidum, after treatment, showed a rise in levels of IL-1β, TNF-α, and...
IL-6 by many folds. Moreover, the administration resulted in the release of IFN-γ from T lymphocytes showing their role in the antitumor activity of this extract [124].

The 6-branched 1,3-β-D-glucan (SCG), derived from the Sparassiscrispa has antitumor activity [125]. The administration of SCG enhanced the hematopoietic response in cyclosporine-induced leukopenic mice by the intraperitoneal route. The monocytes and granulocytes present in the peritoneal cavity, liver, and spleen showed faster recovery in control. Moreover, the ratio of natural killer cells and γ delta T cells in the liver and spleen increased. However, the CD4+ and CD8+ cells decreased, and production of IL-6 and BMCs increased. Thus, this shows the possibility that IL-6 may contribute towards the enhanced hematopoietic response. Researchers studied the effect of Agaricus blazeiMurrill, Antrodia cinnamomea, Ganoderma lucidum, and Hirsutella Sinensis [126]. The water and ethanol-based extracts showed remarkable effects on NK cells. The water extracts enhanced NK cell cytotoxicity against the cancer cells, while ethanol extract inhibited the cytotoxicity. The presence of water in extract stimulates the expression and production of perforin and granulysin and activates the signaling kinases such as ERK, JNK, and p38, while with ethanol, inhibition in the expression of cytolytic and cell surface receptors was reported. This finding shows that the mode of extraction of mushroom proteins may cause different pharmacological actions.

Similarly, another group of researchers found that the alkali-soluble polysaccharide and water-soluble polysaccharide-protein complex derived from the Pleurotus rhinoceros showed immunomodulatory effects in murine bone marrow-derived dendritic cells [127]. The extracts caused morphological changes in the cells and induced phenotypic and functional maturation of dendritic cells. The alkali-based polysaccharide upregulates the expression of CD86, while the water-soluble polysaccharide upregulates CD40, CD80, and 86 cells and also binds to the dectin-1 receptor and stimulates the release of MIP-1α, MIP-2, and IL-2. The water-based polysaccharide binds to complement receptor 3 and toll-like receptor 2 with upregulation of IL-2, IL-6, MIP-1α, MIP-2, RANTES, IL-12p40p70, IL-12p70, TIMP-1, IFN-γ, KC, MCP-1, and GCSF [127]. Polyporus rhinoceros produces the immunologically active novel micro-particulate β-glucan known as PRA-1p. PRA-1p is produced via emulsification and crosslinking of PRA-1, which is chemically hyper-branched (1→3), (1→6)-β-d-glucan [128]. The PRA-1p pharmacologically induces the morphological changes in RAW 264.7 cells and generates nitric oxide and reactive oxygen species formation. Moreover, PRA-1p enhances the secretion of cytokines, granulocyte colony-stimulating factor, macrophages inflammatory protein, etc., while with RAW 264.7, cells’ activation of nitric oxide synthase, NF-κB, extracellular signal-regulated kinase, and protein kinase B takes place. Many of the other papers citing the immunomodulatory effect of mushrooms have been tabulated in Table 4.

| Source | Immunomodulatory Effect | References |
|--------|-------------------------|------------|
| Auricularia auricula-judae | Induces apoptosis of cancer cell | [129] |
| Agaricus blazei | Activates the NK cells, macrophages, dendritic cells, and granulocytes | [130] |
| Agaricus bisporus | Obstruct multiplying of L1210 and HT-29 cells | [41] |
| Agrocybe aegerita | Obstruct multiplying of 4T1, HeLa, SW480 SGC7901, MGC803, BGC823, HL-60, and S180 cells | [95] |
| Amanita phalloides | Obstruct multiplying of L1210 cells | [131] |
| Boletus edulis | Arouse mice splenocytes mitogenicity and obstruct multiplying of human hepatocyte carcinoma G2 (HepG2) and HT-29 cells | [132] |
| Boletus speciosus | Obstruct multiplying of HepG2 and L1210 cells | [98] |
| Cryptoporus volvatus | Diminutions of TLR2 and activate NF-κB | [133] |

Table 4. Mushrooms having an immunomodulatory effect.
Table 4. Cont.

| Source | Immunomodulatory Effect | References |
|--------|-------------------------|------------|
| Cerioporus squamosus (syn. Polyporus squamosus) | Obstruct multiplying of HeLa cells | [134] |
| Clitocybe nebularis | Obstruct multiplying of human leukemic T cells | [99] |
| Chroogomphis rutilus | Arouse the proliferation of murine splenocytes and improved the secretion of IL-2 | [135] |
| Flammulina velutipes | Upsurge NO, IL-1 production, and TNF-α secretion | [137] |
| Flammulina velutipes | Excite mice splenocytes mitogenicity and obstruct multiplying of L1210 cells | [100] |
| Flammulina velutipes | Excite mice splenocytes mitogenicity and stimulate proliferation of L1210, Mouse myeloma MBL2 and HeLa cells | [97] |
| Flammulina velutipes | Excite mitogenesis in human peripheral lymphocytes, suppress systemic anaphylaxis reaction, improve transcription of IL-3, IFN-γ | [138] |
| Ganoderma lucidum | Excite TNF-α, IL-1, IFN-γ production, activates NF-κB | [139] |
| Grifola frondosa | Macrophage activation, induction of IL-1, IL-6, and TNF-α secretion | [140] |
| Gymnoporus dryophilus (syn. Collybia dryophila) | Constrain proliferation of HeLa cells | [102] |
| Ganoderma capense | Arouse mice splenocytes mitogenicity and inhibit proliferation of L1210, Mouse myeloma MBL2 and HeLa cells | [101] |
| Grifola frondosa | Constrain the proliferation of HeLa | [102] |
| Cantharellus cibarius | Arouse proliferation of IL-2, IL-3, IL-4, IFN-γ, TNF-α | [142] |
| Ganoderma microsporum | Downregulation of TNF-α | [143] |
| Ganoderma tsugae | Persuade cytokine secretion, cellular multiplication of human peripheral mononuclear cells (HPBMCs) enhancing IFN-γ expression | [144] |
| Ganoderma lucidum | Trigger THP-1 macrophages and induce proinflammatory cytokine transcription | [145] |
| Ganoderma lucidum | Augment transcription of IL-2, IL-3, IL-4, IFN-γ, TNF-α | [146] |
| Hericium erinaceus | Persuades NO production, increases expression of TNF-α, IL-1β, IL-12 | [147] |
| I. obliquus | Augment expression of IL-1β, IL-6, TNF-α, and inducible nitric oxide synthase (iNOS) in macrophages | [148] |
| Intragenic shuffled library | Encourage U-251 MG cells apoptosis | [149] |
| Kurokawa leucomeles | Constrain the proliferation of U937 cells | [150] |
| Lentinula edodes (syn. Lentinus edodes) | Encourage non-specific cytotoxicity in macrophage and augment cytokine production | [151] |
| Lentinus squarrosulus | Stimulation of macrophages, splenocytes, and thymocytes | [152] |
| Lignosus rhinocerotis | Hinder the multiplication of HeLa, MCF7, and A549 cells | [153] |
| Lactarius flavidulus | Obstruct the multiplying of HepG2 and L1210 cells | [154] |
| Leucocalocybe mongolica (syn. Tricholoma mongolicum) | Hinder the production of S180 cells | [155] |
| Macrocybe gigantea | Upsurge phagocytic function of macrophages by activating macrophages to release mediators such as NO and TNF-α and inhibits S180 and HL-60 cells | [156] |
| Marasmius oreades | Hinder the proliferation of SW480, HepG2, and NIH-3T3 cells | [157] |
| Morchella esculenta | Macrophage activation, trigger NF-κB | [158] |
### Table 4. Cont.

| Source                                                | Immunomodulatory Effect                                                                 | References |
|-------------------------------------------------------|----------------------------------------------------------------------------------------|------------|
| Morchella conica                                      | Encourages NO, IL-1β, IL-6 making                                                      | [159]      |
| Naematelia aurantialba                                | Improves mouse spleen lymphocyte multiplication                                         | [160]      |
| Pleurotus sp. 'Florida'                               | Arouses macrophages, splenocytes, and thymocytes                                        | [161]      |
| Poria cocos                                           | Promotes the immune reaction; increases the expression of cytokines                     | [162]      |
| Pleurotus ostreatus                                   | Encourages IL-4 and IFN-γ production                                                   | [163]      |
| Pseudosperma umbrinellum (syn. Inocybe umbrinella)    | Obstruct multiplication of HepG2 and MCF7 cells                                         | [164]      |
| Pleurotus eous                                        | Obstruct multiplication of MCF7, K562, and HepG2                                        | [165]      |
| Pleurotus citrinopileatus                            | Arouse mice splenocytes mitogenicity and obstruct multiplication of S180 cells         | [33]       |
| Pholiota adiposa                                      | Obstruct multiplication of HepG2 and MCF7 cells                                         | [64]       |
| Postia placenta                                       | Arouse mouse splenocyte cell proliferation and enhance interleukin-2 (IL-2) release, obstruct multiplication and persuade apoptotic effects on gastric tumor cells (MGC823) | [166]      |
| Poria cocos                                           | Enhance production of IL-1β, IL-6, IL-18, TNF-α, NO                                    | [167]      |
| Russula delica                                        | Obstruct multiplication of HepG2 and MCF7 cells                                         | [34]       |
| Russula lepida                                        | Obstruct multiplication of HepG2 and MCF7 cells                                         | [168]      |
| Schizophyllum commune                                 | Instigation of T cell increases interleukin and TNF-α production                        | [169]      |
| Sparassis crispa                                      | Boosts IL-6 and IFN-γ production                                                       | [170]      |
| Sarcodon aspratus                                     | Upsurges the discharge of TNF-α and NO in macrophage                                    | [171]      |
| Schizophyllum commune                                 | Excite mice splenocytes mitogenicity and obstruct multiplication of KB, HepG2, and S180 cells | [172]      |
| Stropharia rugosoannulata                             | Obstruct multiplication of HepG2 and L1210 cells                                        | [173]      |
| Trametes versicolor                                   | Upsurges the expression of cytokines; stimulates the macrophage phagocytes              | [174]      |
| Taiwanofungus camphoratus (syn. Antrodia camphorate)  | Stimulation of IFN-γ, TNF-α                                                            | [175]      |
| Tropicoporus linteus (syn. Phellinus linteus)         | Instigation of murine B cells, Induces IL-12 and IFN-γ production                      | [176]      |
| Tremella succiformis                                  | Encourages human monocytes to express interleukins                                     | [177]      |
| Taiwanofungus camphoratus (Syn. Antrodia camphorate)  | Induce expression of different cytokines (IL-1β, IL-6, IL-12, TNF-α)                    | [178]      |
| Trametes versicolor                                   | Increase human peripheral blood lymphocytes, enhanced production of TNF-α, NO           | [179]      |
| Volvariella volvacea                                  | Enhance expression of IL-2, IL-4, IFN-γ, TNF-α                                        | [180]      |
| Xylaria nigripes                                      | Inhibits NO, IL-1β, IL-6, TNF-α, and IFN-γ production                                  | [181]      |
| Xerocomellus chrysenteron (syn. Xerocomus chrysenteron)| Inhibit the proliferation of NIH-3T3 and HeLa cells                                     | [182]      |
| Xylaria hypoxylon                                     | Inhibit the proliferation of HepG2 cells                                               | [183]      |

### 2.5. Antioxidant and Antibacterial Action of Mushrooms

The reactive oxygen species (ROS) plays a vital role in the pathogenesis of various acute and chronic diseases. Antioxidants try to act via lowering the reaction in the cellular environment and thus the levels of ROS. The secondary products derived from mushrooms also play an essential role in the scavenging of ROS. Researchers exploited *Pleurotus ostreatus* and *Coprinus conatus* as ethanolic extracts for their antioxidant potential [184]. The study
showed the extraction of α-tocopherol, rutin, and apigenin, essential in skin protection as antioxidants. The flavonoid contents extracted from *Lentinus edodes*, *Volvariella volvacea*, *Pleurotus satusor-caju*, and *Auricularia auricula* have been shown to possess antioxidant properties [185]. The ethanolic extract from *L. edodes* was found to have higher phenolic and flavonoid content than the rest. In addition, the extract showed the highest radical scavenging assay compared to the standard. Other researchers reported similar results for the *Lentinus edodes* and *Volvariella volvacea* [186].

Yoon et al. reported the antioxidant effect of *Lentinus lepideus* and observed that the hot water extract of mushrooms showed the strongest β carotene-linoleic acid inhibition compared to others [187]. In addition, the methanolic extract with a concentration of 8 mg/mL showed the highest reducing power. However, the acetone and methanolic extract showed more effectiveness in scavenging action. The acetone and methanolic extract of *Pleurotus floria* also possesses strong inhibitory activity against the β-carotene-linoleic acid [188]. The extracts caused induction of nitric oxide production and expression of inducible nitric oxide synthase in RAW 264.7 cells and showed inhibition on the dose-dependent level. Xu et al. extracted the antioxidants from *Thelephora ganbajun* using ultrasound-assisted extraction [189]. The extraction was carried out using the design of experiments and was perfected as 57.38% ethanol, 70.15 mL/g solvents to solid ratio, 10.58 min extraction time, 40 °C extraction temperature, and 500 W ultrasound power. Compared to the traditional extraction method involving the soxhlet apparatus, the ultrasound-assisted method showed better output in a shorter time interval. Moreover, the extracts also showed anti-proliferative action against the A549, MCF-7, HepG2, and HT-29 cell lines. The antioxidant and anti-proliferative activity was accounted for due to rutin, 2-hydrocinnamic acid, and epicatechin in extracts. Polysaccharides from *Oudemansiella radicata* mushroom were extracted, termed as *Oudemansiella radicata* polysaccharides (ORP) [190]. Three extracts were ORP-1, ORP-2, and ORP-3 with an average molecular weight of 13,921 Da, 14,942 Da, and 10,209 Da. The chemical composition of extracts varied as mannose, ribose, glucose, galactose, and xylose. The ORP-1 showed the highest DPPH radical scavenging activity, while the ORP-3 showed the highest hydroxy radical scavenging activity, along with ferrous ion chelating activity. Researchers reported the exopolysaccharides extraction from *Ganoderma lingzhi* using a unique media for growth; the growth increased about three times compared to growth on basal media [191]. The exopolysaccharide showed higher uronic acid content, d-mannose, l-rhamnose, and d-glucose, thus possessing higher antioxidant properties such as radical scavenging, reductive capacity, and chelation transition metal catalysis. A tabulated form of papers citing the antioxidant potential of mushrooms has been reported in Table 5.

The antibacterial activity of methanol extract from the *C. versicolor* fruiting body was studied by Matijašević et al. [192]. The MIC values for different bacteria varied from 0.625 to 20 mg mL$^{-1}$. Both Gram-positive and Gram-negative bacteria were killed by *C. versicolor*. The extract inhibited *Staphylococcus aureus* and *Salmonella enterica* serovar Enteritidis as measured at 630 nm and verified by macro dilution. *S. aureus* cells exposed to *C. versicolor* MIC looked elongated and deformed, whereas *S. enteritidis* treated cells seemed shorter and aggregated, with torn cell walls. The treated *S. enteritidis* had a larger periplasmic gap and distorted and dispersed cell envelope components. The loss of 260-nm-absorbing material showed that the extract’s cytoplasmic membrane disrupting activity was more apparent in *S. aureus* than *S. enteritidis*. Similarly, Janeš et al. reported the antibacterial activity of extracts derived from mushrooms *Amanita virosa*. (Fr.) Bertill. (Amanitaceae) and *Cortinarius praestans*. Cordier (Cortinariaceae) against *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, respectively, and extract of endophytic fungus *Trucatella hartii*. (Tubeuf) Steyaert (Amphisphaeriaceae) against *Enterococcus faecalis* and *S. aureus* [193]. The coprophilous mushroom *Coprinopsis cinerea* has a genome-wide transcriptional response to *Bacillus subtilis* and *Escherichia coli* [194]. As the genes activated by co-cultivation with each bacterium mirrored each other, it is likely that the fungal effectors used by the fungus are identical. Interestingly, comparative proteomics of the *C. cinerea* secretome revealed that
the upregulated genes encode mainly secreted peptides and proteins with antibacterial activity. The cysteine-stabilized-defensins (Cs-defensins) and GH24-type lysozymes (GH24-lysozymes) were isolated, and their antibacterial activity was verified.

Table 5. Mushrooms and their antioxidant-derived compounds.

| The Scientific Name of the Mushroom | Antioxidant Compounds                                      | References          |
|------------------------------------|------------------------------------------------------------|---------------------|
| *Agaricus arvensis*                | β-Carotene, ascorbic acid, lycopene, phenolic compounds    | [195,196]           |
| *Agaricus bisporus*                | Pyrogallol, α-ergothioneine, α- and β-glucans, Catechin, gallic acid, rutin, caffeic acid | [197–199]          |
| *Agaricus blazei*                  | Benzoic acid, myricetin, quercetin, pyrogallol α- and β-Glucans | [200–202]          |
| *Agaricus romagnesi*               | Phenolic compounds, β-carotene                             | [203,204]          |
| *Agaricus silvaticus*              | Phenolic compounds, β-carotene                             | [205,206]          |
| *Agaricus silvicola*               | β-Carotene, ascorbic acid, lycopene, phenolic compounds    | [207,208]          |
| *Agrocybe cylindracea*             | α-Tocopherol, β-tocopherol                                 | [65]                |
| *Amanita rubescens*                | Phenolics compounds, flavonoids                            | [209,210]          |
| *Armillaria mellea*                | Antioxidant components, ascorbic acid, flavonoids, and phenolic compounds | [211–213]         |
| *Armillaria ostoyae*               | Phenolic compounds                                         | [214]               |
| *Auricularia auricula-judae*       | Polysaccharides, phenolic compounds                         | [215–217]          |
| *Auriculariapolytricha*            | Phenolic compounds                                         | [218,219]          |
| *Boletus badius*                   | β-Carotene, α-tocopherol, phenolic compounds, flavonoids   | [220,221]          |
| *Boletus edulis*                   | β-Carotene, ascorbic acid, flavonoids, tocopherols          | [222,223]          |
| *Calocybe gambosa*                 | Phenolic compounds, flavonoids                              | [224]               |
| *Cantharellus cibarius*            | Phenolic compounds, flavonoids                              | [225–227]          |
| *Cantharellus clavatus*            | Phenolic compounds                                          | [228]               |
| *Chlorophyllum rhacodes*           | Phenolic compounds                                          | [229,230]          |
| *Clavaria vermicularis*            | Flavonoids, ascorbic acid                                  | [231,232]          |
| *Clitocybe alexandra*              | Tocopherols, phenolic compounds                             | [233,234]          |
| *Clitocybe geotropa*               | Phenolic compounds                                          | [235,236]          |
| *Coprinopsis atramentaria*         | β-Glucans                                                  | [237,238]          |
| *Coprinus comatus*                 | β-Carotene, ascorbic acid, lycopene, phenolic compounds     | [239]               |
| *Coriolus versicolor*              | Gallic, p-coumaric, protocatechin, caffeic, and vanillie acids | [240–242]         |
| *Cortinarius clausus*              | Tocopherols, phenolic compounds                             | [240]               |
| *Craterellus cornucopioides*       | Phenolic compounds, flavonoids                              | [243–246]          |
| *Fistulina hepatica*               | Tocopherols, phenolic compounds                             | [247,248]          |
| *Flammulina velutipes*             | Gallic acid, pyrogallol, homogentisic acid, 5-sulfosalicylic acid, protocatechuic acid, quercetin, caffeic acid | [249,250]         |
| *Ganoderma applanatum*             | Gallic, p-coumaric, protocatechin, caffeic, and vanillie acids | [251,252]         |
| *Ganoderma lucidum*                | Quercetin, kaempferol, Triterpenoids, polysaccharides       | [253–255]          |
### Table 5. Cont.

| The Scientific Name of the Mushroom | Antioxidant Compounds | References |
|-------------------------------------|-----------------------|------------|
| *Ganoderma tsugae*                  | Polysaccharides       | [256,257]  |
| *Gomphus clavatus*                  | Ergosterol, phenolic compounds | [258,259]  |
| *Grapes frondosa*                   | Phenolic compounds, β-1,6 and β-1,3-glucan | [260]      |
| *Helvelia crispa*                   | Phenolic compounds    | [261]      |
| *Hericium erinaceus*                | Phenolic compounds    | [262]      |
| *Hydnum repandum*                   | Tocopherols, phenolic compounds | [263,264]  |
| *I. obliquus*                       | p-Hydroxybenzoic acid, quercetin, kaempferol | [265,266]  |
| *Lactarius deliciosus*              | Phenolic compounds, flavonoids | [269–271]  |
| *Lactarius piperatus*               | Phenolic compounds, flavonoids | [236,272]  |
| *Leucopaxillus giganteus*           | β-Carotene, α-tocopherol | [278–281]  |
| *Macrolepiota procera*              | Phenolic compounds    | [283]      |
| *Marasmius oraeus*                  | Flavonoids, ascorbic acid | [284,285]  |
| *Meripilus giganteus*               | Gallic, p-coumaric, protocatechuic acid, caffeic, and vanillic acids | [286–288]  |
| *Phellinus igniarius*               | Hispidin              | [289,290]  |
| *Phellinus linteus*                 | β-Tocopherol, protocatechuic acid, gallic acid; pyrogallol; homogentisic acid, α- and β-glucans | [291]      |
| *Pleurotus ostreatus*               | β-Glucans             | [292–294]  |
| *Pleurotus pulmonarius*             | Flavonoids, ascorbic acid | [295,296]  |
| *Pycnoporus sanguineus*             | Phenolic compounds    | [297,298]  |
| *Ramaria botrytis*                  | Tocopherols, phenolic compounds, ascorbic acid, β-carotene | [299–301]  |
| *Russula vinosa*                    | Phenolic compounds    | [302,303]  |
| *Schizophyllum commune*             | α- and β-Glucans, phenolic compounds | [304–306]  |
| *Sparassis crispa*                  | Protocatechuic acid, benzoic acid, p-hydroxybenzoic acid | [307]      |

### 2.6. Hepatoprotective Potentials of Mushrooms

Several researchers reported the protective action of mushrooms on experimentally induced liver injuries. Morel mushrooms have been reported to have beneficial action against the CCL₄ and ethanol-induced hepatotoxicity [308]. Treatment with mushroom extract resulted in lowering the levels of GOT (Glutamic oxaloacetic transaminase), GPT (Glutamic pyruvic transaminase), and ALP (Alkaline phosphatase) in a dose-dependent manner. A similar kind of result was reported by Wu et al. to use *Ganoderma lucidum* [309]. Liu et al. extracted the polysaccharides such as water-soluble polysaccharides and alkali-soluble polysaccharides from the *Oudemansiella radicata* [310]. Administration of polysaccharides resulted in lower serum alanine aminotransferase and aspartate aminotransferase, and it stimulated the hepatic superoxide dismutase and glutathione peroxidase. Nisar et al.
reported the hepatoprotective action of actives isolated from *Lentinus edodes* in hypercholesterolemic rats [311].

### 2.7. Anti-Inflammatory Action of Mushroom

The anti-inflammatory action of mushrooms is based on macrophages mediating via inhibiting the signaling pathways such as prostaglandins release, ROS production, activation of transcription 1 and STAT6, and NF-κB [312,313]. Chien et al. studied the anti-inflammatory action of the *Grifola frondosa* and *Ophiocordyceps* spp. It was reported that the production of nitric oxide affected tumor necrosis factor-α, while the production of nitric oxide interleukin-10 was increased [314]. Yuan et al. reported the role of bioactive protein PEP derived from *Pleurotus eryngii*. PEP showed anti-inflammatory activity in RAW 264.7 macrophages, inhibiting pro-inflammatory mediators’ production and inhibiting inducible nitric oxide synthase expression, showing its potency for anti-inflammatory activity in the colon [315]. Liu et al. reported the action of polysaccharides derived from *Hypsizygus marmoreus* on LPS in lungs [316].

### 3. Clinical Trails

The clinical trials were searched using clinicaltrials.gov (accessed on 27 August 2021). The criteria for searching the trials included trials completed and results reported. The number of clinical trials was reported for the use of mushrooms in treatment, and therapeutic interventions were relatively low (Total 8 nos, 6 nos was relevant to the use of mushrooms; two clinical trials were excluded). Table 6 outlines many of the useful clinical trials which provide evidence of the usefulness of mushrooms. Many other researchers had also summed up the role of mushrooms on cancer risk, gut health, and mortality [317–322].

**Table 6.** Tabulated data about Clinical trials involving mushrooms.

| Clinical Trial No. | Intervention Model | Details of Trial and Outcome | References |
|--------------------|--------------------|------------------------------|------------|
| NCT01398176        | Parallel Assignment| Consuming *Lentinula edodes* daily resulted in improvement in immunity and cellular proliferation. | [323,324] |
| NCT01099917        | Single Group Assignment | Administration of Maitake mushroom showed improvement in Hematopoiesis in Myelodysplastic Patients during Phase II evaluation | [325,326] |
| NCT01414010        | Parallel Assignment | The comparative analysis of administering Trametes Versicolor, Saccharomyces Boulardii, and amoxicillin to subjects. The Trametes versicolor administration showed a significant reduction in bacterial percentage in the stool. | [327] |
| NCT01402115        | Parallel Assignment | Administration of polycan (a purified β-glucan from *Aureobasidium pullulans*) resulted in a reduction in bone loss and biomarkers present due to bone metabolism | [328] |
| NCT00465595        | Crossover Assignment | The use of Psilocybin This resulted in a decrease in mood anxiety and depression and increased well-being/life satisfaction | [329,330] |
| NCT04186780        | Parallel Assignment | Consumption of *L. edodes* Bars This resulted in a decrease in oxidative stress and Dyslipidemia in border line patients | [331] |

### 4. Recommendations and Future Perspectives

Various mushrooms have been found and tested to possess a bioactive role in treating multiple disorders besides their beneficial health effects. They have been included in dietary supplements by multiple organizations. The role of the bioactive is determined by the type of extraction procedure carried out. It has been found that the choice of solvent used for extraction determines the quantity and quality of the bioactive derived.
The primary and secondary metabolites showed outstanding properties for treating and preventing many life-threatening diseases. Bioactive compounds showing therapeutic action include polysaccharides, proteins, peptides, enzymes, and other compounds. They have been based on inhibiting viral proteins, enhance immunity, etc. Many formulations of mushrooms such as paste and powder present low amounts of fats and can be used as antioxidants to prevent oxidative stress and aging. However, due to many mushroom varieties existing, many of them have been remained untouched, and their pharmacological action has not been determined. Thus, there is a need to explore the other side of the coin complemented with advanced interventions and additional clinical trials.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/jof7090728/s1, Table S1: Name and a molecular formula of constituent compounds of APH (hexane crude extract of Auricularia polytricha).

Author Contributions: Conceptualization, H.C. and Y.K.M.; original draft preparation, H.C., A.K.M., Y.K.M., and A.A.B.; writing—review and editing, A.K.M., T.K.M., Y.K.M., and K.-H.B.; visualization, H.C.; supervision, K.-H.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Research Foundation of Korea [NRF2019R1F1A1052625], Republic of Korea.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: This work was supported by the National Research Foundation of Korea, Republic of Korea [Grant number-NRF2019R1F1A1052625].

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Alves, M.; Ferreira, I.F.R.; Dias, J.; Teixeira, V.; Martins, A.; Pintado, M. A review on antimicrobial activity of mushroom (basidiomycetes) extracts and isolated compounds. Planta Med. 2012, 78, 1707–1718. [CrossRef]
2. Reis, F.S.; Barros, L.; Martins, A.; Ferreira, I.C.F.R. Chemical composition and nutritional value of the most widely appreciated cultivated mushrooms: An inter-species comparative study. Food Chem. Toxicol. 2012, 50, 191–197. [CrossRef] [PubMed]
3. Blumfield, M.; Abbott, K.; Duve, E.; Cassettari, T.; Marshall, S.; Fayet-Moore, F. Examining the health effects and bioactive components in Agaricus bisporus mushrooms: A scoping review. J. Nutr. Biochem. 2020, 84, 108453. [CrossRef] [PubMed]
4. Ndong’u, S.W.; Otieno, C.A.; Onyango, C.; Musieba, F. Nutritional composition, physical qualities and sensory evaluation of wheat bread supplemented with Oyster Mushroom. Am. J. Food Technol. 2015, 10, 279–288. [CrossRef]
5. Bernas, E. Monosodium glutamate equivalents and B-group vitamins in frozen mushrooms. Int. J. Food Prop. 2018, 10, 1948. [CrossRef]
6. Cardwell, G.; Bornman, J.F.; James, A.P.; Black, L.J. A review of mushrooms as a potential source of dietary vitamin D. Nutrients 2018, 10, 1948. [CrossRef]
7. Keflie, T.S.; Nölle, N.; Lambert, C.; Nohr, D.; Biesalski, H.K. Impact of the natural resource of UVB on the content of vitamin D2 in oyster mushroom (Pleurotus ostreatus) under subtropical settings. Saudi J. Biol. Sci. 2019, 26, 1724–1730. [CrossRef]
8. Jiang, Q.; Zhang, M.; Mujumdar, A.S. UV induced conversion during drying of ergosterol to vitamin D in various mushrooms: Effect of different drying conditions. Trends Food Sci. Technol. 2020, 105, 200–210. [CrossRef]
9. Fischer, M.W.F.; Money, N.P. Why mushrooms form gills: Efficiency of the lamellate morphology. Fungal Biol. 2010, 114, 57–63. [CrossRef]
10. Mapoung, S.; Umsumarrang, S.; Semmarath, W.; Arjari, P.; Thippraphan, P.; Yodkeeree, S.; Pornngarm, L. Skin wound-healing potential of polysaccharides from medicinal mushroom Auricularia auricula-judae (Bull.). J. Fungi 2021, 7, 247. [CrossRef]
11. Dunnill, C.; Patton, T.; Brennan, J.; Barrett, J.; Dryden, M.; Cooke, J.; Leaper, D.; Georgopoulos, N.T. Reactive oxygen species (ROS) and wound healing: The functional role of ROS and emerging ROS-modulating technologies for augmentation of the healing process. Int. Wound J. 2017, 14, 89–96. [CrossRef]
12. Veeraperumal, S.; Qiu, H.M.; Zeng, S.S.; Yao, W.Z.; Wang, B.P.; Liu, Y.; Cheong, K.L. Polysaccharides from Gracilaria lemanceiformis promote the HaCaT keratinocytes wound healing by polarised and directional cell migration. Carbohydr. Polym. 2020, 241, 116310. [CrossRef] [PubMed]
13. Batterbury, M.; Tebbs, C.A.; Rhodes, J.M.; Grierson, I. Strategies and Therapies for Wound Healing: A Review. *Curr. Drug Targets* 2021, 22. (online ahead of print). [CrossRef]

14. De Jesus, L.I.; Smiderle, F.R.; Ruthes, A.C.; Vilaplana, F.; Dal’Lin, F.T.; Maria-Ferreira, D.; Werner, M.F.; Van Griensven, L.J.L.D.; Iacomini, M. Chemical characterization and wound healing property of a β-D-glucan from edible mushroom *Piptoporus betulinus*. *Int. J. Biol. Macromol.* 2018, 117, 1361–1366. [CrossRef]

15. Rao, K.M.; Suneetha, M.; Park, G.T.; Babu, A.G.; Han, S.S. Hemostatic, biocompatible, and antibacterial non-animal fungal mushroom-based carboxymethyl chitosan-ZnO nanocomposite for wound-healing applications. *Int. J. Biol. Macromol.* 2020, 155, 71–80. [CrossRef] [PubMed]

16. Kwon, A.H.; Qiu, Z.; Hashimoto, M.; Yamamoto, K.; Kimura, T. Effects of medicinal mushroom (*Sparassis crispa*) on wound healing in streptozotocin-induced diabetic rats. *Am. J. Surg.* 2009, 197, 503–509. [CrossRef] [PubMed]

17. Kaplan, O.; Gökşen Tosun, N.; Ozgür, A.; Erden Tayhan, S.; Bilgin, S.; Türkekul, I.; Gökce, I. Microwave-assisted green synthesis of silver nanoparticles using crude extracts of *Boletus edulis* and *Coriolus versicolor*: Characterization, anticancer, antimicrobial and wound healing activities. *J. Drug Deliv. Sci. Technol.* 2021, 64, 102641. [CrossRef]

18. Batterbury, M.; Tebbs, C.A.; Rhodes, J.M.; Grierson, I. *Agaricus bisporus* (edible mushroom lectin) inhibits ocular fibroblast proliferation and collagen lattice contraction. *Exp. Eye Res.* 2002, 74, 361–370. [CrossRef] [PubMed]

19. Sui, Z.F.; Yang, R.; Liu, B.; Gu, T.M.; Zhao, Z.L.; Shi, D.F.; Chang, D.Q. Chemical analysis of *Agaricus blazei* polysaccharides and effect of the polysaccharides on IL-1ß mRNA expression in skin of burn wound-treated rats. *Int. J. Biol. Macromol.* 2010, 47, 155–157. [CrossRef]

20. Da Silva, G.R.; Franklin, V.; Cambui, J.M.; de Almeida, D.T.; Wadt, N.S.Y.; Cardoso, V.O.; Bach, E.E. Effect of *Agaricus sytleticus* (Scheffer) extract in rats skin wound healing. *Biomed. J. Sci. Tech. Res.* 2018, 10, 7598–7600. [CrossRef]

21. Khamrai, M.; Banerjee, S.L.; Kundu, P.P. A sustainable production method of mycelium biomass using an isolated fungal strain *Phanerochaete chrysosporium* (accession no: KY593186): Its exploitation in wound healing patch formation. *Biocatal. Agric.* 2018, 16, 548–557. [CrossRef]

22. Gao, Y.; Tang, W.; Gao, H.; Chan, E.; Lan, J.; Zhou, S. *Ganoderma lucidum* polysaccharide fractions accelerate healing of acetic acid-induced ulcers in rats. *J. Med. Food* 2004, 7, 417–421. [CrossRef]

23. Lin, H.J.; Chang, Y.S.; Lin, L.H.; Haung, C.F.; Wu, C.Y.; Ou, K.L. An immunomodulatory protein (Ling Zhi-8) from a *Ganoderma lucidum* induced acceleration of wound healing in rat liver tissues after monopolar electrosurgery. *Evid. Based Complement. Altern. Med.* 2014, 2014, 916531. [CrossRef]

24. Yamamoto, K.; Kimura, T. Orally and topically administered *Sparassis crispa* (hanabiratake) improved healing of skin wounds in mice with streptozotocin-induced diabetes. *Biosci. Biotechnol. Biochem.* 2013, 77, 1303–1305. [CrossRef] [PubMed]

25. Abdulla, M.A.; Fard, A.A.; Sabaratnam, V.; Wong, K.H.; Kuppusamy, U.R.; Abdullah, N.; Ismail, S. Potential activity of aqueous polysaccharide fractions of edible mushroom *Pleurotus citrinopileatus* on wound healing in diabetic rat. *J. Drug Deliv. Sci. Technol.* 2018, 54, 76–80. [CrossRef] [PubMed]

26. Bae, J.S.; Jang, K.H.; Jin, H.K. Polysaccharides isolated from *Phellinus gilvus* accelerates wound healing in streptozotocin-induced diabetic rats. *J. Vet. Sci.* 2009, 13, 33–39. [CrossRef] [PubMed]

27. Kim, J.Y.; Lee, Y.M.; Park, J.P.; Lim, K.T.; Lee, S.J. Phytoglycoprotein isolated from *Dioscorea batatas* Decne promotes intestinal epithelial wound healing. *Chin. J. Nat. Med.* 2020, 18, 738–748. [CrossRef]

28. Chen, F.; Zhang, Q.; Wu, P.; Zhao, Y.; Suo, X.; Xiao, A.; Ke, M.; He, X.; Tong, Z.; Chen, Y. Green fabrication of seedbed-like *Flammulina velutipes* (Bull.: Fr.) Pers. (Aphyllophoromycetidae) in accelerating wound healing in rats. *Int. J. Med. Mushrooms* 2011, 13, 33–39. [CrossRef] [PubMed]

29. Bae, J.S.; Jang, K.H.; Jin, H.K. Polysaccharides isolated from *Phellinus gilvus* enhances dermal wound healing in streptozotocin-induced diabetic rats. *J. Vet. Sci.* 2005, 6, 161–164. [CrossRef] [PubMed]

30. Nor Azlan, A.Y.H.; Katas, H.; Habideen, N.H.; M. Busra, M.F. Dual-action of thermoresponsive gels containing DslRNA-loaded gold nanoparticles for diabetic wound therapy: Characterization, in vitro safety and healing efficacy. *Saudi Pharm. J.* 2020, 28, 1420–1430. [CrossRef]

31. Figueira, M.S.; Sá, L.A.; Vasconcelos, A.S.; Moreira, D.R.; Laurindo, P.S.O.C.; Ribeiro, D.R.G.; Santos, R.S.; Guzzo, P.; Dolabela, M.E.; Percario, S. Nutritional supplementation with the mushroom *Hericium erinaceus* (Bull.: Fr.) Pers. (Aphyllophoromycetidae) in accelerating wound healing in diabetic rats. *Int. J. Biol. Macromol.* 2011, 49, 155–157. [CrossRef] [PubMed]

32. Djoohan, Y.F.; Camara, C.; Monde, A.A.; Koffi, G.; Niamké, G.; Déré, L.; Tiahou, G.; Djessou, P.; Sess, D. Interest of antioxidants in the care of the patients infected by the HIV: The experience of long term administration of *Alternanthera pungens* herb tea. *Ann. Biol. Clin.* 2009, 67, 563–568.

33. Li, Y.R.; Liu, Q.H.; Wang, H.L.; Ng, T.B. A novel lectin with potent antitumor, mitogenic and HIV-1 reverse transcriptase inhibitory activities from the edible mushroom *Polyporus citrinopileatus*. *Biochim. Biophys. Acta Gen. Subj.* 2008, 1780, 51–57. [CrossRef]

34. Zhao, S.; Zhao, Y.; Li, S.; Zhao, J.; Zhang, G.; Wang, H.; Ng, T.B. A novel lectin with highly potent antiproliferative and HIV-1 reverse transcriptase inhibitory activities from the edible wild mushroom *Russula delica*. *Glycoconj. J.* 2010, 27, 259–265. [CrossRef]

35. Singh, R.S.; Bhari, R.; Kaur, H.P. Mushroom lectins: Current status and future perspectives. *Crit. Rev. Biotechnol.* 2010, 30, 99–126. [CrossRef] [PubMed]
36. Li, N.; Li, L.; Fang, J.C.; Wong, J.H.; Ng, T.B.; Jiang, Y.; Wang, C.R.; Zhang, N.Y.; Wen, T.Y.; Qu, L.Y.; et al. Isolation and identification of a novel polysaccharide-peptide complex with antioxidant, anti-proliferative and hypoglycaemic activities from the abalone mushroom. *Biosci. Rep.* 2012, 32, 221–228. [CrossRef]

37. Collins, R.A.; Ng, T.B. Polyasaccharopeptide from *Coriolus versicolor* has potential for use against human immunodeficiency virus type 1 infection. *Life Sci.* 1997, 60, 383–387. [CrossRef]

38. Adotey, G.; Quarcoo, A.; Holloway, J.C.; Fofie, S.; Saaka, B. Effect of immunomodulating and antiviral agent of medicinal mushrooms (Immune Assist 24/7™) on CD4+ T-Lymphocyte Counts of HIV-infected patients. *Int. J. Med. Mushrooms* 2011, 13, 109–113. [CrossRef]

39. Fleréz-Sampedro, L.; Zapata, W.; Orozco, L.P.; Mejía, A.I.; Arboleda, C.; Rugeles, M.T. In vitro anti-HIV-1 activity of the enzymatic extract enriched with laccase produced by the fungi *Ganoderma* sp. and *Lentinus* sp. *Vitae* 2016, 23, 109–118. [CrossRef]

40. Zhao, S.; Rong, C.B.; Kong, C.; Liu, Y.; Xu, F.; Miao, Q.J.; Wang, S.X.; Wang, H.X.; Zhang, G.Q. A novel lactose with potent antiproliferative and HIV-1 reverse transcriptase inhibitory activities from mycella of mushroom *Coprinus comatus*. *BioMed Res. Int.* 2014, 2014, 417461. [CrossRef]

41. Zhang, G.Q.; Chen, Q.J.; Hua, J.; Liu, Z.L.; Sun, Y.; Xu, X.; Han, P.; Wang, H.X. An inulin-specific lectin with anti-HIV-1 reverse transcriptase, antiproliferative, and mitogenic activities from the edible mushroom *Agaricus bitotius*. *BioMed Res. Int.* 2019, 2019, 1341370. [CrossRef] [PubMed]

42. Sillapachaiyaporn, C.; Nilkhet, S.; Ung, A.T.; Chuchawankul, S. Anti-HIV-1 protease activity of the crude extracts and isolated compounds from *Auricularia polytricha*. *BMC Complement. Altern. Med.* 2019, 19, 351. [CrossRef] [PubMed]

43. El-Mekkawy, S.; Meselhy, M.R.; Nakamura, N.; Tezuka, Y.; Hattori, M.; Kakiuchi, N.; Shimotohno, K.; Kawahata, T.; Otake, T. Anti-HIV-1 and anti-HIV-1-protease substances from *Ganoderma lucidum*. *Phytochemistry* 1998, 49, 1651–1657. [CrossRef]

44. El Dine, R.S.; El Halawany, A.M.; Ma, C.-M.; Hattori, M. Anti-HIV-1 protease activity of lanostane triterpenes from the Vietnamese mushroom *Ganoderma colossum*. *J. Nat. Prod.* 2008, 71, 1022–1026. [CrossRef]

45. Lv, H.; Kong, Y.; Yao, Q.; Zhang, B.; Leng, F.W.; Bian, H.J.; Balzarini, J.; Van Damme, E.; Bao, J.K. Nebrodeolysin, a novel hemolytic protein from mushroom *Pleurotus nebrodensis* with apoptosis-inducing and anti-HIV-1 effects. *Phytomedicine* 2009, 16, 198–205. [CrossRef]

46. Wang, C.R.; Zhou, R.; Ng, T.B.; Wong, J.H.; Qiao, W.T.; Liu, F. First report on isolation of methyl gallate with antioxidant, anti-HIV-1 and HIV-1 enzyme inhibitory activities from a mushroom (*Pholiota adipsa*). *Environ. Toxicol. Pharmacol.* 2014, 37, 626–637. [CrossRef]

47. Wang, J.; Wang, H.X.; Ng, T.B. A peptide with HIV-1 reverse transcriptase inhibitory activity from the medicinal mushroom *Russula paludosa*. *Peptides* 2007, 28, 560–565. [CrossRef] [PubMed]

48. Sillapachaiyaporn, C.; Chuchawankul, S. HIV-1 protease and reverse transcriptase inhibition by tiger milk mushroom (*Russula* species) sclerotium extracts: In vitro and in silico studies. *J. Tradit. Complement. Med.* 2020, 10, 396–404. [CrossRef] [PubMed]

49. El Dine, R.S.; El Halawany, A.M.; Ma, C.-M.; Hattori, M. Inhibition of the dimerization and active site of HIV-1 protease by secondary metabolites from the Vietnamese mushroom *Ganoderma colossum*. *J. Nat. Prod.* 2009, 72, 2019–2023. [CrossRef] [PubMed]

50. Wang, S.X.; Liu, Y.; Zhang, G.Q.; Zhao, S.; Xu, F.; Geng, X.L.; Wang, H.X. Cordyosbin, a novel alkaline serine protease with HIV-1 reverse transcriptase inhibitory activity from the medicinal mushroom *Cordyceps sobolifera*. *J. Biosci. Bioeng.* 2012, 113, 42–47. [CrossRef]

51. Seniuk, O.F.; Gorovoj, L.F.; Beketova, G.V.; Savichuk, H.O.; Rytik, P.G.; Kucherov, I.I.; Prilutskay, P.G.; Prilutsky, A.I. Anti-infective properties of the melainin-glucan complex obtained from medicinal tinder bracket mushroom, *Coriolus versicolor* (L.: Fr.) Fr. *(Aphyllophoromycetideae).* *Int. J. Med. Mushrooms* 2011, 13, 109–118. [CrossRef]

52. Bruggemann, R.; Orlandi, J.M.; Benati, F.J.; Faccin, L.C.; Mantovani, M.S.; Nozawa, C.; Linhares, R.E.C. Antiviral activity of *Agaricus blazei* Murill ss. Heinem extract enriched with laccase produced by the fungi *Ganoderma* sp. and *Lentinus* sp. *Vitae* 2016, 23, 109–118. [CrossRef]

53. Ullrich, R.; Le, M.H.; Nguyen, L.D.; Hofrichter, M. Laccase from the medicinal mushroom *Agaricus blazei*: Production, purification and characterization. *Appl. Microbiol. Biotechnol.* 2005, 67, 357–363. [CrossRef] [PubMed]

54. Kawagishi, H.; Nomura, A.; Yumen, T.; Mizuno, T.; Hagiwara, T.; Nakamura, T. Isolation and properties of a lectin from the fruiting bodies of *Agaricus blazei*. *Carbohydr. Res.* 2013, 183, 150–154. [CrossRef]

55. Pavlova, N.I.; Savinova, O.V.; Nikolaeva, S.N.; Boreko, E.I.; Flekhter, O.B. Antiviral activity of betulin, betulinic and betulonic acids against some enveloped and non-enveloped viruses. *Fitoterapia* 2003, 74, 489–492. [CrossRef]

56. Ma, L.; Chen, H.; Zhang, Y.; Zhang, N.; Fu, L. Chemical modification and antioxidant activities of polysaccharide from mushroom *Inonotus obliquus*. *Carbohydr. Polym.* 2012, 89, 371–378. [CrossRef]

57. Duru, K.C.; Kovalkeva, E.G.; Daniilova, I.G.; van der Bijl, P. The pharmacological potential and possible molecular mechanisms of action of *Inonotus obliquus* from preclinical studies. *Phyther. Res.* 2019, 33, 1966–1980. [CrossRef]

58. Lee, I.K.; Yun, B.S. Styrlypyrone-class compounds from medicinal fungi *Phellinus* and *Inonotus* spp., and their medicinal importance. *J. Antibiot.* 2011, 64, 349–359. [CrossRef]

59. Lindequist, U.; Niedermeyer, T.H.J.; Jülich, W.D. The pharmacological potential of mushrooms. *Evid.-Based Complement. Altern. Med.* 2005, 2, 285–299. [CrossRef]
60. Zapora, E.; Wolkoowcyki, M.; Bakier, S.; Zjawiony, J.K. Phellinus igniarius: A pharmacologically active polypore mushroom. Nat. Prod. Commun. 2016, 11, 1043–1046. [CrossRef]

61. Wang, H.; Ng, T.B. Isolation and characterization of velutin, a novel low-molecular-weight ribosome-inactivating protein from winter mushroom (Flammulina velutipes) fruiting bodies. Life Sci. 2001, 68, 2151–2158. [CrossRef]

62. Wong, J.H.; Wang, H.X.; Ng, T.B. Marmorin, a new ribosome inactivating protein with antiproliferative and HIV-1 reverse transcriptase inhibitory activities from the mushroom Hypsizigus marmoreus. Appl. Microbiol. Biotechnol. 2008, 81, 669–674. [CrossRef] [PubMed]

63. Wang, H.X.; Ng, T.B. Isolation of a novel ubiquitin-like protein from Pleurotus ostreatus mushroom with anti-human immunodeficiency virus, translation-inhibitory, and ribonuclease activities. Biochem. Biophys. Res. Commun. 2000, 276, 587–593. [CrossRef]

64. Zhang, G.Q.; Sun, J.; Wang, H.X.; Ng, T.B. A novel lectin with antiproliferative activity from the medicinal mushroom Pholiota adiposa. Acta Biochim. Pol. 2009, 56, 415–421. [CrossRef] [PubMed]

65. Ngai, P.H.K.; Zhao, J.; Ng, T.B. Agrocybin, an antifungal peptide from the edible mushroom Agrocybe cylindracea. Peptides 2005, 26, 191–196. [CrossRef]

66. Ho Wong, J.; Bun Ng, T.; Jiang, Y.; Liu, F.; Cho Wing Sze, S.; Yanbo Zhang, K. Purification and characterization of a laccase with inhibitory activity toward HIV-1 reverse transcriptase and tumor cells from an edible mushroom (Pleurotus cornucopiae). Protein Pept. Lett. 2010, 17, 1040–1047. [CrossRef] [PubMed]

67. Zhao, Y.C.; Zhang, G.Q.; Ng, T.B.; Wang, H.X. A novel ribonuclease with potent HIV-1 reverse transcriptase inhibitory activity from cultured mushroom Schizophyllum commune. J. Microbiol. 2011, 49, 803–808. [CrossRef]

68. Ngai, P.H.K.; Ng, T.B. Lentin, a novel and potent antifungal protein from shiitake mushroom with inhibitory effects on activity of human immunodeficiency virus-1 reverse transcriptase and proliferation of leukemia cells. Life Sci. 2003, 73, 3363–3374. [CrossRef]

69. Li, Y.; Zhang, G.; Ng, T.B.; Wang, H. A novel lectin with antiproliferative and HIV-1 reverse transcriptase inhibitory activities from dried fruiting bodies of the monkey head mushroom hericium erinaceum. J. Biomed. Biotechnol. 2010, 2010, 716515. [CrossRef]

70. Wang, C.R.; Ng, T.B.; Li, L.; Fang, J.C.; Jiang, Y.; Wen, T.Y.; Qiao, W.T.; Li, N.; Liu, F. Isolation of a polysaccharide from Lactarius deliciosus. Biomed. Pharmacother. 2007, 61, 190–193. [CrossRef] [PubMed]

71. Zeng, D.; Zhu, S. Purification, characterization, antioxidant and anticancer activities of novel polysaccharides extracted from Macrolepiota procera. Int. J. Biol. Macromol. 2018, 107, 1086–1092. [CrossRef] [PubMed]

72. Blagodatskaya, A.; Yatsunskaya, M.; Mikhailova, V.；Tiasto, V.；Kagansky, A.; Katanaev, V.；Wong, J.H.; Wang, H.X.; Ng, T.B. Marmorin, a new ribosome inactivating protein with antiproliferative and HIV-1 reverse transcriptase inhibitory activities from the fruiting bodies of the abalone mushroom Pleurotus abalonus. J. Pharm. Pharmacol. 2011, 63, 825–832. [CrossRef]

73. Li, Y.; Zhang, G.; Ng, T.B.; Wang, H. A novel lectin with antiproliferative and HIV-1 reverse transcriptase inhibitory activities from dried fruiting bodies of the monkey head mushroom hericium erinaceum. J. Biomed. Biotechnol. 2010, 2010, 716515. [CrossRef]

74. Park, B.T.; Na, K.H.; Jung, E.C.; Park, J.W.; Kim, H.H. Antifungal and anticancer activities of a protein from the mushroom Cordyceps militaris. Korean J. Pharm. Pharmacol. 2009, 13, 49–54. [CrossRef]

75. Kosanić, M.; Ranković, B.; Rančić, A.; Stanojković, T. Evaluation of metal concentration and antioxidant, antimicrobial, and anticancer potentials of two edible mushrooms Lactarius deliciosus and Macrolepiota procera. J. Food Drug Anal. 2016, 24, 477–484. [CrossRef]

76. Kim, D.H.; Han, K.H.; Song, K.Y.; Lee, K.H.; Jo, S.Y.; Lee, S.W.; Yoon, T.J. Activation of innate immunity by Lepiota procera enhances antitumor activity. Korean J. Pharmacogn. 2010, 41, 115–121.

77. Boobalan, T.; Sethupathi, M.; Sengottuvelan, N.; Kumar, P.; Balaj, P.; Gulyás, B.; Padmanabhan, P.; Selvan, S.T.; Arun, A. Mushroom-derived carbon dots for toxic metal ion detection and as antibacterial and anticancer agents. ACS Appl. Nano Mater. 2020, 3, 9509–9519. [CrossRef]

78. Zeng, D.; Zhao, J.; Suk, K.H.; Cheung, S.T.; Wong, K.H.; Chen, T. Potentiation of in vivo anticaner efficacy of Selenium nanoparticles by mushroom polysaccharides surface decoration. J. Agric. Food Chem. 2019, 67, 2865–2876. [CrossRef] [PubMed]

79. Zeng, D.; Zhu, S. Purification, characterization, antioxidant and anticancer activities of novel polysaccharides extracted from Baciu mushroom. Int. J. Biol. Macromol. 2018, 107, 1086–1092. [CrossRef] [PubMed]

80. Elkhateeb, W.A.; Zaghlol, G.M.; El-Garawani, I.M.; Ahmed, E.F.; Rateb, M.E.; Abdel Moneim, A.E. Canaderma aplanatum secondary metabolites induced apoptosis through different pathways: In vivo and in vitro anticancer studies. Biomed. Pharmacocher. 2018, 101, 264–277. [CrossRef] [PubMed]

81. Shomali, N.; Onar, O.; Cihan, A.C.; Akata, I.; Yildirim, O. Antioxidant, anticancer, antimicrobial, and antibiofilm properties of the culinary-medicinal fairy ring mushroom, Marasmius oreades (Agaricomycetes). Int. J. Med. Mushrooms 2019, 21, 571–582. [CrossRef] [PubMed]

82. Gu, Y.H.; Leonard, J. In vitro effects on proliferation, apoptosis and colony inhibition in ER-dependent and ER-independent human breast cancer cells by selected mushroom species. Oncol. Rep. 2006, 15, 417–423. [CrossRef] [PubMed]
84. Wang, Y.; Bao, L.; Liu, D.; Yang, X.; Li, S.; Gao, H.; Yao, X.; Wen, H.; Liu, H. Two new sesquiterpenes and six norsesquiterpenes from the solid culture of the edible mushroom Flammulina velutipes. *Tetrahedron* 2012, 68, 3012–3018. [CrossRef]

85. Wang, Y.; Bao, L.; Yang, X.; Li, L.; Li, S.; Gao, H.; Yao, X.S.; Wen, H.; Liu, H.W. Bioactive sesquiterpenoids from the solid culture of the edible mushroom *Flammulina velutipes* growing on cooked rice. *Food Chem.* 2012, 132, 1346–1353. [CrossRef] [PubMed]

86. Leung, M.Y.K.; Fung, K.P.; Choy, Y.M. The isolation and characterization of an immunomodulatory and anti-tumor polysaccharide preparation from *Flammulina velutipes*. *Immunopharmacology* 1997, 35, 255–263. [CrossRef]

87. Jiang, S.M.; Xiao, Z.M.; Xu, Z.H. Inhibitory activity of polysaccharide extracts from three kinds of edible fungi on proliferation of human hepatoma SMMC-7721 cell and mouse implanted S180 tumor. *World J. Gastroenterol.* 1999, 5, 404–407. [CrossRef]

88. Zhao, C.; Zhao, K.; Liu, X.; Huang, Y.F.; Liu, B. In vitro antioxidant and antitumor activities of polysaccharides extracted from the mycelia of liquid-cultured *Flammulina velutipes*. *Food Sci. Technol. Res.* 2013, 19, 661–667. [CrossRef]

89. Yi, C.; Zhong, H.; Tong, S.; Cao, X.; Frempong, C.K.; Liu, H.; Fu, M.; Yang, Y.; Feng, Y.; Zhang, H.; et al. Enhanced oral bioavailability of a sterol-loaded microemulsion formulation of *Flammulina velutipes*, a potential antitumor drug. *Int. J. Nanomed.* 2012, 7, 5067–5078.

90. Ikekawa, T.; Miyano, T.; Okura, A.; Maruyama, H.; Kawamura, K.; Sawasaki, Y.; Shiratori, K.; Naito, K. Proflamin, a new antitumor agent: Preparation, physicochemical properties and antitumor Activity. *Jpn. J. Cancer Res. GANN* 1985, 76, 142–148. [PubMed]

91. Lau, M.-F.; Chua, K.-H.; Sabaratnam, V.; Kuppusamy, U.R. In vitro and in silico anticancer evaluation of a medicinal mushroom, *Ganoderma neo-japonicum* Imazeki, against human colon canceric cells. *Biotechnol. Appl. Biochem.* 2021, 68, 902–917. [CrossRef] [PubMed]

92. Dasgupta, A.; Dey, D.; Ghosh, D.; Lai, T.K.; Bhuvanesh, N.; Dolui, S.; Velayutham, R.; Acharya, K. Astrakurkurone, a sesquiterpenoid from wild edible mushroom, targets liver cancer cells by modulating Bcl-2 family proteins. *IUBMB Life* 2019, 71, 992–1002. [CrossRef]

93. Lemieszek, M.K.; Nunes, F.M.; Rzeski, W. Branched mannans from the mushroom: *Grifola frondosa* and cloning of a ricin B-like lectin from mushroom *Agrocybe aegerita*. *Biochem. J.* 2003, 374, 321–327. [CrossRef]

94. Zhao, C.; Sun, H.; Tong, X.; Qi, Y. An antitumour lectin from the edible mushroom *Agrocybe aegerita*. *Biochem. J.* 2006, 398, 167–171. [CrossRef]

95. Yu, L.; Fernig, D.G.; Smith, J.A.; Milton, J.D.; Rhodes, J.M. Reversible inhibition of proliferation of epithelial cell lines by *Agaricus bisporus* (Edible Mushroom) Lectin. *Cancer Res.* 1993, 53, 4627–4632.

96. Feng, K.; Liu, Q.H.; Ng, T.B.; Liu, H.Z.; Li, J.Q.; Chen, G.; Sheng, H.Y.; Xie, Z.L.; Wang, H.X. Isolation and characterization of a novel lectin from the mushroom *Amarillaria luteo-virens*. *Biochem. Biophys. Res. Commun.* 2006, 345, 1573–1578. [CrossRef]

97. Sun, J.; Ng, T.B.; Wang, H.; Zhang, G. A novel hemagglutinin with antiproliferative activity against tumor cells from the hallucinogenic mushroom boletus speciesicus. *BioMed Res. Int.* 2014, 2014, 340467. [CrossRef]

98. Zhao, C.; Sun, H.; Tong, X.; Qi, Y. An antitumour lectin from the edible mushroom *Agrocybe aegerita*. *Biochem. J.* 2003, 374, 321–327. [CrossRef]

99. Pohleven, J.; Obermajer, N.; Sabotič, J.; Anžlovar, S.; Sepšć, K.; Kos, J.; Kralj, B.; Štrukelj, B.; Brzin, J. Purification, characterization and cloning of a ricin B-like lectin from mushroom *Agrocybe aegerita*. *Biochem. Biophys. Acta Gen. Subj.* 2009, 1790, 173–181. [CrossRef]

100. Ng, T.B.; Ngai, P.H.K.; Xia, L. An agglutinin with mitogenic and antiproliferative activities from the mushroom *Flammulina velutipes*. *Mycolologia* 2006, 98, 167–171. [CrossRef]

101. Ngai, P.H.K.; Ng, T.B. A mushroom (*Ganoderma capense*) lectin with spectacular thermostability, potent mitogenic activity on splenocytes, and antiproliferative activity toward tumor cells. *Biochem. Biophys. Res. Commun.* 2004, 314, 988–993. [CrossRef] [PubMed]

102. Kawagishi, H.; Nomura, A.; Mizuno, T.; Kimura, A.; Chiba, S. Isolation and characterization of a lectin from *Grifola frondosa* fruiting bodies. *BBA Gen. Subj.* 1990, 1034, 247–252. [CrossRef]

103. Pires, A.D.R.A.; Ruthes, A.C.; Cadena, S.M.S.C.; Iacomini, M. Cytotoxic effect of a mannogalactoglucon extracted from *Agaricus bisporus* on HepG2 cells. *Carbohydr. Polym.* 2017, 170, 33–42. [CrossRef] [PubMed]

104. Jiang, D.; Wang, L.; Zhao, T.; Zhang, Z.; Zhang, R.; Jin, J.; Cai, Y.; Wang, F. Restoration of the tumor-suppressor function to mutant p53 by *Ganoderma lucidum* polysaccharides in colorectal cancer cells. *Oncol. Rep.* 2017, 37, 594–600. [CrossRef] [PubMed]

105. Zhao, X.; Zhou, D.; Li, Y.; Li, C.; Zhao, X.; Li, Y.; Li, W. *Ganoderma lucidum* polysaccharide inhibits prostate cancer cell migration via the protein arginine methyltransferase 6 signaling pathway. *Mol. Med. Rep.* 2018, 17, 147–157. [CrossRef] [PubMed]

106. Wang, C.; Shi, S.; Chen, Q.; Lin, S.; Wang, R.; Wang, S.; Chen, C. Antitumor and immunomodulatory activities of *Ganoderma lucidum* polysaccharides in glioma-bearing rats. *Integr. Cancer Ther.* 2018, 17, 674–683. [CrossRef] [PubMed]

107. Zhang, Y.; Sun, D.; Meng, Q.; Guo, W.; Chen, Q.; Zhang, Y. *Grifola frondosa* polysaccharides induce breast cancer cell apoptosis via the mitochondrial-dependent apoptotic pathway. *Int. J. Mol. Med.* 2017, 40, 1089–1095. [CrossRef]

108. Liu, J.Y.; Hou, X.X.; Li, Z.Y.; Shan, S.H.; Chang, M.C.; Feng, C.P.; Wei, Y. Isolation and structural characterization of a novel polysaccharide from *Hericium erinaceus* fruiting bodies and its arrest of cell cycle at S-phase in colon cancer cells. *Int. J. Biol. Macromol.* 2020, 157, 288–295. [CrossRef]

109. Jeff, I.B.; Fan, E.; Tian, M.; Song, C.; Yan, J.; Zhou, Y. In vivo anticancer and immunomodulating activities of mannogalactoglucon-type polysaccharides from *Lentinus edodes* (Berkeley) singer. *Cent. Eur. J. Immunol.* 2016, 41, 47–53. [CrossRef]
110. Ya, G. A *Lentinus edodes* polysaccharide induces mitochondrial-mediated apoptosis in human cervical carcinoma HeLa cells. *Int. J. Biol. Macromol.* 2017, 103, 676–682. [CrossRef]

111. Qi, W.; Zhou, X.; Wang, J.; Zhang, K.; Zhou, Y.; Chen, S.; Nie, S.; Xie, M. Cordyceps sinensis polysaccharide inhibits colon cancer cells growth by inducing apoptosis and autophagy flux blockage via mTOR signaling. *Carbohydr. Polym.* 2020, 237, 116113. [CrossRef] [PubMed]

112. Ren, D.; Wang, N.; Guo, J.; Yuan, L.; Yang, X. Chemical characterization of *Pleurotus eryngii* polysaccharide and its tumor-inhibitory effects against human hepatoblastoma HepG-2 cells. *Carbohydr. Polym.* 2016, 138, 123–133. [CrossRef]

113. Uddin PK, M.; Sayful Islam; M.; Pervin, R.; Dutta, S.; Talukder, R.I.; Rahman, M. Optimization of extraction of antioxidant polysaccharide from *Pleurotus ostrotrus* (Jacq.) P. Kumm and its cytotoxic activity against murine lymphoid cancer cell line. *PLoS ONE* 2019, 14, e0209371. [CrossRef]

114. Lee, M.S.; Kim, Y.J. Signaling pathways downstream of pattern-recognition receptors and their cross talk. *Annu. Rev. Biochem.* 2007, 76, 447–480. [CrossRef]

115. Abbas, A.K.; Lichtman, A.H.; Pillai, S. *Basic Immunology (6th edition): Functions and Disorders of the Immune System*; Elsevier Health Sciences: Amsterdam, The Netherlands, 2019; ISBN 9780323549431.

116. Van de Velde, J.; Wilbers, R.H.P.; Westerhof, L.B.; van Raaij, D.R.; Stavarakaki, I.; Sonnenberg, A.S.; Bakker, J.; Schots, A. Assessing the immunomodulatory potential of high-molecular-weight extracts from mushrooms; an assay based on THP-1 macrophages. *J. Sci. Food Agric.* 2015, 95, 344–350. [CrossRef] [PubMed]

117. Chan, W.K.; Cheung, C.H.; Law, H.K.W.; Lau, Y.L.; Chan, G.C.F. *Ganoderma lucidum* polysaccharides can induce human monocytic leukemia cells into dendritic cells with immuno-stimulatory function. *J. Hematol. Oncol.* 2008, 1, 1–12. [CrossRef]

118. Chanput, W.; Reitsma, M.; Kleinjans, L.; Mes, J.J.; Savelkoul, H.F.; Wichers, H.J. β-Glucans are involved in immune-modulation of THP-1 macrophages. *Mol. Nutr. Food Res.* 2012, 56, 822–833. [CrossRef]

119. Smiderle, F.R.; Alquini, G.; Tadra-Stier, M.Z.; Iacomini, M.; Wichers, H.J.; Van Griensven, L.J.L.D. *Agaricus bisporus* and *Agaricus brasiliensis* (1→6)-β-D-glucans show immunostimulatory activity on human THP-1 derived macrophages. *Carbohydr. Polym.* 2013, 94, 91–99. [CrossRef]

120. Ellertsen, L.K.; Hetland, G.; Johnson, E.; Grinde, B. Effect of a medicinal extract from *Agaricus blazei* Murill on gene expression in a human monocyte cell line as examined by microarrays and immuno assays. *Int. Immunopharmacol.* 2006, 6, 133–143. [CrossRef]

121. Castro-Alves, V.C.; Gomes, D.; Menolli, N.; Sforça, M.L.; do Nascimento, J.R.O. Characterization and immunomodulatory effects of glucans from *Pleurotus albidus*, a promising species of mushroom for farming and biomass production. *Int. J. Biol. Macromol.* 2017, 95, 215–223. [CrossRef]

122. Lin, H.; She, Y.H.; Cassileth, B.R.; Sirotnak, F.; Rundles, S.C. Maitake beta-glucan MD-fraction enhances bone marrow colony formation and reduces doxorubicin toxicity in vitro. *Int. Immunopharmacol.* 2004, 4, 91–99. [CrossRef] [PubMed]

123. Jin, M.; Jeon, H.; Jung, H.J.; Kim, B.; Shin, S.S.; Choi, J.J.; Lee, J.K.; Kang, C.Y.; Kim, S. Enhancement of repopulation and hematopoiesis of bone marrow cells in irradiated mice by oral administration of PG101, a water-soluble extract from *Lentinus lepidus*. *Exp. Biol. Med.* 2003, 228, 759–766. [CrossRef] [PubMed]

124. Wang, Y.S.; Hsu, M.L.; Hsu, H.C.; Tseng, C.H.; Lee, S.S.; Shiao, M.S.; Ho, C.K. The anti-tumor effect of *Ganoderma lucidum* is mediated by cytokines released from activated macrophages and T lymphocytes. *Int. J. Cancer* 1997, 70, 699–705. [CrossRef]

125. Harada, T.; Miura, N.; Adachi, Y.; Nakajima, M.; Yamada, T.; Ohno, N. Effect of SCG, 1,3β-D-Glucan from *Sparassis crispa* on the hematopoietic response in cyclophosphamide induced leukopenic mice. *Biol. Pharm. Bull.* 2002, 25, 931–939. [CrossRef]

126. Lu, C.C.; Hsu, Y.J.; Chang, C.J.; Lin, C.S.; Martel, J.; Ojcius, D.M.; Ko, Y.F.; Lai, H.C., Young, J.D. Immunomodulatory properties of medicinal mushrooms: Differential effects of water and ethanol extracts on NK cell-mediated cytotoxicity. *Innate Immun.* 2016, 22, 522–533. [CrossRef]

127. Liu, C.; Choi, M.W.; Xue, X.; Cheung, P.C.K. Immunomodulatory effect of structurally-characterized mushroom sclerotial polysaccharides isolated from *Polyporus rhinocerus* on bone marrow dendritic cells (BMDCs). *J. Agric. Food Chem.* 2019, 67, 12137–12143. [CrossRef]

128. Liu, C.; Cheung, P.C.K. Structure and immunomodulatory activity of microparticulate mushroom sclerotial β-Glucan prepared from *Polyporus rhinocerus*. *J. Agric. Food Chem.* 2019, 67, 9070–9078. [CrossRef]

129. Ma, Z.; Wang, J.; Zhang, L.; Zhang, Y.; Ding, K. Evaluation of water soluble β-d-glucan from Auricularia auricula-judae as potential anti-tumor agent. *Carbohydr. Polym.* 2010, 80, 977–983. [CrossRef]

130. Firenzueli, F.; Gori, L.; Lombardo, G. The medicinal mushroom *Agaricus blazei* murill: Review of literature and pharmacotoxicological problems. *Evid.-Based Complement. Altern. Med.* 2008, 5, 3–15. [CrossRef]

131. Lutsik-Kordovsky, M.D.; Stasyk, T.V.; Stoka, R.S. Analysis of cytotoxicity of lectin and non-lectin proteins from *Amanita* mushrooms. *Exp. Oncol.* 2001, 23, 43–45.

132. Zheng, S.; Li, C.; Ng, T.B.; Wang, H.X. A lectin with mitogenic activity from the edible wild mushroom *Boletus edulis*. *Process Biochem.* 2007, 42, 1620–1624. [CrossRef]

133. Yao, H.Y.; Zhang, L.H.; Shen, J.; Shen, H.J.; Jia, Y.L.; Yan, X.F.; Xie, Q.M. Cytoporos polysaccharide prevents lipopolysaccharide-induced acute lung injury associated with down-regulating Toll-like receptor 2 expression. *J. Ethnopharmacol.* 2011, 137, 1267–1274. [CrossRef]
185. Boonsong, S.; Klaypradit, W.; Wilaiapun, P. Antioxidant activities of extracts from five edible mushrooms using different extractants. *Agric. Nat. Resour.* 2016, 50, 89–97. [CrossRef]

186. Cheung, L.M.; Cheung, P.C.K.; Ooi, V.E.C. Antioxidant activity and total phenolics of edible mushroom extracts. *Food Chem.* 2003, 81, 249–255. [CrossRef]

187. Yoon, K.N.; Alam, N.; Lee, K.R.; Shin, P.G.; Cheung, J.C.; Yoo, Y.B.; Lee, T.S. Antioxidant and antityrosinase activities of various extracts from the fruiting bodies of *Lentinus lepideus*. *Molecules* 2011, 16, 2334–2347. [CrossRef] [PubMed]

188. Im, K.H.; Nguyen, T.K.; Shin, D.B.; Lee, K.R.; Lee, T.S. Appraisal of antioxidant and anti-inflammatory activities of various extracts from the fruiting bodies of *Pleurotus florida*. *Molecules* 2014, 19, 3310–3326. [CrossRef]

189. Xu, D.P.; Zheng, J.; Zhou, Y.; Li, Y.; Li, S.; Li, H. Bin Extraction of natural antioxidants from the *Thelephora ganbajun* mushroom by an ultrasound-assisted extraction technique and evaluation of antiproliferative activity of the extract against human cancer cells. *Int. J. Mol. Sci.* 2016, 17, 1664. [CrossRef]

190. Wang, Y.; Jia, J.; Ren, X.; Li, B.; Zhang, Q. Extraction, preliminary characterization and *in vitro* antioxidant activity of polysaccharides from *Oudemansiella ralicata* from the northwest Himalayas. *Int. J. Med. Mushrooms* 2019, 21, 1186–1196. [CrossRef] [PubMed]

191. Si, J.; Meng, G.; Wu, Y.; Ma, H.F.; Cui, B.K.; Dai, Y.C. Medium composition optimization, structural characterization, and antioxidant activity of exopolysaccharides from the medicinal mushroom *Ganoderma lingzhi*. *Int. J. Biol. Macromol.* 2019, 124, 588–602. [CrossRef] [PubMed]

192.tractive activity of *Coriolus versicolor* methanol extract and its effect on ultrastructural changes of *Staphylococcus aureus* and *Salmonella enteritidis*. *Front. Microbiol.* 2016, 7, 1226. [CrossRef] [PubMed]

193. Jia, S.; Li, F.; Liu, Y.; Ren, H.; Gong, G.; Wang, Y.; Wu, S. Effects of extraction methods on the antioxidant activities of polysaccharides from *Agaricus blazei* Murrill. *Carbohydr. Polym.* 2011, 86, 66–69. [CrossRef] [PubMed]

194. Carneiro, A.A.J.; Ferreira, I.C.F.R.; Dueñas, M.; Barros, L.; Gomes, E.; Santos-Buelga, C. Chemical composition and antioxidant properties of sixteen different Portuguese wild mushrooms species. *Hortic. Environ. Biotechnol.* 2010, 51, 579–588. [CrossRef]

195. Sharma, S.K.; Gautam, N. Evaluation of nutritional, nutraceutical, and antioxidant composition of eight wild culinary mushrooms (higher basidiomycetes) from the northwest Himalayas. *Int. J. Med. Mushrooms* 2016, 18, 539–546. [CrossRef]

196. Barros, L.; Falcão, S.; Baptista, P.; Freire, C.; Vilas-Boas, M.; Ferreira, I.C.F.R. Antioxidative action of the extracts of dried, edible mushrooms by chemical, biochemical and electrochemical assays. *Food Chem.* 2008, 111, 61–66. [CrossRef]

197. Xu, D.P.; Zheng, J.; Zhou, Y.; Li, Y.; Li, S.; Li, H. Bin Extraction of natural antioxidants from the *Thelephora ganbajun* mushroom by an ultrasound-assisted extraction technique and evaluation of antiproliferative activity of the extract against human cancer cells. *Int. J. Mol. Sci.* 2016, 17, 1664. [CrossRef]

198. Wang, Y.; Jia, J.; Ren, X.; Li, B.; Zhang, Q. Extraction, preliminary characterization and *in vitro* antioxidant activity of polysaccharides from *Oudemansiella ralicata* from the northwest Himalayas. *Int. J. Med. Mushrooms* 2019, 21, 1186–1196. [CrossRef] [PubMed]

199. Si, J.; Meng, G.; Wu, Y.; Ma, H.F.; Cui, B.K.; Dai, Y.C. Medium composition optimization, structural characterization, and antioxidant activity of exopolysaccharides from the medicinal mushroom *Ganoderma lingzhi*. *Int. J. Biol. Macromol.* 2019, 124, 588–602. [CrossRef] [PubMed]

200. Sharma, S.K.; Gautam, N. Evaluation of nutritional, nutraceutical, and antioxidant composition of eight wild culinary mushrooms (higher basidiomycetes) from the northwest Himalayas. *Int. J. Med. Mushrooms* 2016, 18, 539–546. [CrossRef]

201. Jia, S.; Li, F.; Liu, Y.; Ren, H.; Gong, G.; Wang, Y.; Wu, S. Effects of extraction methods on the antioxidant activities of polysaccharides from *Agaricus blazei* Murrill. *Carbohydr. Polym.* 2011, 86, 66–69. [CrossRef] [PubMed]

202. Carneiro, A.A.J.; Ferreira, I.C.F.R.; Dueñas, M.; Barros, L.; Da Silva, R.; Gomes, E.; Santos-Buelga, C. Chemical composition and antioxidant activity of cultivated button mushrooms (*Agaricus bisporus*). *Hortic. Environ. Biotechnol.* 2015, 56, 376–382. [CrossRef]

203. Robaszkiewicz, A.; Bartosz, G.; Lawrynowicz, M.; Soszyński, M. The role of polyphenols, β-carotene, and lycopene in the antioxidative action of the extracts of dried, edible mushrooms. *J. Nutr. Metab.* 2010, 2010, 173274. [CrossRef] [PubMed]

204. Kozarski, M.; Klaus, A.; Niksic, M.; Jakovljevic, D.; Helsper, J.P.F.G.; Van Griensven, L.J.L.D. Antioxidative and immunomodulating activities of polysaccharides extracts from the medicinal mushrooms *Agaricus bisporus, Agaricus brasiliensis, Ganoderma lucidum* and *Phellinus linteus*. *Food Chem.* 2011, 129, 1667–1675. [CrossRef]

205. Wu, S.; Li, F.; Jia, S.; Ren, H.; Gong, G.; Wang, Y.; Lv, Z.; Liu, Y. Drying effects on the antioxidant properties of polysaccharides obtained from *Agaricus blazei* Murrill. *Carbohydr. Polym.* 2014, 103, 414–417. [CrossRef] [PubMed]

206. Jia, S.; Li, F.; Liu, Y.; Ren, H.; Gong, G.; Wang, Y.; Wu, S. Effects of extraction methods on the antioxidant activities of polysaccharides from *Agaricus blazei* Murrill. *Int. J. Biol. Macromol.* 2013, 62, 66–69. [CrossRef]

207. Carneiro, A.A.J.; Ferreira, I.C.F.R.; Dueñas, M.; Barros, L.; Da Silva, R.; Gomes, E.; Santos-Buelga, C. Chemical composition and antioxidant activity of dried powder formulations of *Agaricus blazei* and *Lentinus edodes*. *Food Chem.* 2013, 138, 2168–2173. [CrossRef]

208. Barros, L.; Dueñas, M.; Ferreira, I.C.F.R.; Baptista, P.; Santos-Buelga, C. Phenolic acids determination by HPLC–DAD–ESI/MS in sixteen different Portuguese wild mushrooms species. *Food Chem. Toxicol.* 2009, 47, 1076–1079. [CrossRef]

209. Hellen, S.A.; Barros, L.; Sousa, M.J.; Martins, A.; Ferreira, I.C.F.R. Tocopherols composition of Portuguese wild mushrooms with antioxidant capacity. *Food Chem.* 2010, 119, 1443–1450. [CrossRef]

210. Gasecka, M.; Magdziak, Z.; Siwulski, M.; Mleczek, M. Profile of phenolic and organic acids, antioxidant properties and ergosterol content in cultivated and wild growing species of *Agaricus*. *Eur. Food Res. Technol.* 2018, 244, 259–268. [CrossRef]

211. Garrab, M.; Edziri, H.; El Mokni, R.; Mastouri, M.; Mabrouk, H.; Douki, W. Phenolic composition, antioxidant and antimicrobial activity properties of the three mushrooms *Agaricus silvaticus* Schaeff., *Hydnum rufescens* Pers. and *Meripilus giganteus* (Pers.) Karst. in Tunisia. *S. Afr. J. Bot.* 2019, 124, 359–363. [CrossRef]

212. Ribeiro, B.; de Pinho, P.G.; Andrade, P.B.; Oliveira, C.; Ferreira, A.C.S.; Baptista, P.; Valente, P. Do bioactive carotenoids contribute to the color of edible mushrooms? *Open Chem. Biomed. Methods J.* 2011, 4, 14–18. [CrossRef]

213. Öztürk, M.; Duru, M.E.; Kivrak, S.; Mercan-Doğan, N.; Türkoglu, A.; Özler, M.A. In vitro antioxidant, anticholinesterase and antimicrobial activity studies on three *Agaricus* species with fatty acid compositions and iron contents: A comparative study on the three most edible mushrooms. *Food Chem. Toxicol.* 2011, 49, 1353–1360. [CrossRef] [PubMed]

214. Buruleanu, L.C.; Radulescu, C.; Antonia Georgescu, A.; Dulama, I.D.; Niculescu, C.M.; Lucian Olteanu, R.; Stanescu, S.G. Chemometric assessment of the interactions between the metal contents, antioxidant activity, total phenolics, and flavonoids in mushrooms. *Anal. Lett.* 2019, 52, 1195–1214. [CrossRef]
210. Kouassi, K.A.; Kouadio, E.J.P.; Konan, K.H.; Dédé, A.E.; Kouamé, L.P. Phenolic compounds, organic acid and antioxidant activity of Lactarius subsericus, Cantharellus platyphyllus and Amanita rubescens, three edible ectomycorrhizal mushrooms from center of Côte d'Ivoire. *Eurasion J. Anal. Chem.* 2016, 11, 127–139.

211. Lai, M.N.; Ng, L.T. Antioxidant and antiedema properties of solid-state cultured honey mushroom, *Armillaria mellea* (Higher Basidiomycetes), extracts and their polysaccharide and polyphenol contents. *Int. J. Med. Mushrooms* 2013, 15, 1–8. [CrossRef]

212. Muszyńska, B.; Sulikowska-Ziaja, K.; Erikt, H. Phenolic acids in selected edible basidiomycota species: *Armillaria mellea*, *Boletus badius*, *Cantharellus cibarius*, *Lactarius deliciosus* and *Pleurotus ostreatus*. *Acta Sci. Pol. Hortorum Cultus* 2013, 12, 107–116.

213. Strapáč, I.; Baranová, M.; Smrčová, M.; Bedlovičová, Z. Antioxidant activity of honey mushrooms (*Armillaria mellea*). *Folia Vet.* 2016, 60, 37–41. [CrossRef]

214. Keleş, A.; Koca, I.; Gençcelep, H. Antioxidant properties of wild edible mushrooms. *J. Food Process. Technol.* 2011, 2, 2–6.

215. Cai, M.; Lin, Y.; Luo, Y.L.; Liang, H.H.; Sun, P.L. Extraction, antimicrobial, and antioxidant activities of crude polysaccharides from the wood ear medicinal mushroom *Auricularia auricula-judae* (higher basidiomycetes). *Int. J. Med. Mushrooms* 2015, 17, 591–600. [CrossRef]

216. Kho, Y.S.; Vikineswary, S.; Abdullah, N.; Kuppusamy, U.R.; Oh, H.I. Antioxidant capacity of fresh and processed fruit bodies and mycelium of *Auricularia auricula-judae* (Fr) quel. *J. Med. Food* 2009, 12, 167–174. [CrossRef] [PubMed]

217. Yu, S.C.; Oh, T.J. Antioxidant activities and antimicrobial effects of extracts from *Auricularia auricula-judae*. *J. Korean Soc. Food Sci. Nutr.* 2016, 45, 327–332. [CrossRef]

218. Teoh, H.L.; Ahmad, I.S.; Johari, N.M.K.; Aminudin, N.; Abdullah, N. Antioxidant properties and yield of wood ear mushroom, *Auricularia polytricha* (Agaricomycetes), cultivated on rubberwood sawdust. *Int. J. Med. Mushrooms* 2018, 20, 369–380. [CrossRef]

219. Bai, S.; Zhang, X.; Ma, X.; Chen, J.; Chen, Q.; Shi, X.; Hou, M.; Xue, P.; Kang, Y.; Xu, Z. Acid-active supramolecular anticancer nanoparticles based on cyclodextrin polyrotaxanes damaging both mitochondria and nuclei of tumor cells. *Biomater. Sci.* 2018, 6, 3126–3138. [CrossRef]

220. Sun, L.; Bae, X.; Zhuang, Y. Effect of different cooking methods on total phenolic contents and antioxidant activities of four Boletus mushrooms. *J. Food Sci. Technol.* 2014, 51, 3362–3368. [CrossRef]

221. Jaworska, G.; Pogon, K.; Skrzypczak, A.; Bernaś, E. Composition and antioxidant properties of wild mushrooms *Boletus edulis* and *Xerocomus badius* prepared for consumption. *J. Food Sci. Technol.* 2015, 52, 794–7953. [CrossRef]

222. Zhang, A.; Xiao, N.; He, P.; Sun, P. Chemical analysis and antioxidant activity in vitro of polysaccharides extracted from *Boletus edulis*. *Int. J. Biol. Macromol.* 2011, 49, 1092–1095. [CrossRef] [PubMed]

223. Vamanu, E.; Nita, S. Antioxidant capacity and the correlation with major phenolic compounds, anthocyanin, and tocopherol content from various extracts of the wild edible *Boletus edulis* mushroom. *BioMed Res. Int.* 2013, 2013, 313905. [CrossRef] [PubMed]

224. Vaz, J.A.; Barros, L.; Martins, A.; Santos-Buelga, C.; Vasconcelos, M.H.; Ferreira, I.C.F.R. Chemical composition of wild edible mushrooms and antioxidant properties of their water soluble polysaccharidic and Ethanolic fractions. *Food Chem.* 2011, 126, 610–616. [CrossRef]

225. Vamanu, E.; Nita, S. Bioactive compounds, antioxidant and anti-inflammatory activities of extracts from *Cantharellus cibarius*. *Rev. Chim.* 2014, 65, 372–379.

226. Ebrahimzadeh, M.A.; Safdari, Y.; Khalili, M. Antioxidant activity of different fractions of methanolic extract of the golden chanterelle mushroom *Cantharellus cibarius* (higher basidiomycetes) from Iran. *Int. J. Med. Mushrooms* 2015, 17, 557–565. [CrossRef] [PubMed]

227. Zhao, D.; Ding, X.; Hou, Y.; Hou, W.; Liu, L.; Xu, T.; Yang, D. Structural characterization, immune regulation and antioxidant activity of a new heteropolysaccharide from *Cantharellus cibarius* Fr. *Int. J. Mol. Med.* 2018, 41, 2744–2754. [CrossRef]

228. Palacios, I.; Lozano, M.; Moro, C.; D’Arrigo, M.; Rostagno, M.A.; Martínez, J.A.; Garcia-Lafuente, A.; Guillamón, E.; Villares, A. Antioxidant properties of phenolic compounds occurring in edible mushrooms. *Food Chem.* 2011, 128, 674–678. [CrossRef]

229. Barreira, J.C.M.; Ferreira, I.C.F.R.; Oliveira, M.B.P.P. Triacylglycerol profile as a chemical fingerprint of mushroom species. Evaluation by principal component and linear discriminant analyses. *J. Agric. Food Chem.* 2012, 60, 10592–10599. [CrossRef]

230. Šima, J.; Vondruška, J.; Svoboda, L.; Šeda, M.; Rokos, L. The accumulation of risk and essential elements in edible mushrooms *Cantharellus platyphyllus*, *Suillus grevillei*, *Inulaea bidaia*, and *Xerocomellus chrysenteron* growing in the Czech Republic. *Chem. Biodivers.* 2019, 16, e1800478.

231. Sharma, S.K.; Gautam, N. Chemical and bioactive profiling, and biological activities of coral fungi from northwestern Himalayas. *Sci. Rep.* 2017, 7, 46570. [CrossRef] [PubMed]

232. Kumari, B.; Upadhayey, R.C.; Atri, N.S. Evaluation of nutraceutical components and antioxidant potential of north indian wild culinary medicinal termitophilous mushrooms. *Int. J. Med. Mushrooms* 2013, 15, 191–197. [CrossRef] [PubMed]

233. Vaz, J.A.; Barros, L.; Martins, A.; Almeida, G.M.; Vasconcelos, M.H.; Ferreira, I.C.F.R. Wild mushrooms *Clitocybe alexandri* and *Lepista inversa*: In vitro antioxidant activity and growth inhibition of human tumour cell lines. *Food Chem. Toxicol.* 2010, 48, 2881–2884. [CrossRef]

234. Ersel, F.Y.; Cavas, L. Enzyme-based scavengers and lipid peroxidation in some wild edible Agaricales s.l. mushrooms from Mugla (Turkey). *Int. J. Med. Mushrooms* 2008, 10, 269–277. [CrossRef]

235. Sarikurkcu, C.; Tepe, B.; Semiz, D.K.; Solak, M.H. Evaluation of metal concentration and antioxidant activity of three edible mushrooms from Mugla, Turkey. *Food Chem. Toxicol.* 2010, 48, 1230–1233. [CrossRef]
236. Kosanić, M.; Petrović, N.; Stanojković, T. Bioactive properties of Clitocybe geotropa and Clitocybe nebularis. J. Food Meas. Charact. 2020, 14, 1046–1053. [CrossRef]

237. Schüßler, A. Secondary metabolites of basidiomycetes. In Physiology and Genetics the Mycota (A Comprehensive Treatise on Fungi as Experimental Systems for Basic and Applied Research); Anke, T., Schüßler, A., Eds.; Springer: Cham, Switzerland, 2018; pp. 231–275. ISBN 978-3-319-71739-5.

238. Helelo, S.A.; Ferreira, I.C.F.R.; Calhelha, R.C.; Esteves, A.P.; Martins, A.; Queiroz, M.J.R.P. Cytotoxicity of Coprinopsis atramentaria extract, organic acids and their synthesized methylated and glucuronate derivatives. Food Res. Int. 2014, 55, 170–175. [CrossRef]

239. Stilinović, N.; Capo, I.; Vukmirović, S.; Rašković, A.; Tomas, A.; Popović, M.; Sabo, A. Chemical composition, nutritional profile and in vivo antioxidant properties of the cultivated mushroom Crumatus conatus. R. Soc. Open Sci. 2020, 7, 200900. [CrossRef] [PubMed]

240. Scuto, M.; Di Mauro, P.; Ontario, M.L.; Amato, C.; Modafferi, S.; Ciavardelli, D.; Salinario, A.T.; Maiolino, L.; Calabrese, V. Nutritional mushroom treatment in meniere’s disease with Coriolus versicolor: A rationale for therapeutic intervention in neuroinflammation and antineurodegeneration. Int. J. Mol. Sci. 2020, 21, 284. [CrossRef]

241. Stojanova, M.; Pantić, M.; Karadelev, M.; Čuleva, B.; Nikšić, M. Antioxidant potential of extracts of three mushroom species collected from the Republic of North Macedonia. J. Food Process. Preserv. 2021, 45, e15155. [CrossRef]

242. Kozarski, M.; Klaus, A.; Vunduk, J.; Nikšić, M. The influence of mushroom Coriolus versicolor and hazelnuts enrichment on antioxidant activities and bioactive content of dark chocolate. Food Feed Res. 2020, 47, 23–32. [CrossRef]

243. Costea, T.; Hudiță, A.; Olaru, O.T.; Gălațeanu, B.; Gîrd, C.E.; Mocanu, M.M. Chemical composition, antioxidant activity and cytotoxic effects of occultus Craterellus cornucopioides (L.) pers. mushroom. Farmaciu. 2020, 68, 340–347. [CrossRef]

244. Liu, T.; Zhang, N.; Zhou, N.; Li, W.; Xie, X.; Deng, Y.; Ren, L.; Long, X.; Li, S.; Zhou, L.; et al. Resveratrol inhibits the TRIF-dependent pathway by upregulating sterile alpha and armadillo motif protein, contributing to anti-inflammatory effects after respiratory syncytial virus infection. J. Virol. 2018, 84, 4229–4236. [CrossRef]

245. Kosanić, M.; Ranković, B.; Stanojković, T.; Radović-Jakovljević, M.; Ćirić, A.; Grujičić, D.; Milošević-Djordjević, O. Craterellus cornucopioides edible mushroom as source of biologically active compounds. Nat. Prod. Commun. 2019, 14, 1–6. [CrossRef]

246. Liu, Y.; Duan, X.; Zhang, M.; Li, C.; Zhang, Z.; Liu, A.; Hu, B.; He, J.; Wu, D.; Chen, H.; et al. Cooking methods effect on the nutrients, bioaccessibility and antioxidant activity of Craterellus cornucopioides. IWT 2020, 131, 109768. [CrossRef]

247. Velygodskas, A.K.; Fedotov, O.V. The production and analysis of carotenoid preparations from some strains of xylotrophic Basidiomycetes. Biostover. Divers. 2016, 24, 290–294. [CrossRef]

248. Vaz, J.A.; Barros, L.; Martins, A.; Morais, J.S.; Vasconcelos, M.H.; Ferreira, I.C.F.R. Phenolic profile of seventeen Portuguese wild mushrooms. IWT Food Sci. Technol. 2011, 44, 343–346. [CrossRef]

249. Krüzselevi, D.; Móricz, A.M.; Vetter, J. Comparison of different morphological mushroom parts based on the antioxidant activity. IWT 2020, 127, 109436. [CrossRef]

250. Ukaegbu, C.I.; Shah, S.R.; Hamid, H.A.; Alara, O.R.; Sarker, M.Z.I. Phenolic compounds of aqueous and methanol extracts of Fistulina hepatica (Fistulinaceae) and antioxidant activities and bioactive contents of dark chocolate. Food Sci. Technol. 2015, 38, 649. [CrossRef]

251. Payamnoor, V.; Kavosi, M.R.; Nazari, J. Polypore fungi of Caucasian alder as a source of antioxidant and antitumor agents. J. Food Meas. Charact. 2020, 14, 3181–3193. [CrossRef]

252. Mohammadifar, S.; Gharaghoz, S.F.; Shayan, M.R.A.; Vaziri, A. Comparison between antioxidant activity and bioactive compounds of Ganoderma applanatum (Pers.) Pat. and Ganoderma lucidum (Curt.) P. Karst from Iran. J. Plant Physiol. 2020, 11, 3417–3424.

253. Xu, Y.; Zhang, X.; Yan, X.H.; Zhang, J.L.; Wang, L.Y.; Xue, H.; Jiang, G.C.; Ma, X.T.; Liu, X.J. Characterization, hypolipidemic and antioxidant activities of degraded polysaccharides from Ganoderma lucidum. Int. J. Biol. Macromol. 2019, 135, 706–716. [CrossRef]

254. Cör, D.; Knez, Ž.; Hrnčić, M.K. Anti-tumour, antimicrobial, antioxidant and anticancer activities of a novel polysaccharide from Ganoderma lucidum terpenoids and polysaccharide. Molecules 2018, 23, 649. [CrossRef]

255. Uddin Pk, M.; Talukder, R.I.; Sarkar, M.K.I.; Rahman, T.; Pervin, R.; Rahman, M.; Zenat, E.A.; Akther, L. Effect of solvents on phytochemicals content and antioxidant activity of Ganoderma lucidum. Open Microbiol. J. 2019, 13, 10–15. [CrossRef]

256. Ribeiro, B.; Valentão, P.; Baptista, P.; Seabra, R.M.; Andrade, P.B. Phenolic compounds, organic acids profiles and antioxidative properties of beefsteak fungus (Fistulina hepatica). Food Chem. Toxicol. 2007, 45, 805–813. [CrossRef] [PubMed]

257. Mau, J.L.; Tsai, S.Y.; Tseng, Y.H.; Huang, S.J. Antioxidant properties of hot water extracts from Ganoderma tsugae Murrill. IWT Food Sci. Technol. 2005, 38, 589–597. [CrossRef]

258. Ding, X.; Hou, Y.; Zhu, Y.; Wang, P.; Fu, L.; Zhu, H.; Zhang, N.; Qin, H.; Qu, W.; Wang, F.; et al. Structure elucidation, anticancer and antioxidant activities of a novel polysaccharide from Coprinus clavatus Gray. Oncol. Rep. 2015, 33, 3162–3170. [CrossRef]

259. Makropoulou, M.; Alijannis, N.; Gouou-Zagou, Z.; Pratsinis, H.; Skaltsounis, A.L.; Fokialakis, N. Antioxidant and cytotoxic activity of the wild edible mushroom Coprinus clavatus. J. Med. Food. 2012, 15, 216–221. [CrossRef]

260. Zhang, J.C.; Kong, X.H.; Zhang, P.Q.; Liu, J.N.; Ma, Y.P.; Dai, X.D.; Han, Z.H.; Ma, Q.F.; Wang, X.Y.; Yu, L.P. Identification of a new fungal pathogen causing white villous disease on the fruiting body of the culinary-medicinal mushroom Auricularia auricula-judae (Agaricomycetes) in China. Int. J. Med. Mushrooms 2017, 19, 155–161. [CrossRef] [PubMed]

261. Kaul, S.; Choudhary, M.; Gupta, S.; Agrawal, D.C.; Dhar, M.K. Diversity and medicinal value of mushrooms from the Himalayan region, India. In Medicinal Mushrooms; Agrawal, D.C., Dhanasekaran, M., Eds.; Springer: Singapore, 2019; pp. 371–389. ISBN 978-981-13-6381-8.
262. Lew, S.Y.; Yow, Y.Y.; Lim, L.W.; Wong, K.H. Antioxidant-mediated protective role of Hericium erinaceus (Bull.: Fr.) pers. against oxidative damage in fibroblasts from friedreich's ataxia patient. Food Sci. Technol. 2020, 40, 264–272. [CrossRef]

263. Tubić, J.; Grujičić, D.; Jakovljević, M.R.; Ranković, B.; Kosanić, M.; Stanojković, T.; Ćirić, A.; Mišošević-Djordjević, O. Investigation of biological activities and secondary metabolites of Hydnium repandum acetone extract. Farmacia 2019, 67, 174–183. [CrossRef]

264. Bakir, T.K.; Boufars, M.; Karadenez, M.; Unal, S. Amino acid composition and antioxidant properties of five edible mushroom species from Kastamonu, Turkey. Afr. J. Tradit. Complement. Altern. Med. 2018, 15, 80–87.

265. Ahmad, A.; Abuizinadah, M.; Alkreathy, H.; Kutbi, H.; Shaik, N.; Ahmad, V.; Saleem, S.; Husain, A. A novel polyherbal formulation containing thymoquinone attenuates carbon tetrachloride-induced hepatoportal injury in a rat model. Asian Pac. J. Trop. Biomed. 2020, 10, 147–155. [CrossRef]

266. Vieira, V.; Barros, L.; Martins, A.; Ferreira, I.C.F.R. Expanding current knowledge on the chemical composition and antioxidant properties of Lactarius deliciosus. Int. J. Med. Mushrooms 2020, 22, 931–942. [CrossRef] [PubMed]

267. Zavastin, D.E.; Miron, A.; Gherman, S.P.; Boerescu, C.M.; Breaban, I.G.; Gavrilescu, C.M. Antioxidant activity, total phenolic and carbohydrate contents of Lepista nuda (Agaricomycetes) from Romania. Food Sci. Technol. 2021, 1, 724. [CrossRef]

268. Stojković, D.S.; Kovačević-Grujičić, N.; Reis, F.S.; Davidović, S.; Barros, L.; Popović, J.; Petrović, I.; Pavić, A.; Glamočlija, J.; Ćirić, A.; et al. Chemical composition of the mushroom Meripils giganteus Karst. and bioactive properties of its methanolic extract. LWT Food Sci. Technol. 2017, 79, 454–462. [CrossRef]

269. Bozdoğan, A.; Ulukanli, Z.; Bozk, F.; Eker, T.; Dogan, H.H.; Buyukalaca, S. Antioxidant potential of Actinomycetes from amanos mountains. Adv. Food Nutr. 2018, 3, 113–120.

270. Rosa, G.B.; Sganzerla, W.G.; Ferreira, A.L.A.; Xavier, L.O.; Veloso, N.C.; da Silva, J.; de Oliveira, G.P.; Amaral, N.C.; de Veeck, A.P.L.; Ferrareze, J.P. Investigation of nutritional composition, antioxidant compounds, and antimicrobial activity of wild culinary–medicinal mushrooms Boletus edulis and Lactarius deliciosus (Agaricomyces) from Brazil. Int. J. Med. Mushrooms 2020, 22, 931–942. [CrossRef] [PubMed]

271. Chen, J.; Liu, D.; Liu, L.; Liu, P.; Xu, Q.; Xia, L.; Ling, Y.; Huang, D.; Song, S.; Zhang, D.; et al. A pilot study of hydroxychloroquine and chloroquine formulations containing thymoquinone attenuates carbon tetrachloride-induced hepatoportal injury in a rat model. Asian Pac. J. Trop. Biomed. 2020, 10, 147–155. [CrossRef]

272. Bozdoğan, A.; Ulukanli, Z.; Bozk, F.; Eker, T.; Dogan, H.H.; Buyukalaca, S. Antioxidant potential of Lactarius deliciosus and Pleurotus ostreatus from amanos mountains. Adv. Food Nutr. 2018, 3, 113–120.

273. Athanasakis, G.; Aligiannis, N.; Gonou-Zagou, Z.; Skaltsounis, A.L.; Fokialakis, N. Antioxidant properties of the wild edible mushroom Lactarius deliciosus from two countries. Int. J. Med. Mushrooms 2020, 22, 931–942. [CrossRef] [PubMed]

274. Garcia, I.M.; S., A.R.; Montero, D.; Arellano, M. Evaluation of total polyphenols and antioxidant capacity in mushroom extracts from amanos mountains. J. Food Meas. Charact. 2021, 15, 2842–2853. [CrossRef] [PubMed]

275. Garcia, J.; Afonso, A.; Fernandes, C.; Nunes, F.M.; Marques, G.; Saavedra, M.J. Comparative antioxidant and antimicrobial properties of some wild edible mushrooms from Romania. Agronomy 2020, 10, 1972. [CrossRef]

276. Vieira, V.; Barros, L.; Martins, A.; Ferreira, I.C.F.R. Expanding current knowledge on the chemical composition and antioxidant activity of the genus Lactarius. Molecules 2014, 19, 20650–20663. [CrossRef]

277. Bozdoğan, A.; Ulukanli, Z.; Bozk, F.; Eker, T.; Dogan, H.H.; Buyukalaca, S. Antioxidant potential of Lactarius deliciosus and Pleurotus ostreatus from amanos mountains. Adv. Food Nutr. 2018, 3, 113–120.

278. Chen, J.; Liu, D.; Liu, L.; Liu, P.; Xu, Q.; Xia, L.; Ling, Y.; Huang, D.; Song, S.; Zhang, D.; et al. A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020, 49, 215–229.

279. Garcia, J.; Afonso, A.; Fernandes, C.; Nunes, F.M.; Marques, G.; Saavedra, M.J. Comparative antioxidant and antimicrobial properties of Lentinula edodes Donko and Koshin varieties against priority multidrug-resistant pathogens. S. Afr. J. Chem. Eng. 2021, 35, 98–106. [CrossRef]

280. Do, J.; Guo, H.B.; Li, Q.; Forsythe, A.; Chen, X.H.; Yu, X.D. Genetic diversity of Lepista nuda (Agaricales, Basidiomycota) in Northeast China as indicated by SRAP and ISSR markers. PLoS ONE 2018, 13, e0202761. [CrossRef]

281. Mercan, N.; Duru, M.E.; Turko Glu, A.; Gezer, K.; Kivrak, I.; Turko Glu, H. Antioxidant and antimicrobial properties of ethanolic extract from Lepista nuda (Bull.) Cooke. Ann. Microbiol. 2006, 56, 339–344. [CrossRef]

282. Erbilai, E.H.; Pinto da Silva, L.; Saidi, R.; Lamrani, Z.; Esteves da Silva, J.C.G.; Maouni, A. Chemical composition, bioactive compounds and antioxidant activity of two wild edible mushrooms Armillaria mellea and Macrolepiota procera from two countries (Morocco and Portugal). Biomolecules 2021, 11, 575. [CrossRef]

283. Queirós, B.; Barreira, J.C.M.; Sarmento, A.C.; Ferreira, I.C.F.R. In search of synergistic effects in antioxidant capacity of combined edible mushrooms. Int. J. Food Sci. Nutr. 2009, 60, 160–172. [CrossRef] [PubMed]

284. Stojković, D.S.; Kovačević-Grujičić, N.; Reis, F.S.; Davidović, S.; Barros, L.; Popović, J.; Petrović, I.; Pavić, A.; Glamočlija, J.; Ćirić, A.; et al. Chemical composition of the mushroom Meripils giganteus Karst. and bioactive properties of its methanolic extract. LWT Food Sci. Technol. 2017, 79, 454–462. [CrossRef]
287. Maity, P.; Nandi, A.K.; Manna, D.K.; Pattanayak, M.; Sen, I.K.; Bhanja, S.K.; Samanta, S.; Panda, B.C.; Paloi, S.; Acharya, K.; et al. Structural characterization and antioxidant activity of a glucan from *Meripilus giganteus*. Carbohydr. Polym. 2017, 157, 1237–1245. [CrossRef]

288. Sárközy, A.; Béni, Z.; Dékány, M.; Zomborszki, Z.P.; Rudolf, K.; Papp, V.; Hohmann, J.; Ványoló, A. Cerebroside and steroids from the edible mushroom *Meripilus giganteus* with antioxidant potential. Molecules 2020, 25, 1395. [CrossRef]

289. Zhang, H.N.; Ma, H.L.; Zhou, C.S.; Yan, Y.; Yin, X.L.; Yan, J.K. Enhanced production and antioxidant activity of endo-polysaccharides from *Phellinus igniarius* mutants screened by low power He-Ne laser and ultraviolet induction. Bioact. Carbohydr. Diet. Fibre 2018, 15, 30–36. [CrossRef]

290. Guo, J.; Liu, X.; Li, Y.; Ji, H.; Liu, C.; Zhou, L.; Huang, Y.; Bai, C.; Jiang, Z.; Wu, X. Screening for proteins related to the biosynthesis of hspidin and its derivatives in *Phellinus igniarius* using iTRAQ proteomic analysis. BMC Microbiol. 2021, 21, 1–16. [CrossRef]

291. Yan, J.K.; Wang, Y.Y.; Ma, H.L.; Wang, Z. Bin Ultrasonic effects on the degradation kinetics, preliminary characterization and antioxidant activities of polysaccharides from *Phellinus linteus* mycelia. Ultrason. Sonochem. 2016, 29, 251–257. [CrossRef]

292. Wu, J.J.; Zhu, Y.F.; Guo, Z.Z.; Lou, Y.M.; He, S.G.; Guan, Y.; Zhu, L.J.; Liu, Z.Q.; Lu, L.L.; Liu, L. Aconitum alkaloids, the major components of Aconitum species, affect expression of multidrug resistance-associated protein 2 and breast cancer resistance protein by activating the Nrf2-mediated signalling pathway. Phytotherapeutics 2018, 44, 87–97. [CrossRef]

293. Rahimah, S.B.; Djunaedi, D.D.; Soeroto, A.Y.; Bisri, T. The phytochemical screening, total phenolic contents and antioxidant activities of *Pleurotus ostreatus* in vitro preparations. Open Access Maced. J. Med. Sci. 2019, 7, 2404–2412. [CrossRef]

294. Bakir, T.; Karadeniz, M.; Unal, S. Investigation of antioxidant activities of *Pleurotus ostreatus* stored at different temperatures. Food Sci. Nutr. 2018, 6, 1040–1044. [CrossRef]

295. Nguyen, T.K.; Im, K.H.; Choi, J.; Shin, P.G.; Lee, T.S. Evaluation of antioxidant, anti-cholinesterase, and anti-inflammatory effects of culinary mushroom *Pleurotus pulmonarius*. Mycobiology 2016, 44, 291–301. [CrossRef]

296. Contato, A.G.; Inacio, F.D.; de Araujo, C.A.V.; Brugnari, T.; Maciel, G.M.; Haminiuk, C.W.I.; Bracht, A.; Peralta, R.M.; de Souza, C.G.M. Comparison between the aqueous extracts of mycelium and basidioma of the edible mushroom *Pleurotus pulmonarius*: Chemical composition and antioxidant analysis. J. Food Meas. Charact. 2020, 14, 830–837. [CrossRef]

297. Gambato, G.; Todescato, K.; Pavão, E.M.; Scortegagna, A.; Fontana, R.C.; Salvador, M.; Camassola, M. Evaluation of productivity and antioxidant profile of solid-state cultured macrofungi *Pleurotus albidus* and *Pyrenomorph sanguineus*. Biore sourc. Technol. 2016, 207, 46–51. [CrossRef] [PubMed]

298. Cao, J.; Zhang, H.J.; Xu, C.P. Culture characterization of exopolysaccharides with antioxidant activity produced by *Pyrenomorph sanguineus* in stirred-tank and airlift reactors. J. Taiwan Inst. Chem. Eng. 2014, 45, 2075–2080. [CrossRef]

299. Bhanja, S.K.; Samanta, S.K.; Mondal, B.; Jana, S.; Ray, J.; Pandey, A.; Tripathy, T. Green synthesis of Ag@Au bimetallic composite nanoparticles using a polysaccharide extracted from *Ramaria botrytis* mushroom and performance in catalytic reduction of 4-nitrophenol and antioxidant, antibacterial activity. Environ. Nanotechnol. Monit. Manag. 2020, 14, 100341. [CrossRef]

300. Han, S.R.; Kim, K.H.; Kim, H.J.; Jeong, S.H.; Oh, T.J. Comparison of biological activities using several solvent extracts from *Ramaria botrytis*. Indian J. Sci. Technol. 2016, 9, 1–6. [CrossRef]

301. Li, H. Extraction, purification, characterization and antioxidant activities of polysaccharides from *Ramaria botrytis* (Pers.) Ricken. Chem. Cent. J. 2017, 11, 1–9. [CrossRef]

302. He, T.; Yan, S.F.; Chen, J. Structure and antioxidant activity of HAP-I in *Russula vinosa*. Mod. Food Sci. Technol. 2015, 31, 63–68.

303. Liu, Q.; Tian, G.; Yan, H.; Geng, X.; Cao, Q.; Wang, H.; Ng, T.B. Characterization of polysaccharides with antioxidant and hepatoprotective activities from the wild edible mushroom *Russula vinosa* mutants screened by low power He-Ne laser and ultraviolet induction. Bioact. Carbohydr. Diet. Fibre 2018, 15, 30–36. [CrossRef]

304. Abd Razak, D.L.; Mohd Fadzil, N.H.; Jamaluddin, A.; Abd Rashid, N.Y.; Sani, N.A.; Abdul Manan, M. Effects of different extracting conditions on anti-tyrosinase and antioxidant activities of *Schizophyllum commune* fruit bodies. Biocatal. Agric. Biotechnol. 2019, 19, 101116. [CrossRef]

305. Wanna, C.; Sudhadham, M. The effect of coconut water and boiling on antioxidant activity and total phenolic contents in *Schizophyllum commune* Fr. Pharmacogn. J. 2018, 10, 925–931. [CrossRef]

306. Basso, V.; Schiavenin, C.; Mendonça, S.; de Siqueira, F.G.; Salvador, M.; Camassola, M. Chemical features and antioxidant profile of *Schizophyllum commune* produced on different agroindustrial wastes and byproducts of biodiesel production. Food Chem. 2020, 329, 127089. [CrossRef] [PubMed]

307. Ngoc, L.T.N.; Oh, Y.K.; Lee, Y.J.; Lee, Y.C. Effects of sparsariis crispa in medical therapeutics: A systematic review and meta-analysis of randomized controlled trials. Int. J. Mol. Sci. 2018, 19, 1487. [CrossRef] [PubMed]

308. Nitha, B.; Fijesh, P.V.; Janardhanan, K.K. Hepatoprotective activity of cultured mycelium of Morel mushroom, *Morchella esculenta*. Exp. Toxicol. Pathol. 2013, 65, 105–112. [CrossRef]

309. Wu, X.; Zeng, J.; Hu, J.; Liao, Q.; Zhou, R.; Zhang, P.; Chen, Z. Hepatoprotective effects of aqueous extract from lingzhi or reishi medicinal mushroom *Ganoderma lucidum* (Higher Basidiomycetes) on α-amanitin-induced liver injury in mice. Int. J. Med. Mushrooms 2013, 15, 383–391. [CrossRef]

310. Liu, Q.; Zhu, M.; Geng, X.; Wang, H.; Ng, T.B. Characterization of polysaccharides with antioxidant and hepatoprotective activities from the edible mushroom *Oudemansiella radicata*. Molecules 2017, 22, 234. [CrossRef] [PubMed]
311. Nisar, J.; Mustafa, I.; Anwar, H.; Sohail, M.U.; Hussain, G.; Ullah, M.I.; Faisal, M.N.; Bukhari, S.A.; Basit, A. Shiitake culinary-medicinal mushroom, *Lentinus edodes* (Agaricomycetes): A species with antioxidant, immunomodulatory, and hepatoprotective activities in hypercholesterolemic rats. *Int. J. Med. Mushrooms* 2017, 19, 981–990. [CrossRef]

312. Chang, C.W.; Lur, H.S.; Lu, M.K.; Cheng, J.J. Sulfated polysaccharides of *Armillariella mellea* and their anti-inflammatory activities via NF-κB suppression. *Food Res. Int.* 2013, 54, 239–245. [CrossRef]

313. Talero, E.; Avila-Roman, J.; Motivá, V. Chemoprevention with phytoneutrients and microalgae products in chronic inflammation and colon cancer. *Curr. Pharm. Des.* 2012, 18, 3939–3965. [CrossRef]

314. Chien, R.C.; Lin, L.M.; Chang, Y.H.; Lin, Y.C.; Wu, P.H.; Asatiani, M.D.; Wasser, S.G.; Krakhmalnyi, M.; Agbarya, A.; Wasser, S.P.; et al. Anti-inflammation properties of fruiting bodies and submerged cultured mycelia of culinary-medicinal higher basidiomycetes mushrooms. *Int. J. Med. Mushrooms* 2016, 18, 999–1009. [CrossRef]

315. Yuan, B.; Zhao, L.; Rakarlyatham, K.; Han, Y.; Gao, Z.; Muinde Kimatu, B.; Hu, Q.; Xiao, H. Isolation of a novel bioactive protein from an edible mushroom *Pleurotus eryngii* and its anti-inflammatory potential. *Food Funct.* 2017, 8, 2175–2183. [CrossRef]

316. Li, J.; Zou, L.; Chen, W.; Zhu, B.; Shen, N.; Ke, J.; Lou, J.; Song, R.; Zhong, R.; Miao, X. Dietary mushroom intake may reduce the risk of breast cancer: Evidence from a meta-analysis of observational studies. *Nutrients* 2018, 10, 1402. [CrossRef] [PubMed]

317. Ahn, W.S.; Kim, D.J.; Chae, G.T.; Lee, J.M.; Bae, S.M.; Sin, J.I.; Kim, Y.W.; Namkoong, S.E.; Lee, I.P. Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, *Agaricus blazei* Murill Kyowa, in gynecological cancer patients undergoing chemotherapy. *Int. J. Gynecol. Cancer* 2004, 14, 589–594. [CrossRef] [PubMed]

318. Therkelsen, S.P.; Hetland, G.; Lyberg, T.; Lygren, I.; Johnson, E. Cytokine levels after consumption of a medicinal *Agaricus blazei* Murill-based mushroom extract, AndoSan™, in patients with Crohn’s disease and ulcerative colitis in a randomized single-blinded Placebo-controlled study. *Scand. J. Immunol.* 2016, 84, 323–331. [CrossRef] [PubMed]

319. Hess, J.M.; Wang, Q.; Kraft, C.; Slavin, J.L. Impact of *Agaricus bisporus* mushroom consumption on satiety and food intake. *Appetite* 2017, 117, 179–185. [CrossRef] [PubMed]

320. Hess, J.; Wang, Q.; Gould, T.; Slavin, J. Impact of *Agaricus bisporus* mushroom consumption on gut health markers in healthy adults. *Nutrients* 2018, 10, 1402. [CrossRef] [PubMed]

321. Ba, D.M.; Gao, X.; Muscat, J.; Al-Shaar, L.; Chinchilli, V.; Zhang, X.; Ssentongo, P.; Beelman, R.B.; Richie, J.P. Association of mushroom consumption with all-cause and cause-specific mortality among American adults: Prospective cohort study findings from NHANES III. *Nutr. J.* 2021, 20, 38. [CrossRef]

322. Li, J.; Zou, L.; Chen, W.; Zhu, B.; Shen, N.; Ke, J.; Lou, J.; Song, R.; Zhong, R.; Miao, X. Dietary mushroom intake may reduce the risk of breast cancer: Evidence from a meta-analysis of observational studies. *PLoS ONE* 2014, 9, e93437. [CrossRef] [PubMed]

323. Dai, X.; Stanilka, J.M.; Rowe, C.A.; Esteves, E.A.; Nieves, C., Jr.; Spaiser, S.J.; Christman, M.C.; Langkamp-Henken, B.; Percival, S.S. Immune Benefits from Mushroom Consumption. (20 July 2011–30 December 2013). Identifier NCT01398176. Available online: https://clinicaltrials.gov/ct2/show/NCT01398176 (accessed on 27 August 2021).

324. Dai, X.; Stanilka, J.M.; Rowe, C.A.; Esteves, E.A.; Nieves, C., Jr.; Spaiser, S.J.; Christman, M.C.; Langkamp-Henken, B.; Percival, S.S. Consuming Shiitake (Shiitake) mushrooms daily improves human immunity: A randomized dietary intervention in healthy young adults. *J. Am. Coll. Nutr.* 2015, 34, 478–487. [CrossRef]

325. Wesa, K.M.; Cunningham-Rundles, S.; Klimek, V.M.; Vertosick, E.; Coleton, M.I.; Yeung, K.S.; Lin, H.; Nimer, S.; Cassileth, B.R. Does Maitake Mushroom Extract Enhance Hematopoiesis in Myelodysplastic Patients? (8 April 2010–19 May 2016). Identifier NCT01099917. Available online: https://clinicaltrials.gov/ct2/show/NCT01099917 (accessed on 27 August 2021).

326. Wesa, K.M.; Cunningham-Rundles, S.; Klimek, V.M.; Vertosick, E.; Coleton, M.I.; Yeung, K.S.; Lin, H.; Nimer, S.; Cassileth, B.R. Maitake mushroom extract in myelodysplastic syndromes (MDS): A phase II study. *Cancer Immunol. Immunother.* 2017, 66, 237–247. [CrossRef] [PubMed]

327. Kelly, C.P. Effects of Pre-, Pro- & Anti-Biotics on Gut Microbiota. (11 August 2011–24 July 2017). Identifier NCT01414010. Available online: https://clinicaltrials.gov/ct2/show/results/NCT01414010 (accessed on 27 August 2021).

328. Chae, S.-W. A 12-week Human Trial to Compare the Efficacy and Safety of Poly cane on Bone Metabolism. (26 July 2011–12 October 2012). Identifier NCT01402115. Available online: https://clinicaltrials.gov/ct2/show/results/NCT01402115 (accessed on 27 August 2021).

329. Griffiths, R.R.; Johnson, M.W.; Carducci, M.A.; Umbricht, A.; Richards, W.A.; Richards, B.D.; Cosimano, M.P.; Klinedinst, M.A. Psychopharmacology of Psilocybin in Cancer Patients. (25 April 2007–19 July 2018). Identifier NCT00465595. Available online: https://www.clinicaltrials.gov/ct2/show/NCT00465595 (accessed on 27 August 2021).

330. Griffiths, R.R.; Johnson, M.W.; Carducci, M.A.; Umbricht, A.; Richards, W.A.; Richards, B.D.; Cosimano, M.P.; Klinedinst, M.A. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J. Psychopharmacol.* 2016, 30, 1181–1197. [CrossRef] [PubMed]

331. Lopes, L.C. Effects of *Lentinula edodes* Bars on Dyslipidemia and Oxidative Stress in Cholesterol Individuals: Randomized Study. (5 December 2019–27 October 2020). Identifier NCT04186780. Available online: https://clinicaltrials.gov/ct2/show/study/NCT04186780 (accessed on 27 August 2021).