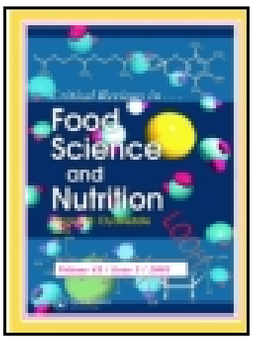

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REVIEW

A comprehensive review on phenolic compounds from edible mushrooms: Occurrence, biological activity, application and future prospective

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ABSTRACT

Phenolic compounds are minor metabolites usually present in mushroom species. Because of their potential advantages for human health, such as antioxidant and other biological activities, these bioactive components have been gaining more interest as functional foods, nutraceutical agents for providing better health conditions. This review aims to comprehensively discuss the recent advances in mushroom phenolic compounds, including new sources, structural characteristics, biological activities, potential uses and its industrial applications as well as the future perspectives. Phenolic acids as well as flavonoids are considered the most common phenolics occurring in mushroom species. These are responsible for its bioactivities, including antioxidant, anti-inflammatory, antitumor, antihyperglycaemic, antiosteoporotic, anti-tyrosinase and antimicrobial activities. Several edible mushroom species with good phenolic content and show higher biological activity were highlighted, in a way for its futuristic applications. Trends on mushroom research highlighting new research areas, such as nanoformulation were discussed. Furthermore, the use of phenolic compounds as nutraceutical and cosmeceutical agents as well as the future perspectives and recommendations were made.

KEYWORDS

Mushrooms polyphenols; biological activity; antioxidant; antitumor; anti-inflammatory; nutraceutical

Introduction

The mushroom is a macrofungus with a distinctive fruiting body which can be either hypogeous (underground) or epigeous (above ground) (Miles and Chang 2004). From long time ago, many mushroom species have been utilized in food preparation or folk medicine in several countries (Aprotosoaie et al. 2017). Besides the desirable flavor, edible mushroom species have a high nutritive value. Mushrooms are considered as the good source of proteins, carbohydrates, elements (generally phosphorous, potassium, calcium, copper, magnesium, iron, zinc), vitamins (mostly thiamin, riboflavin, cobalamin, ascorbate, tocopherols, and β-carotene), and have lower fat content. Moreover, the dietary fibers, including chitin and β-glucans as well as some essential amino acids such as aspartate, glutamate were found in the edible mushrooms (Altaf, Lalotra, and Sharma 2020; Guillamon et al. 2010; Rathore, Prasad, and Sharma 2017).

Also, mushrooms contain secondary metabolites such as polysaccharides (Mingyi et al. 2019) and phenolic compounds (phenols) which have a range of beneficial effects including, antioxidant, antimicrobial, antitumor, and anti-inflammatory activities (Kalac 2013; Khoshnoudi-Nia, Sharif, and Jafari 2020; Muszyńska et al. 2018). Among various secondary metabolites reported from mushrooms, polyphenols are widely explored and found effective against various health complications (Ferreira, Barros, and Abreu 2009; Gąsecka, Siwulski, and Mleczek 2018; Islam, Yu, and Xu 2016). The occurrence of phenolic acids, including caffeic, *p*-coumaric, gallic, cinnamic, protocatechuic, ferulic, chlorogenic, sinapic, *p*-hydroxybenzoic, vanilic, salicylic, and syringic acids as well as flavonoid compounds were reported from mushroom species extracts (Bahadori et al. 2019; Mutukwa et al. 2019; Yahia, Gutiérrez-Orozco, and Moreno-Pérez 2017).

The mushroom constituents were added to various health-promoting products as active ingredients for antioxidants and others essential compounds (Elkhateeb et al. 2019). In this context, there is an increasing interest with nutraceutical effects of mushroom extract and isolated phenolic compounds and potential for its use as functional foods (Stoffel et al. 2019). In past few years, mushroom bioactive components and its health effects were reviewed. For instance, Mingyi et al. (2019) reviewed mushroom polysaccharides and its health effects, Wieczorek et al. (2015) reviewed mushroom alkaloids and its health effects. However, realizing the role of mushroom polyphenols as an active health ingredient, a comprehensive discussion on the

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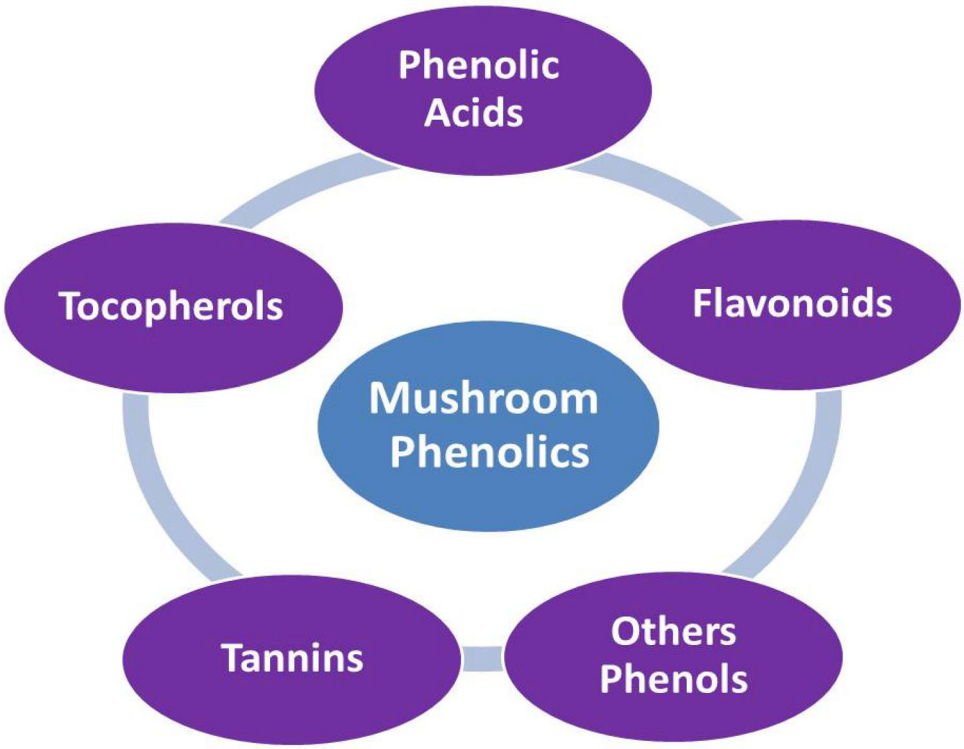

Figure 1. Classification of mushroom polyphenols.

functional activities of mushroom polyphenols is lacking. Thus the present review highlighted the recent advances in mushroom phenolic compounds, including its new sources, structural characteristics, biological activities and their potential mechanism of action, trends of its applications as nutraceuticals and cosmeceuticals and the future perspectives in industrial applications. Also, recommendations were made highlighting the potential gaps in the study.

Classification and distribution of mushroom phenols

Phenolic compounds have one aromatic ring (C_6) at least and one or more (OH) groups. The structures of these compounds can extend from simple molecules to complicated polymers (Michalak 2006). Different kinds of phenolic compounds observed by mushroom species extracts (Figures 1 and 2) were discussed below.

Phenolic acids

Phenolic acids such as gallic, caffeic and *p*-coumaric acids are non-flavonoid molecules which have two major groups, benzoic acid derivatives (C_1–C_6 backbone) and cinnamic acid derivatives (C_3–C_6 backbone). Several studies stated that many biological activities of mushrooms were related to their significant content of phenolic acids which can be considered the major phenolic group in the mushroom species (Muszyńska, Sułkowska-Ziaja, and Ekiert 2013; Nowacka et al. 2014; Taofiq et al. 2015). Cinnamic, *p*-hydroxybenzoic, caffeic, *p*-coumaric, protocatechuic, and gallic acids are phenolic acids most commonly found in mushroom species extracts (Alkan et al. 2020; Muszyńska, Sułkowska-Ziaja, and Ekiert 2013).

Bach et al. (2019) stated that *p*-hydroxybenzoic (4-hydroxybenzoic), gentisic (2,5-dihydroxybenzoic), gallic (3,4,5-trihydroxybenzoic), *p*-coumaric (4-hydroxycinnamic), benzoic, trans-cinnamic, fumaric, and ferulic acids were quantified from *Agaricus brasiliensis* mushroom extract, ferulic acid followed by gallic acid had the highest concentrations (0.75 ± 0.002, 0.49 ± 0.001 mg/g DW, respectively) among other phenolic compounds. Additionally, Lin et al. (2017) observed the occurrence of 4-OH-benzoic, ferulic, syringic, vanillic, *p*-coumaric, protocatechuic, salicylic, and caffeic acids in *Agrocybe aegerita* mushroom. Furthermore, salicylic, *p*-coumaric, syringic, caffeic, 4-OH-benzoic, protocatechuic, synapic, and rosmarinic acids were determined in *Hyphodontia paradoxa* species, synapic and rosmarinic acids were the major detected phenolic acids (Nowacka et al. 2015).

In another study, 3,4-dihydroxybenzaldehyde and syringic acids were measured with a significant concentrations in *Inonotus obliquus* mushroom species, besides other phenolic acids, including gallic, protocatechuic, and caffeic acids (Hwang et al. 2019). Additionally, Islam and coworker studied the phenolic composition of 43 mushroom species extracts, and they observed the occurrence of gallic, 3,4-dihydroxybenzoic and gentisic acids in the most tested mushroom extracts; the observed phenolic components in *Lentinus edodes* species were gallic acid with the highest concentration 0.22, mg/g DW, besides *p*-hydroxybenzoic and 3,4-dihydroxybenzoic acids, while gentisic acid with the highest concentration 0.087 mg/g DW in addition of 3,4-dihydroxybenzaldehyde, 3,4-dihydroxybenzoic and gallic

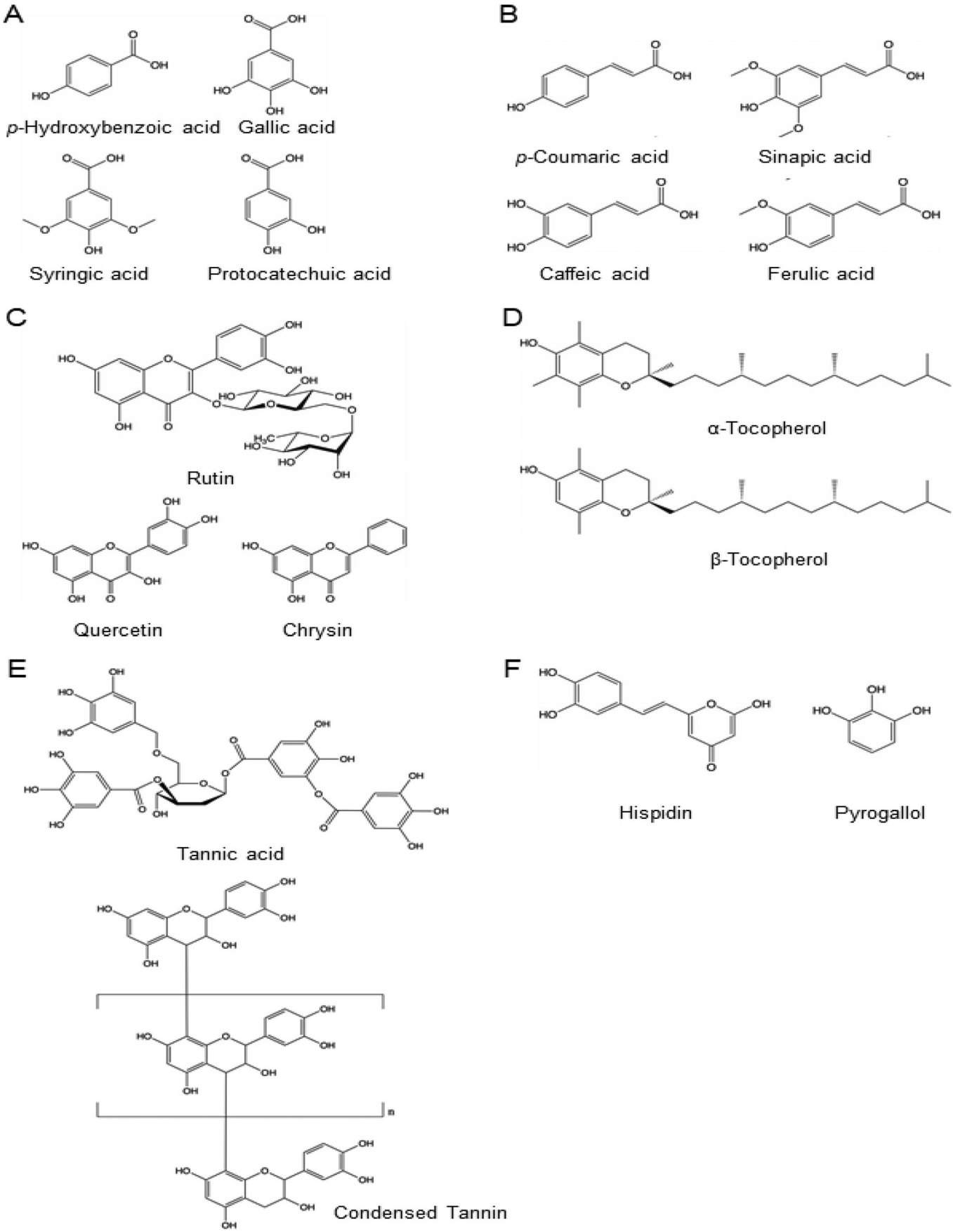

Figure 2. Chemical structure of some phenolic compounds presented in mushroom species: (A) benzoic acid derivatives, (B) cinnamic acid derivatives, (C) flavonoid compounds, (D) tannins, (E) tocopherols and (F) others phenols.

acids were observed in *Umbilicaria esculenta* species extracts (Islam, Yu, and Xu 2016).

Using HPLC technique, six phenolic components were determined in *Melanoleuca cognata* and *Melanoleuca stridula* mushroom extracts, including benzoic, *p*-coumaric, protocatechuic, syringic, trans-cinnamic, and *p*-hydroxybenzoic acids. Meanwhile, the main phenolic components in two *Melanoleuca* species were benzoic acid (0.032 mg/g DW) in *Melanoleuca cognata* and syringic acid (0.034 mg/g DW) in *Melanoleuca stridula* species; besides, the water extract was richer in phenolic content than other solvent extracts (Bahadori et al. 2019). Also, Contato and coworkers stated that, cafeic, gallic and ferulic acids were the main phenolic compounds detected in the mycelium aqueous extract of *Pleurotus pulmonarius* mushroom; cafeic acid displayed the highest value (0.217 mg/g DW) followed by gallic acid (0.066 mg/g DW) (Contato et al. 2020).

Phenolic compounds identification of 18 edible mushroom species collected from Turkey were studied using HPLC combined with photodiode array detector (HPLC–DAD). The results indicated that, the trans-cinnamic, *p*-hydroxybenzoic, protocatechuic, fumaric and gallic acids besides catechin hydrate were the major phenolic compounds presented in the most studied species. Furthermore, the highest concentration of gallic acid (2.96 ± 0.56 µg/g FW) in *Russula aurora* mushroom, the highest value of protocatechuic acid (4.89 ± 0.32 µg/g FW) in *Russula delica*, the higher value of catechin hydrate (16.59 ± 0.71 µg/g FW) in *Suillus granulatus*, the highest concentration of both *p*-hydroxybenzoic acid (5.44 ± 0.67 µg/g FW) and fumaric acid (53.70 ± 3.66 µg/g FW) in *Lepista nuda*, while, the maximum amount of *trans*-cinnamic acid (0.45 ± 0.02 µg/g FW) in *Agaricus bisporus* were detected among selected mushroom species (Çayan et al. 2020).

Also, the phenolic acids, *p*-Hydroxybenzoic, protocatechuic and cinnamic acids were determined in *Suillus belinii* species extract while, *p*-hydroxybenzoic, *p*-coumaric, and cinnamic acids were determined in *Suillus eryngii* species extract. *p*-Hydroxybenzoic acid presented the highest value in both mushroom species 1.82 ± 0.097, 0.273 ± 0.01 mg/g of extract, respectively (Souilem et al. 2017). As such, many researchers found several phenolic acids in mushroom species such as gallic, caffeic, protocatechuic, salicylic, syringic, and vanillic acids in *Morchella esculenta* species (Gąsecka, Siwulski, and Mleczek 2018), *p*-coumaric, cinnamic, and homogentisic acids in *Pleurotus ostreatus* species (de Souza Campos Junior et al. 2019), *p*-coumaric acid in *Agaricus subrufescens* mushroom (Ferrari et al. 2020).

Flavonoid compounds

Flavonoids are phenolic compounds with the C_6–C_3–C_6 common basic backbone by two C_6 rings (A and B) (Lewandowska et al. 2016). These compounds can be further classified to various sub-groups such as flavones and flavonols (Gonzalez-Vallinas et al. 2013). Numerous studies have demonstrated the occurrence of flavonoids in many extracts of mushroom species (Bahadori et al. 2019; Ozen et al. 2011).

In this context, flavonoid compounds, including quercetin, kaempferol, hesperetin and naringenin were observed in *Ganoderma lucidum* species extract (Veljovic et al. 2017). Liu et al. (2012) measured quercetin and catechin flavonoid compounds in *Laccaria amethystea* and *Laccaria ventricosum* extracts. Catechin was the most abundant compound (0.03 ± 0.006 mg/g DW) in *Laccaria amethystea* extract, while quercetin was the highest flavonoid compound (0.07 ± 0.006 mg/g DW) in *Laccaria ventricosum* extract.

Additionally, Yahia, Gutiérrez-Orozco, and Moreno-Pérez (2017) determined flavonoid components, including myricetin, procyanidin, quercetin-hexoside, isoquercetin-hexoside, and kaempferol in *Lactarius indigo* species extract and myricetin displayed the highest level (0.053 mg/g DW) compared to other detected flavonoids. In the same study, catequin hexosemalonate-carboxyl and isoramnethin were observed in *Ramaria flava* species extract at concentration of 0.36 and 0.065 mg/g DW, respectively. Moreover, catechin (0.013 mg/g DW) and quercetin (0.017 mg/g DW) were observed in *Russula emetic* species extract, while *Rugiboletus extremiorientalis* species extract showed significant values of catechin (0.013 mg/g DW) and rutin (0.01 mg/g DW) (Kaewnarin et al. 2016).

In similar study, myricetin was the main flavonoid compound detected in seven mushroom species, including *Agaricus bisporus*, *Boletus edulis*, *Calocybe gambosa*, *Cantharellus cibarius*, *Craterellus cornucopioides*, *Lactarius deliciosus*, and *Pleurotus ostreatus*. *C. cornucopioides* showed the highest concentration of myricetin (0.04 mg/g DW) followed by *C. cibarius* (0.02 mg/g DW), while *B. edulis* species extract presented the lowest myricetin concentration (0.018 mg/g DW). Catechin was only observed in two mushroom species, including *C. cibarius* (0.006 mg/g DW) and *A. bisporus* (0.0005 mg/g DW) (Palacios et al. 2011).

Additionally, flavonoids rutin (2.1 ± 0.1 mg/g DW) and quercetin (0.091 ± 0.001 mg/g DW) were identified in *Lentinus edodes* (Xiaokang et al. 2020). Also, flavonoid compounds, rutin and quercetin as well as other phenolic compounds such as gallic and caffeic acids were detected in *Pleurotus citrinopileatus* mushroom extract and produced several biological benefits such as antioxidant activity (Gogoi et al. 2019).

However, most of previous researches studied the presence of common phenolic acids such as gallic, syringic, vanillic, and caffeic acids and flavonoids such as quercetin, rutin, and kaempferol in various mushroom species, so the detection of new phenolic compounds must be considered in the future researches.

Tannins

Tannins are phenolic compounds that bind to and precipitate protein from aqueous solutions and are commonly distributed in many species of plants. Also, tannins are capable of binding with some types of amino acids, alkaloids, nucleic acids, and polysaccharides (Okuda and Ito 2011). Many

studies observed the occurrence of tannins in mushroom species such as *Pleurotus tuber-regium (fries)*, which has total tannins content 310 µg CAE/g DW (Akindahunsi and Oyetayo 2006). Garrab and coworker determined the total tannins content for three mushroom species, including *Agaricus silvaticus*, *Hydnum rufescens*, and *Meripilus giganteus,* they found that, the total tannins content for the studied mushroom species were 45,200, 48,400, 82,360 µg CAE/g DW, respectively (Garrab et al. 2019).

In another study, *Astraeus hygrometricus* mushroom species was tested for its tannins content, the results indicate that the tannins content of mushroom species extract was 620 µg CAE/g DW (Pavithra et al. 2016). On the other hand, Yıldız et al. (2017) demonstrated that, the total tannins of *Pleurotus ostreatus* and *Pleurotus citrinopileatus* mushroom species extracts were 3690 and 3670 µg CAE/g DW, respectively. However, tannin compounds of edible mushrooms require further quantitative and qualitative studies to obtain more data about this important phenolic group.

Tocopherols

Another class of mushroom polyphenols are tocopherols, these compounds are divided to four types, including α, β, γ and δ tocopherol (Shahidi 2000). Barros et al. (2008) stated that, the total tocopherols content of five mushrooms species, including *Agaricus silvicola*, *Agaricus silvaticus*, *Agaricus romagnesii*, *Agaricus arvensis*, and *Agaricus bisporus* were 1.16, 3.23, 1.29, 1.22, and 2.41 µg/g, respectively. Furthermore, eighteen wild mushroom species were tested for its total tocopherols content, the highest concentration of total tocopherols were in *Laccaria laccata* 8.04, *Mycena rosea* 4.89 and *Clitocybe alexandri* mushroom species 3.55 µg/g. In the same study, *Lepista inversa* mushroom species showed the largest quantity of α-tocopherol compound (0.28 µg/g), *Laccaria laccata* mushroom species showed the largest quantity of β-tocopherol compound (7.06 µg/g), *Clitocybe alexandri* mushroom species showed the largest quantity of γ-tocopherol compound (1.34 µg/g), while, *Lepista inversa* mushroom species showed the largest quantity of δ-tocopherol compound (0.64 µg/g) (Heleno et al. 2010). In addition, Jayakumar, Thomas, and Geraldine (2009) observed that the occurrence of α-tocopherol by 303 µg/g in *Pleurotus ostreatus* mushroom species extract.

Moreover, *Morchella esculenta* mushroom extract showed significant contents of total tocopherols (0.038 mg/g of extract) and other phenolic compounds including cinnamic acid, ellagic acid, quercetin, hyperoside, rutin, catechol and *p*-coumaric acid (Wagay et al. 2019).

The occurrence of α-tocopherol was observed in methanolic extracts of dried *Russula delica, Boletus badius* and *Agaricus bisporus* mushroom species by 4200, 8800 and 9200 µg/g, respectively (Elmastas et al. 2007). Also, the total tocopherols were determined in many mushroom species such as *Pleurotus ostreatus*, *Pleurotus eryngii*, and *Ganoderma lucidum*, the concentrations were 687, 473, 718 $\mu g\ mL^{-1}$, respectively (Bouzgarrou et al. 2018). Besides this, *Laccaria amethystea, Craterellus cornucopioides, Catathelasma ventricosum* and *Clitocybe maxima* mushroom species showed that they contain different concentration of α-tocopherol and the first species was the highest in α-tocopherol concentration (2.12 µg/g) (Liu et al. 2012).

Other mushroom phenols

Many other phenolic components have been obtained from some mushroom species such as pyrogallol component from *Lactarius deliciosus*, *Cantharellus cibarius*, and *Agaricus bisporus* species (Witkowska, Zujko, and Mirończuk-Chodakowska 2011), grifolin derivatives from *Boletus pseudocalopus* species (Song, Manir, and Moon 2009), and from *Albatrellus ovinus* species (Nukata et al. 2002), benzophenone compounds, daldinals A, B and C of *Daldinia childiae* (Japanese fungus) (Quang et al. 2006), diaporthin and orthosporin components from *Daldinia concentrica* species (Lee et al. 2006), and Hispidin from *Phellinus linteus* species (Park et al. 2004).

Many studies have showed the high concentration of polyphenols in mushroom fruiting bodies or their different extracts (Table 1).

Biological activities of mushroom phenols

Several studies stated that mushroom phenolic compounds are responsible for many biological activities, including antitumor, anti-inflammatory, antioxidant, antihyperglycemic, antiosteoporotic, anti-tyrosinase, and antimicrobial activities. In this section, we have covered all these major biological activities of mushroom polyphenols and their potential mechanisms in mitigating the health consequences (Table 2, Figure 3).

Antioxidant activity

Oxidative stress conditions are the main reason for the excessive production of reactive oxygen species (ROS) in the cellular organisms. Extravagant (ROS) generation causes macromolecules oxidative damage such as DNA, RNA, lipids, and proteins leading to tissue injury or death (Vaz et al. 2011). Some of the ROS are superoxide radicals (O_2), hydrogen peroxide (H_2O_2), and Hydroxyl radicals (-OH), which can stimulate nucleic acids destruction and destroy structure of proteins and enzymes. Also, ROS molecules are implicated in the chronic diseases pathogenesis, such as diabetes, cardiovascular, cataracts, cancer, aging, rheumatoid arthritis as well as many others (Circu and Aw 2010; Jeong et al. 2012).

The antioxidant compounds of mushroom extracts have also come to be an important source for the medicine industries and food to take the place of synthetic antioxidant materials and to supply products by bioactive components (Zielinski, Haminiuk, and Beta 2016). The quantitative and qualitative traits of mushroom phenolic contents are responsible for the variations of antioxidant activity of mushroom species extracts (Abd Razak et al. 2019; Aljadi and

Table 1. Occurrence and distribution of phenolic compounds in some mushroom species.

Mushroom species	Used part/Edibility	Extraction Method	Phenols contents (T.P.C and T.F.C)	Identified phenolic compounds	References
Agaricus brasiliensis	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 13.16 ± 0.06 (mg GAE/g DW) T.F.C: NA	Gallic, Ferulic, Benzoic, *p*-Hydroxybenzoic, Gentisic, trans-Cinnamic, *p*-Coumaric, Fumaric acids, Catechol	Bach et al. (2019)
Agaricus subrufescens	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 0.74 ± 0.006 (mg GAE/g DW) T.F.C: NA	*p*-Coumaric	Ferrari et al. (2020)
Agrocybe aegerita	Fruiting Bodies/Edible	Water Extraction	T.P.C: NA T.F.C: NA	Sinapic, Chlorogenic, Gallic, Protocatechuic, Ferulic acids	Lin et al. (2017)
Amanita crocea	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 9.33 ± 0.06 (mg GAE/g DW) T.F.C: NA	Cinnamic, *p*-Hydroxybenzoic, *p*-Coumaric acids	Alkan et al. (2020)
Calocybe indica	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: NA T.F.C: NA	Gallic, Vanillin, Protocatechuic acid, Naringin, Naringenin, Homogentisic acid, Hesperetin, Ferulic acid, Caffeic acid and Formononetin	Alam et al. (2019)
Cantharellus cibarius	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 2.1 ± 0.08 (mg GAE/g DW) T.F.C: 1.6 ± 0.06 (mg CAE/g DW)	Gallic, Homogentisic, Caffeic, Catechin, Ferulic, Gentisic, *p*-Hydroxybenzoic, Protocatechuic acids, Pyrogallol, Myricetin	Palacios et al. (2011)
Ganoderma lucidum	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 139 ± 3.1 (mg CAE/g DW) T.F.C: NA	Kaempferol, Hesperetin, Trans-cinnamic acid, Gallic acid, Quercetin, Naringenin	Veljovic et al. (2017)
Hyphodontia paradoxa	Fruiting Bodies/Edible	Ultrasound-Assisted Extraction	T.P.C: 38.44 ± 1.7 (mg GAE/g DE) T.F.C: NA	Synapic, Rosmarinic, Salicylic, Protocatechuic, 4-OH-benzoic acid, *p*-Coumaric, Caffeic, Syringic acids	Nowacka et al. (2015)
Inonotus obliquus	Fruiting Bodies/Edible	High Temperatur-e, Pressure Extraction	T.P.C: 204 ± 8.9 (mg GAE/g DW) T.F.C: NA	3,4-dihydroxybenzaldehyde, Syringic, Gallic, Protocatechuic, Caffeic acids	Hwang et al. (2019)
Laccaria amethystea	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 9.08 ± 0.54 (mg GAE/g DW) T.F.C: 3.47 ± 0.16 (mg CAE/g DW)	Quercetin, Catechin, *p*-Coumaric acid	Liu et al. (2012)
Lactarius indigo	Fruiting Bodies/Edible	Ultrasound-Assisted Extraction	T.P.C: 0.560 ± 0.007 (mg of GAE/g FW) T.F.C: 0.123 ± 0.01 (mg CAE /g FW)	Myricetin, quercetin-hexoside, isoquercetin-hexoside, Kaempferol, Procyanidin, Coumaric, *p*-Coumaroylmalic, Malic, *p*-Hydroxybenzoic, Sinapic, *o*-Chlorogenic, Succinic acids	Yahia, Gutiérrez-Orozco, and Moreno-Pérez (2017)
Lentinus edodes	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 2.72 ± 0.15 (mg GAE/g DW) T.F.C: 0.40 ± 0.02 (mg CAE/g DW)	*p*-Hydroxybenzoic, Gallic, 3,4-Dihydroxybenzoic acids	Islam, Yu, and Xu (2016)
Melanoleuca cognate	Fruiting Bodies/Edible	Water Extraction	T.P.C: 255 ± 8.0 (μmol GAE/g DW) T.F.C: 7.0 ± 0.1 (μmol QE/g DW)	Benzoic, syringic, *p*-hydroxybenzoic, protocatechuic, *p*-Coumaric, Trans-cinnamic acids	Bahadori et al. (2019)
Morchella esculenta (L.) Pers.	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 7.24 ± 0.27 (mg GAE/g E) T.F.C: 0.53 ± 0.01 (mg GAE/g E)	Gallic, Protocatechuic, Caffeic, Salicylic, Syringic, Vanillic acids	Gąsecka, Siwulski, and Mleczek (2018)
Pleurotus citrinopileatus	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 3.62 ± 0.02 (mg GAE/ g E) T.F.C: 0.4 ± 0.03 (mg QE/g E)	Rutin, quercetin, gallic acid, caffeic acid	Gogoi et al. (2019)
Pleurotus ostreatus	Fruiting Bodies/Edible	Aqueous Extraction	T.P.C: NA T.F.C: NA	Homogentisic, *p*-Coumaric, Cinnamic acids	de Souza Campos Junior et al. (2019)
Pleurotus pulmonarius	Mycelium/Edible	Aqueous Extraction	T.P.C: NA T.F.C: NA	Cafeic, Gallic, Ferulic acids	Contato et al. (2020)
Ramaria flava	Fruiting Bodies/Edible	Ultrasound-Assisted Extraction	T.P.C: 0.54 (mg GAE/g FW) T.F.C: 0.35 (mg CAE/g FW)	hexosemalonate-carboxyl, catequin	Yahia, Gutiérrez-Orozco, and Moreno-Pérez (2017)
Russula aurora	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 0.005 (mg of GAE/g FW) T.F.C: NA	Gallic, Ellagic, Rosmarinic, trans-Cinnamic acids	Çayan et al. (2020)

(*continued*)

Table 1. Continued.

Mushroom species	Used part/Edibility	Extraction Method	Phenols contents (T.P.C and T.F.C)	Identified phenolic compounds	References
Russula emetic	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 9.4 ± 0.3 (mg GAE/g DW) T.F.C: 0.009 ± 0.0005 (mg QE /g DW)	Protocatechuic acid, Catechin, Rutin, Gallic, Vanillic, Rosmarinic acids	Kaewnarin et al. (2016)
Suillus belinii	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: NA T.F.C: NA	*p*-Hydroxybenzoic acid, Protocatechuic acid , Cinnamic acid	Souilem et al. (2017)
Umbilicaria esculenta	Fruiting Bodies/Edible	Solvent Extraction	T.P.C: 26.21 ± 0.40 (mg GAE/g DW) T.F.C: 2.09 ± 0.07 (mg CAE/g DW)	Gallic acid, Gentisic acid, 3,4-Dihydroxybenzaldehyde, 3,4-Dihydroxybenzoic acid	Islam, Yu, and Xu (2016)

CAE: catechin equivaent; DE: dry extract; DPPH: 1,1-diphenyl-2-picrylhydrazyl; DW: dry weight; E: Extract; FW: fresh weight; GAE: gallic acid equivalent; QE: quercetin equivalent; T.F.C: total flavonoids content; T.P.C: total phenolic content

Kamaruddin 2004). Moreover, a strong correlation was detected between the amount of polyphenols and antioxidant activity of mushroom species due to the scavenging capability by their hydroxyl groups (Abd Razak et al. 2019; Contato et al. 2020; Smolskaitė, Venskutonis, and Talou 2015).

Additionally, the antioxidant activity of methanolic and acetic ester extracts of different mushroom species, including *Meripilus giganteus*, *Agaricus Hydnum*, and *rufescens silvaticus* was due to high polyphenols content. These results increase the use of these extracts for improving the human health, by food or pharmaceutical products (Garrab et al. 2019). The extracts of some mushroom species showed good DNA protective impacts, decreasing capacities and scavenging of free radicals against H_2O_2-induced destruction (Aprotosoaie et al. 2017). Moreover, Ahmad et al. (2014) showed that the antioxidant characteristics of mushroom polyphenols due to redox reaction, which let these bioactive compounds to act as reducing agents or hydrogen atom granters.

Also, Bahadori et al. (2019) illustrated that the water phenolic extracts of mushroom species *Melanoleuca stridula* and *Melanoleuca cognata* have the strongest in vitro antiradical activity in DPPH assay (12.1 and 11.7 μmol TEs/g DW, respectively) followed by methanolic extracts. However, the lowest value was found in ethyl acetate extract (0.21 μmol TEs/g DW for both).

The ethanol extracts of selected mushroom species obtained from Turkey, including *Trametes versicolor*, *Lactarius deliciosus*, *Cantharellus cibarius*, *Polyporus badius*, *Polyporus stevenii*, *Polyporus fomentarius*, *Polyporus volvatus*, *Polyporus pinicola*, *Polyporus radiatus*, *Polyporus annosus*, *Polyporus sulphureus*, and *Polyporus gilvus* showed various antioxidant activities, among them, *Polyporus pinicola* followed by *Polyporus volvatus* extracts showed the highest in vitro scavenging activities may be because of their high phenolic contents (29.27 ± 1.51, 21.58 ± 0.35, mg GAE/g of extract, respectively), while *Polyporus badius* had the lowest effect in vitro scavenging activity may be due to its low phenolic content (4.27 ± 0.26 mg GAE/g of extract) (Orhan and Üstün 2011).

Among of five solvent extracts, including ethanol, acetone, ethyl acetate, chloroform, and n-hexane solvents, besides the pure water extract obtained from five edible mushroom species, including *Lycoperdon utriforme*, *Chlorophyllum agaricoides*, *Neolentinus cyathiformis*, *Tricholoma populinum*, and *Tricholoma scalpturatum*, acetone and ethanol extracts showed the most effective solvents in extraction efficiency and antioxidant activities. *T. populinum*, *C. agaricoides*, and *L. utriforme* displayed the highest antioxidant activities and phenolic contents. Chlorogenic, gallic and protocatechuic acids were the main phenolic acids responsible for the high antioxidant activities of mushroom species extracts (Sezgin, Dalar, and Uzun 2020).

Ćirić et al. (2019) revealed that three Macrolepiota species extracts, including *M. mastoidea*, *M. rhacodes* and *M.procera* presented a significant reducing power and *M. rhacodesand* had the highest reducing power value (39.5 mg GAE/g of extract). Also, *Macrolepiota procera* mushroom extract showed the highest phenolic content (0.013 mg/g DW), and cinnanic acid was the main phenolic compound was observed (0.009 mg/g DW).

Similarly, Islam, Yu, and Xu (2016) studied the antioxidant activities of 43 commonly consumed mushroom species in China and illustrated that all mushroom species showed a significant antioxidant activity. *Boletus aereus* (porcino nero), *Boletus pinophilus* (pine bolete), and *Boletus aereus* (porcino nero) showed the higher DPPH scavenging ability 18.56, 17.74, 17.58 mmol TE/g DW, respectively. On the other hand, *Tricholoma matsutake* (Pine mushroom) and *Poria cocos* (tuckahoe) displayed the least DPPH scavenging ability 1.36, 3.37 mmol TE/g DW, respectively. Relatively similar results were observed with other antioxidant determination methods such as FRAP, ABTS radical scavenging activities and metal chelating ability of mushrooms.

Potential antioxidant mechanism of isolated phenolic compounds from mushroom species or mushroom phenolic extract exert in different ways. As such, they may act as electron donor thus neutralizing free radical kinds besides keeping cells versus oxidative effects. Also, polyphenols are able to chelating some elements such as Cu and Fe, which produce ROS. Furthermore, phenolic compounds prevent the free radical formation by enzymes inhibition, primarily oxidases, such NADH oxygenase, microsomal monooxygenase, lipoxygenase, and cyclooxygenase in addition of S-

Table 2. Some biological activities of mushroom phenolic compounds and its potential mechanism of action.

Observed activity	Phenolic compound types	Test model	Potential mechanism of action	References
Antioxidant activity	Phenolic extract	Ferrous ion chelation, Reducing power, ABTS radical cation scavenging activity, 15-Lipoxygenase inhibition	Redox reactions, acting as reducing agents or hydrogen atom donors	Aprotosoaie et al. (2017)
	Phenolic extract	DPPH assay, ABTS radical cation scavenging activity	Redox reactions, acting as reducing agents or hydrogen atom donors	Bahadori et al. (2019)
	Phenolic extract	Catalase activity assay, Ferric-reducing antioxidant power assay, ABTS cation radical scavenging assay, DPPH radical scavenging assay	Redox reactions, acting as reducing agents or hydrogen atom donors	Garrab et al. (2019)
	Phenolic extract	Ferrous-ion chelating effect, DPPH radical scavenging activity, Ferric-reducing antioxidant power assay (FRAP), Beta-carotene bleaching microplate assay	Redox reactions, acting as reducing agents or hydrogen atom donors	Orhan and Üstün (2011)
Antitumor activity	Phenolic extract	liver cancer cell lines HepG2, Prostate cancer lines PC3 and DU145 and lung cancer cell lines A549	Inhibition migration and invasion of PC3, A549 and HepG2 cells	Liu et al. (2017)
	Grifolin	A2780 cell line	Decreasing the phosphorylation of Akt and ERK1/2	Yan et al. (2017)
	Grifolin	The human gastric cancer cell lines BGC823 and SGC-7901	Inducing apoptosis and suppressing the ERK1/2 pathway	Wu and Li (2017)
	Phenolic extract	Human lung cancer cell lines A549, H441, H661	Inhibition of the Akt/mTOR signaling pathway	Chen et al. (2016)
	Phenolic extract	HL-60 (human leukemia cell), U937 (human histiocytic lymphoma cell), PA-1 (human teratocarcinoma ovary cell), IMR90 (human fetal lung cell) and A549 (human lung adenocarcinoma cell)	Leading cancer cells to apoptosis without affecting normal cells	Nakajima et al. (2009)
	Phenolic extract	Human promonocytic U937 cells	Induction of DNA damage and apoptosis	Saltarelli et al. (2019)
	Phenolic extract	An adult human colorectal cancer cell line, Caco-2 (HTB-37, ATCC) A normal monkey kidney epithelial cell line, Vero (CCL-81)	lowering the intracellular ROS level and the VEGF secretion in cancer cells (Caco-2 cells) and inhibiting the proliferation	Lin et al. (2017)
	5,7-Dihydroxyisobenzofuran-1(3H)-one and 5-(hydroxymethyl)-1,3-benzenediol	human umbilical vein endothelial cells (HUVECs)	Inhibition of angiogenesis	Lee et al. (2017)
	gallic and *p*-coumaric acids	Liver cancer (HepG2) cell line	Antioxidant activity (DPPH), Cell growth inhibitory potential	Sadi et al. (2016)
Anti-inflammatory activity	Phenolic acids	RAW264.7 macrophages	Inhibiting the overproduction of pro-inflammatory mediators (NO), (ROS)	Hu et al. (2018)
	Phenolic acids	LPS-activated RAW 264.7 macrophages	Influence on the expression of inflammation markers, such as IL-1β and IL-6, inhibition the production of nitric oxide (NO)	Palacios et al. (2011)
	Pyrogallol	LPS-stimulated RAW 364.7 macrophage cells	Inhibited NO production and expression of iNOS, IL-1$\beta$and IL6 mRNAs	Moro et al. (2012)
	Grifolins	RAW 264.7 cells	Inhibition NO production	Quang et al. (2006)
	Phenolic acids	Mouse macrophage-like cell line RAW 264.7	Decreasing NO levels	Taofiq et al. (2015)
Antihyperglycemic activity	Phenolic extract	α-glucosidase and α-amylase inhibition assays	Inhipation of α-glycosidase and α-amylase enzymes	Liu et al. (2012)
	Phenolic extract	α-glucosidase inhibition assays	α-glucosidase inhibition	Kaewnarin et al. (2016)
	Phenolic extract			Stojkovic et al. (2019)

(*continued*)

Table 2. Continued.

Observed activity	Phenolic compound types	Test model	Potential mechanism of action	References
		α-Amylase and α-glucosidase inhibition assays	Inhipation of α-glucosidase and α-amylase enzymes	
	Phenolic extract	Aldose reductase and α-glucosidase inhibition assays	Inhipation of α-glycosidase and Aldose reductase	Wu and Xu (2015)
Anti-osteoporotic effects	Syringic and vanilic acids	Murine monocytic RAW 264.7 cells	Inhibition of NFkB transcriptional activity through antioxidant mechanisms	Tanaka et al. (2019)
	Syringic acid	Female mice	Protection of cells from oxidative stress and inflammation	Tanaka et al. (2017)
Anti-tyrosinase activity	Phenolic extract	L-DOPA	The antioxidant activity	Kaewnarin et al. (2016)
	Flavonoid	L-DOPA	Alternative enzyme substrates	Chang (2009)
	Phenolic extract	L-DOPA	The antioxidant activity, decreasing enzymatic activity	Yoon et al. (2011)
	Phenolic extract	L-DOPA	Decreasing enzyme activity	Alam, Yoon, and Lee (2011)
Antimicrobial activity	Phenolic extract	Pathogenic bacteria	Inhibition of cell wall, protein and nucleid acid synthesis	Erjavec et al. (2016)
	Phenolic extract	Pathogenic bacteria	Inhibition of cell wall, protein and nucleid acid synthesis.	Nowacka et al. (2014)
	Phenolic extract	Pathogenic bacteria and fungi	Inhibition of cell wall, protein and nucleid acid synthesis.	Kosanić et al. (2016)
	Hispidin, hypholomine B, inoscavin A, davallialactone, phelligridin	Influenza viruses	Neuraminidase inhibition	Hwang et al. (2015)
	Phenolic extract	Pathogenic bacteria	Inhibition of cell wall, protein and nucleid acid synthesis	Bach et al. (2019)
	Phenolic extract	Pathogenic bacteria	Mechanism of action should be better understood	Alves et al. (2013)

ABTS: 2,2-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid; CPE: cytopathic effect; DPPH: 1,1-diphenyl-2-picrylhydrazyl; E_2: estrogen; ER: estrogen receptor; FRAP: Ferric reducing antioxidant power; H_2O_2: hydrogen peroxide; HepG2: human liver cancer cell line; HUVECs: human umbilical vein endothelial cells; iNOS, IL-1β, IL6: proinflammatory cytokines; L-DOPA: 3,4-dihydroxy-1-phenylalanine; NADH: nicotinamide adenine dinucleotide hydrogen; NFkB: nuclear factor-kB; NO: nitric oxide; O_2: superoxide radicals; OH: hydroxyl radicals; RAW 264.7: macrophage-like cell line; ROS: reactive oxygen species; VEGF: vascular endothelial growth factor.

glutathione transferase or C protein kinase (Ferreira, Barros, and Abreu 2009).

Antitumor activity

Recently, significance of mushroom species as antitumor agent has been observed, suggested its usage as a biological factor in the cancer control (Ding, Hou, and Hou 2012). They exert antitumor activity by inhibiting the tumor growth and cancer cell proliferation as seen both in vivo and in vitro investigations (Hu and Luo 2016; Liu et al. 2017; Nowacka-Jechalke, Olech, and Nowak 2018).

Several studies showed the potential anticancer activity of mushroom species containing phenolic compounds such as *Albatrellus confluence* against Human ovarian cancer (A2780) cell line (Yan et al. 2017) and Human gastric cancer cell lines SGC-7901 and BGC823 (Wu and Li 2017), *Auricularia polytricha* species against kidney cancer (ACHN), breast cancer (MCF-7) and colon cancer (COLO-205) cell lines (Arora et al. 2013), *Clitocybe alexandri* against Nonsmall cell lung cancer (NCI-H460) cell line (Vaz et al. 2012), *Coprinus atramentarius* against Human colon cancer (Colo-205) (Khan et al. 2016), *Ganoderma lucidum* against Human lung cancer (A549, H441, and H661) cell lines (Chen et al. 2016), and *Inonotus obliquus* against leukemia (HL-60) (Nakajima et al. 2009). The potential mechanisms of mushroom phenolic compounds as antitumor agents were illustrated in Table 2.

On the other hand, the fraction of polyphenols content *for Ganoderma lucidum* ethanol extract is generally containing of flavonoid compounds such as myricetin, rutin, naringenin, quercetin, morin, and hesperetin. Significant relationship has been detected among these components occurrence and anti-proliferative influence in mushroom species extracts (Saltarelli et al. 2019; Veljovic et al. 2017). Moreover, the phenolic-rich water extract of *Agrocybe aegerita* mushroom may be overlap with multiple phases of angiogenesis through solid tumor growth, including the tubule development in VEGF-induced HUVECs, migration, preventing proliferation, secretion of VEGF in cancer cells (Caco-2 cells) as well as decreasing of intracellular ROS levels (Araujo, Goncalves, and Martel 2011).

Ukaegbu et al. (2020) examined the antiproliferative influence of the methanol and aqueous extracts from *Flammulina velutipescaps* (Enoki) and *Hypsizygus tessellatus* (Bunapi shimeji) mushroom against two cell lines of breast cancer (MDA-MB-231 and MCF-7). Compared to the methanol extract, aqueous extract of *F. velutipes* and *H. tessellatus* presented higher antiproliferative activity against MDA-MB-231 (IC_{50} = 151.57–227.99, and 238.63–260.76 µg/mL, respectively) and MCF-7 cells (IC_{50} = 14.42–24.84 and 16.46–33.57 µg/mL, respectively), also the aqueous extract showed a better antioxidant activity against

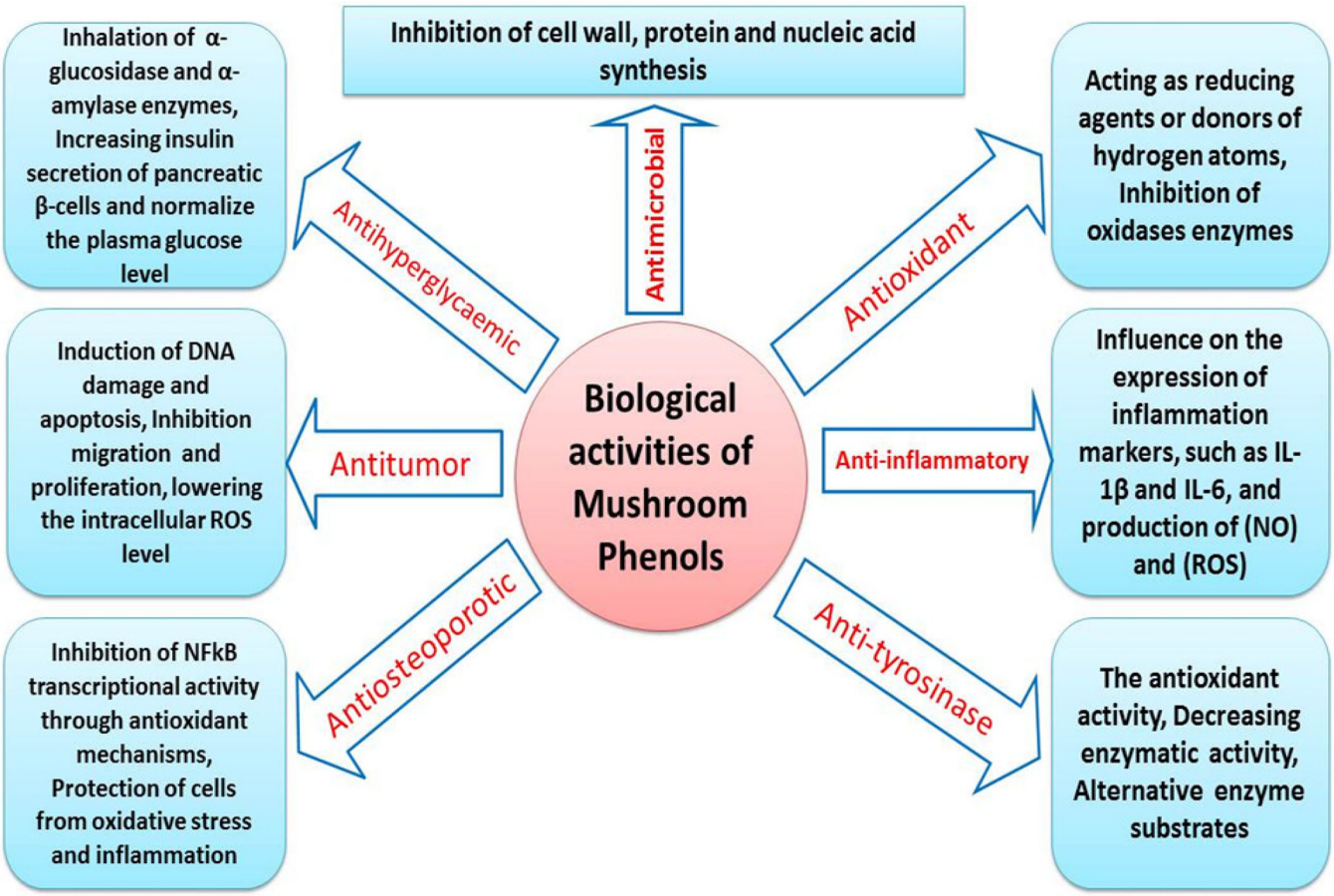

Figure 3. Some biological activities of mushroom phenolic compounds and its potential mechanism of action.

DPPH (IC_{50} were 0.202 and 0.573 mg/mL, respectively). The antiproliferative effects of mushroom aqueous extracts could be due to their higher contents of total phenolic content 198.05 ± 0.16 and 145.22 ± 0.22 mg GAE/g of extract and total flavonoid content 106.33 ± 0.11 and 102.26 ± 0.22 mg QE/g of extract, respectively. The potential mechanism of the detected antiproliferative activity of mushroom extracts may be the apoptosis induction by the hydroxyl groups interaction contained in the phytochemical compounds such as polyphenols with the polar receptor site of the mitochondrial cytochrome P450 enzyme.

Therefore, *Agrocybe aegerita* mushroom showed a potential antitumor activity by its phenolic-rich water extract with low cytotoxicity effects and it has promising future in control and treatment of cancer disease. Ferulic, chlorogenic, protocatechuic, gallic and sinapic acids were the main phenolic compounds measured in the phenolic-rich water extract. The potential antitumor activity may be due to inhibition of the vascular endothelial growth factor (VEGF)-induced proliferation in HUVECs observed by MTT (3-(4, 5-Dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) assay. Also, secretion of VEGF was detected in Caco-2 cells processed with mushroom extracts (Lin et al. 2017).

Additionally, the phenolic compounds 5-(hydroxymethyl)-1,3-benzenediol and 5,7-Dihydroxyisobenzofuran-1(3H)-one separated from methanolic extracts of *Calvatia nipponica* mushroom species demonstrated antitumor activities against (HUVECs) by inhibition of angiogenesis (Lee et al. 2017). Also, gallic and *p*-coumaric acids from *Volvopluteus gloiocephalus* mushroom extract were tested for their potential antitumor activity against liver cancer (HepG2) cell line, the results showed that the antitumor activity for tested phenolic compounds may be due to their antioxidant activity or cell growth inhibitory potential (Sadi et al. 2016). However, examination of purified phenolic compounds obtained from mushroom extracts for their antitumor activity provides more accurate results than extracts.

Anti-inflammatory activity

Inflammation is a normal reaction of the body immunity to harmful effects which associated with pathogenic microorganisms and chemical or physical agents (Dennis and Norris 2015). Mushroom species have exhibited anti-inflammatory activity due to their efficiency to decrease the inflammatory mediators produces (Elsayed et al. 2014).

Moro and coworkers stated that the different compounds in mushroom have been used as potential anti-inflammatory agents, including polyphenols (Moro et al. 2012). More interestingly, they observed that pyrogallol isolated from *Lactarius deliciosus, Cantherellus cibarius*, and *Agaricus bisporus* extracts decreased produce of NO, iNOS, IL-1β, and IL6 mRNAs expression in response to LPS stimulated RAW 364.7 macrophages (Moro et al. 2012). Moreover, the phenolic-rich extracts of *Pleurotus eryngii* mushroom species

were demonstrated to showed anti-colon cancer and anti-inflammatory characteristics, by inhibiting the inflammatory mediators production such as ROS and NO, at least via suppression of NF κB signaling pathway in LPS-induced RAW 264.7 macrophages (Hu et al. 2018).

Furthermore, Anti-inflammatory activity of phenolic components, including homogentisic, ferulic, caffeic, gentisic, *p*-hydroxybenzoic, protocatechuic, gallic acids, catechin, myricetin, and pyrogallol from some edible mushroom species, including *Pleurotus ostreatus*, *Boletus edulis*, *Cantharellus cibarius*, *Agaricus bisporus*, *Calocybe gambosa*, *Hygrophorus marzuolus*, *Cratarellus cornucopioides*, and *Lactarius deliciosus* were examined in in vitro model by LPS-activated RAW 264.7 macrophages. It was noticed that the anti-inflammatory effects of mushroom extracts on the expression of inflammation markers, including production of nitric oxide (NO), IL-6 and IL-1β. However, *Lactarius deliciosus*, *Cantharellus cibarius*, and *Agaricus bisporus* mushroom species recorded the highest anti-inflammatory effect. Phenolic contents of selected mushroom species were between 1 to 6 mg/g DW and *Boletus edulis* extract presented the highest concentration of phenolic content, while flavoined contents were between 0.9 to 3.0 mg/g DW and *Lactarius deliciosus* showed the highest concentration of flavoined contents (Palacios et al. 2011). Also, grifolin derivatives from *Albatrellus caeruleoporus* mushroom were found to significantly inhibit NO produce induced by LPS in RAW 264.7 cells, with IC_{50} values ranging between 22.9 and 29μM (Quang et al. 2006).

Moreover, Taofiq et al. (2015) stated that phenolic extracts of the mushroom species *Agaricus bisporus*, *Boletus impolitus*, *Macrolepiota procera*, and *Pleurotus ostreatus* induced the highest anti-inflammatory potential by inhibiting NO produce. *Pleurotus ostreatus* mushroom extracts showed the strongest reduction of NO production (EC_{50} 96 μg/mL) might be due to its largest content of cinnamic acid (619 μg/g), which was also the strongest anti-inflammatory activity (Taofiq et al. 2015).

Antihyperglycemic activity

Diabetes mellitus (Diabetes disease) is a chronic disease caused via irregular increase in the blood glucose levels due to unbalance insulin hormone insensitivity and/or production in the body (Shobana, Sreerama, and Malleshi 2009). Inhibition of pancreatic α-amylase enzyme or intestinal α-glucosidase enzyme which directly influence of polysaccharides hydrolysis and absorption is the most effective strategies to control the risk of diabetes type-2 (Koike, Yamadera, and DiMagno 1995).

Garduno-Diaz and Khokhar (2012) stated that many mushroom species claimed to be active for controlling and management of diabetes disease and also found to be effectively control its associated complications such hypertension and cardiovascular diseases. As such, antioxidants in mushrooms, such as polyphenols and flavonoids, have exhibited significant anti-diabetic properties via inhibition of some enzymes activity such aldose reductase enzyme (Kato et al. 2009), α-glucosidase and α-Amylase (Liu et al. 2012).

The antihyperglycemic activity was observed in some edible mushroom species such as *Phlebopus portentosus*, *Russula sp.*, *Russula emetica*, and *Rugiboletus extremiorientalis* collected in Thailand (Kaewnarin et al. 2016). Among them, *Rugiboletus extremiorientalis* exhibited higher α-glucosidase enzyme inhibition activity than other mushroom species, which may be due to its high content of polyphenols (18 mg GAE/g) and flavonoids (0.95 mg QE/g). Moreover, the water and methanolic extracts of *Rugiboletus extremiorientalis* displayed high α-glucosidase inhibitory activity (54.4 ± 1.2 and $55.5 \pm 3.9\%$ inhibition) (Kaewnarin et al. 2016).

In another study, Stojkovic and coworkers investigated in in vitro anti-diabetic activity for some medicinal and edible mushroom species methanolic extract, including *Coprinus comatus*, *Phellinus linteus*, *Inonotus obliquus*, *Cordyceps militaris*, *Agaricus blazei*, and *Morchella conica*. *p*-coumaric acid (0.003 mg/g DW) and cinnamic acid (0.001 mg/g DW) were the major phenolic components found in the mushroom extracts. The authors found that α-glucosidase enzyme inhibition was detected with all selected mushrooms and *Inonotus obliquus* mushroom extract showed the highest inhibition level (IC_{50} 220.31 μg/mL), while *Morchella conica* mushroom extract showed the lowest inhibition level (IC_{50} 521.12 μg/mL). Also, α-amylase inhibition was observed with all except *Cordyceps militaris and Morchella conica*. *Coprinus comatus* mushroom extract displayed the highest inhibition activity (IC_{50} 714.45 μg/mL) among other extracts. The antihyperglycemic activity was observed with mushroom extracts could be related to the presence of mushroom phenolic compounds. Overall, the results indicated that *Inonotus obliquus* was the most promising potential mushroom species for anti-diabetic activity (Stojkovic et al. 2019).

Akata et al. (2019) studied the antihyperglycemic activity of six mushroom species extracts by methanol solvent from Turkey including *Leucoagaricus leucothites*, *Macrolepiota procera*, *Lycoperdon utriforme*, *Agaricus campestris*, *Macrolepiota mastoidea*, and *Coprinus comatus* by α-amylase,α-glucosidase enzymes inhibition. The results indicated that *Lycoperdon utriforme* mushroom extract produced the higher level of inhibition of α-amylase and α-glucosidase enzymes 0.22 ± 0.01, 2.97 ± 0.14 mmol ACAE/g of extract, respectively may be due to the significant content of phenolic content (13.11 mg GAE/g of extract). *Agaricus* campestris mushroom extract had the maximum value of phenolic content (15.63 mg GAE/g of extract), besides the highest antioxidant activities using DPPH, CUPRAC, FRAP and ABTS tests.

Additionally, eight mushroom species selected from china were investigated for their anti-diabetic effects including, *Agrocybe aegerita*, *Tremella fuciformis*, *Ganoderma lucidum*, *Auricularia auriculajudae*, *Hericium erinaceus*, *Russula sanguinea*, *Lentinus edodes*, and *Grifola frondosa* (Wu and Xu 2015). The study illustrated the anti-diabetic effect of tested mushroom species such *Ganoderma lucidum* which has the highest values of the total phenolic content (39.3 mg GAE/g

of extract) and total flavonoids content (15.1 mg CE/g of extract); also, it exhibited the highest α-glycosidase and aldose reductase inhibition. Moreover, the study illustrated the relationships among the antioxidant activities and anti-diabetic effects (Wu and Xu 2015).

Nevertheless, In vitro antihyperglycemic activity of mushroom extracts or their bioactive phenols may be give less reliable results than In vivo studies due to the different conditions which can decrease the activity of mushroom phenols such as digestion conditions in the human gut.

Anti-osteoporotic activity

Osteoporosis disease is described by skeleton lack due to the imbalance between bone deposition and bone resorption, these disease can cause the bone weakness as well as increasing the risk of fractures (Faienza et al. 2013; Tella and Gallagher 2014). Estrogen (E2) deficiency is one of the most important reasons of osteoporosis disease for menopausal females. Recently, the patient's numbers of osteoporosis disease have increased in many countries. Osteoporosis is affected by eating habits, so the healthy nutrition is effective part of the solution for this problem (Martinkovich et al. 2014).

The phenolic components vanilic and syringic acids extracted from *Pholiota microspora* (butterscotch), *Pleurotus eryngii* (king trumpet), *Grifola frondosa* (maitake), *Lentinula edodes* (shiitake), and *Hypsizygus marmoreus* (buna shimeji) mushroom species were tested to study their antiosteoporotic effects using human breast cancer MCF-7 cells, ovariectomized mice and murine monocytic RAW264.7 cells. The authors stated that *Lentinula edodes* had the highest concentrations of syringic and vanilic acids (0.45, 0.31 mg/g DW, respectively), these phenolic acids are prospective natural ingredients for treatment of osteoporosis. Nevertheless, more researches are required to explain the mechanism of action of these compounds as anti-osteoporotic agents (Tanaka et al. 2019).

Moreover, Tanaka et al. (2017) demonstrated that dietary syringic acid present in *Lentinula edodes* (shiitake mushroom) can prevent bone mass decreasing and microarchitectural injury without influence on Ovariectomized mice uterus. Moreover, the study suggested that syringic acid may affect in bone formation and bone resorption and it can potentially useful for osteoporosis disease prevention. Anti-osteoporotic activity of some phenolic acids such as vanilic and syringic acids may be through inhibition of the DNA-binding activity of nuclear factor-kB (NFkB), an oxidative stress responsive factor in human colorectal cells (Abaza et al. 2013).

Anti-tyrosinase activity

Tyrosinase is an oxidase enzyme containing of copper active sites and responsible for melanin synthesis, it presents in the tissues of human, plant and animal. The hyper pigmentation occurs as a result of the increased activities of tyrosinase enzyme which increase melanin production of human skin. Also high activity of tyrosinase enzyme cause undesirable effects (browning) for fresh-cut vegetables and fruits. So, tyrosinase inhibitors have growing interest to prevent vegetable and fruit browning and skin hyper pigmentation (Carcelli et al. 2020; Perluigi et al. 2003; Zolghadri et al. 2019).

Apigenin, rutin, catechin, hydroxycinnamic, ferulic, sinapic, syringic, vanillic, protocatechuic and gallic acids are the main phenolic composites associated with several edible mushrooms and showed strong anti-tyrosinase activity. The Anti-tyrosinase activity for these compounds may be by their antioxidant activities (Kaewnarin et al. 2016). Additionally, the flavonoid compounds of mushroom species extracts may be used as a natural anti-tyrosinase substance (Chang 2009).

Tricholosporum goniospermum mushroom extracts including methanol, ethyl acetate and n-hexane extracts were examined to recognize their anti-tyrosinase activity. Ethyl acetate extract presented the highest tyrosinase inhibition value (554.30 ± 9.41 mg KAE/g FW) may be its content of catechin (albeit partially) (Angelini et al. 2020).

Among eight edible mushroom extracts, *Hemileccinum depilatum* and *Cyclocybe cylindracea* mushroom species extracts showed the highest inhibition activities of tyrosinase enzyme by 54.18 ± 0.17 and 53.24 ± 0.12 mg KAE/g DW, respectively. The observed anti-tyrosinase activity may be due to the presence of phenolic components in the mushroom extracts such as *p*-hydroxybenzoic and *p*-coumaric acids which have a significant effect as tyrosinase inhibitors (Alkan et al. 2020).

Calocybe indica (milky white mushroom) extracts by hot water, methanol and acetone were studied to test their antioxidant and antityrosinase activities. Gallic acid, vanillin, protocatechuic acid, naringin, naringenin, homogentisic acid, hesperetin, ferulic acid, caffeic acid, and formononetin were the main phenolic compounds observed in the mushroom extracts, gallic acid presented the highest concentration (0.03 mg/g DW), while formononetin displayed the lowest concentration (0.01 mg/g DW) in the methanolic extract. The methanolic extract recorded the highest reducing power inhibition (2.825), while hot water showed the lowest reducing power inhibition (2.332). Acetone, methanol and hot water mushroom extracts showed various anti-tyrosinase activities ranging from 56.87, 54.59, and 48.82%, respectively. The antioxidant activity of phenolic compounds could be responsible for the anti-tyrosinase effects of mushroom extracts (Alam et al. 2019).

Schizophyllum commune mushroom extract presented a good tyrosinase inhibition with total phenolic content 33.44 mg GAE/g of extract. The authers stated that extraction conditions such as temperature and time extraction significantly influence on the biological activities of mushroom extracts such as antioxidant and anti-tyrosinase activities. Time of 1 hour and temperature of 30 °C were the optimum extraction condition to obtain the highest tyrosinase inhibition (96.6%) (Abd Razak et al. 2019).

Moreover, the methanolic extracts of *Lentinus lepideus* mushroom species showed higher anti-tyrosinase activity

Table 3. Some of available commercial nutraceutical and cosmeceutical products containing mushroom as an active/major ingredient.

		TPC (mg GAE/g fortified product)		DPPH			
Commercial products	Mushroom species	Control	Fortified product	Control	Fortified product	Applications	References
Fortifying brown rice	*Agaricus blazei*	0.12 ± 0.00	1.36 ± 0.07	1.53	8.75 (μmol TEAC/g	NA	Stoffel et al. (2019)
Fortifying canjica corn	*Auricularia fuscosuccinea*	0.08 ± 0.02	2.38 ± 0.05	0.83	8.90 (μmol TEAC/g		
Fortifying wheat	*Pleurotus albidus*	0.17 ± 0.03	0.55 ± 0.01	1.84	7.32 (μmol TEAC/g		
Fortifying muffins (5%)	*Lentinus edodes*	12.24	28.72	9.82	14.33%	NA	Olawuyi and Lee (2019)
Fortifying muffins (15%)			37.71		24.92%		
Fortifying cereal bars (14 %)	*Lentinula edodes*	–	82 ± 5			NA	Spim et al. (2021)
Fortifying extruded snacks (10%)	*Lentinus edodes*	1.10	2.11	0.12	1.98 (μmol TEAC/g	NA	Lu et al. (2020)
	Boletus edulis		4.53		3.02 (μmol TEAC/g		
	Agaricus bisporus		2.84		1.71 (μmol TEAC/g		
Skin care formulations	*Ganoderma lucidum,*	–	–	–	–	CA	Taofiq et al. (2019)
	Pleurotus ostreatus	–	–	–	–		
Mushroom extract	*Volvariella volvacea*	–	–	–	–	CA	Ruksiriwanich et al. (2014)
Mushroom extract	*Pleurotus tuber-regium*	–	–	–	–	CA	Dandapat and Sinha (2015)

NA: nutraceutical agents; CA: cosmeceutical agents; GAE: Gallic acid equivalent; TEAC: Trolox equivalents antioxidant activity; DPPH: 1,1-diphenyl-2-picrylhydrazyl; T.F.C: total flavonoids content; T.P.C: total phenolic content

than the water extracts of the same species (Huang et al. 2014; Yoon et al. 2011). Some correlations were detected between the anti-tyrosinase activity of tested mushroom species and their phenols content such as kojic, *p*-coumaric and gallic acids (Taofiq et al. 2016; Yoon et al. 2011). However, the hydroxyl group numbers of polyphenols may influence on the anti-tyrosinase activity by forming hydrogen bonds with the active sites of enzymes causing of enzyme activity lowering (Alam et al. 2019; Alam, Yoon, and Lee 2011).

Antimicrobial activity

Mushrooms species have antimicrobial activity against several pathogenic microorganisms due to the presence of active compounds which have various molecular weights (Erjavec et al. 2016). It is observed that there are relationships among antimicrobial activities against pathogenic microorganisms and phenolic compound concentrations of mushroom species (Barros et al. 2007; Ozen et al. 2011). The efficiency of mushrooms antimicrobial effects related to mushroom species, its active compounds concentration and selected microorganism (Kosanić, Ranković, and Dašić 2012).

Phenolic extracts of some mushroom species collected from Poland have displayed to possess significant antimicrobial activities versus pathogenic bacteria including Gram-positive bacteria such as *M. luteus*, *B. subtilis*, *S. epidermidis*, and *S. aureus*, and Gram-negative bacteria such as *P. mirabilis*, *P. aeruginosa*, *K. pneumonia*, and *E. coli* (Nowacka et al. 2014). In another study, the potential antimicrobial activities of two mushroom species, i.e., *Lactarius deliciosus* and *Macrolepiota procera* were determined by a microdilution against pathogenic and food spoiler microorganisms including, *Staphylococcus aureus*, *Proteus mirabilis*, *Eschrichia coli*, *Bacillus subtilis*, *Bacillus cereus*, *Aspergillus flavus*, *Aspergillus niger*, *Trichoderma viride*, *Candida albicans*, *Penicillium expansum*, *Penicillium chrysogenum*, *Alternaria alternate*, *Cladosporium cladosporioides*, *Fusarium oxysporum*, and *Mucor mucedo*. Among all tested mushroom species, *Lactarius deliciosus* which has minimum inhibitory concentration values ranged from 2.5 to 20 mg/mL with the better antimicrobial activity (Kosanić et al. 2016).

Additionally, five polyphenolic compounds phelligridin D, davallialactone, inoscavin A, hypholomine B and hispidin were separated from the ethanolic extracts of *Phellinus baumii* fruiting bodies, all compounds exhibited antiviral activity against H3N2, H5N1 and H1N1 influenza viruses and decreased the amount of virally-induced cytopathic effect (CPE) according to an MDCK cell-based assay. The phelligridin D compound presented the higher antiviral activity against all selected viruses (IC_{50} 10.3, 10.9, 8.8, respectively), also the mechanism of influenza viruses inhibition is non-competitive (Hwang et al. 2015). Also, the antimicrobial activity of five mushroom phenolic extracts including, *Lentinula edodes* (Shiitake), *Flammulina velutipes* (Enoki), *Agaricus bisporus* (Champignon and Portobello), and *Agaricus brasiliensis* were observed against some pathogenic bacteria, including *E. coli*, *S. enteritidis*, *S. aureus*, and *B. cereus* (Bach et al. 2019).

Three extracts obtained from *Tricholosporum goniospermum* mushroom by methanol, ethyl acetate and n-hexane extraction was tested to study their antimicrobial activity against some Gram-positive bacteria, including *B. cereus* (PeruMycA 4), *B. subtilis* (PeruMyc 6), and *S. aureus* (ATCC 6538), Gram-negative bacteria, including *E. coli* (ATCC 10536), *E. coli* (PeruMycA 2), *E. coli* (PeruMycA 3), *P. aeruginosa* (PeruMyc 5), and *S. typhy* (PeruMyc 7) and yeasts, including *C. albicans* (YEPGA 6183), *C. albicans* (YEPGA 6379), *C. tropicalis* (YEPGA 6184), and *C. parapsilopsis* (YEPGA 6551). All mushroom extracts showed a potential antimicrobial activity and the ethyl acetate extract exhibited the highest effect with the least minimum inhibitory concentration (MIC) against all selected microbial strains. The authors stated that, the potential antimicrobial activity of these mushroom extracts could be related to its high content of phenolic compounds (70.51 ± 0.06 mg GAE/g FW) such as gallic acid and catechin (Angelini et al. 2020).

Gram-negative bacteria were more resistant to mushroom phenolic extracts than Gram-positive bacteria (Bach et al. 2019; Oyetayo 2009). The higher resistance found in Gram-negative bacteria may be regarding of their complex permeability barrier. The Gram-negative bacteria cell membrane has a supplemental outer lipopolysaccharide barrier that

limits the breakthrough of many compounds while being permeable to nutrients (Oliveira et al. 2016).

Inhibition of cell wall, nucleic acid and cellular protein synthesis is the possible mechanisms of mushroom phenolic compounds as antimicrobial agents. Furthermore, the different antimicrobial properties of selected mushrooms are possibly related to the presence of various compounds at different concentrations (Kosanić, Ranković, and Dašić 2012). Also, Alves et al. (2013) stated that phenolic components could also be used against some pathogenic bacteria which are less sensitive to the antibiotics.

Currently, the novel coronavirus (COVID-19) has been seriously threatening public health across the world. Many papers indicated to the potential role of polyphenols from different plant sources in preventing of COVID-19 (Keflie and Biesalski 2021; Alkhatib 2020). However, there is no study about the effect of polyphenols from edible mushrooms against COVID-19 up to now; this must be considered in the future studies.

Mushroom phenols as nutraceutical and cosmeceutical agents

Mushroom phenolic compounds can be used for nutraceutical and cosmetic applications because they have several biological activities, such antioxidant, antimicrobial and anticancer (Blade et al. 2016; Çayan et al. 2020). Some of these commercial applications of mushrooms rich in phenolic contents are shown in Table 3.

Mushroom phenols as nutraceutical agents

Since ancient times, many ancient folk medicines such as Traditional Chinese Medicine used several mushroom species in traditional medicine (Paul et al. 2018). Also, ancient civilizations of Egypt, Early Greek, Roman and Mexico used mushroom as a delicacies food besides as a medicine (Feeney et al. 2014).

Recently, the use of mushroom bioactive compounds in the functional foods for the promotion of its healthy effects and control of many chronic diseases has been increased (Ma et al. 2018; Tepsongkroh et al. 2020). In this context, the mycelia of some mushroom species which have high phenolic contents such as *Pleurotus albidus*, *Auricularia fuscosuccinea*, and *Agaricus blazei* species were used for fortifying of some grains, including wheat, canjica corn and brown rice to improve their healthy benefits such as antioxidant, anti-diabetic and anti-obesity activities and promote their uses as functional foods (Stoffel et al. 2019).

Porcini (*Boletus edulis*), shiitake (*Lentinula edodes*), and white button (*Agaricus bisporus*) mushroom powders were added into the products of semolina extruded snack by replacement ratios 5 g/100 g, 10 g/100 g and 15 g/100 g (w/w) to enhance the functional properties of these products. The products of semolina extruded snack fortified with selected mushroom powders presented improving of the antioxidant properties and antihyperglycimic activity (by decreasing of the reducing sugars release) and the replacement ratio of porcini followed by white button mushroom at 15 g/100 g (w/w) displayed the highest level in both activities. The authors revealed that, the phenolic content of semolina extruded snack products was increased with the increasing of the replacement ratios of various mushroom and a potential correlation was observed between the phenolic content and antioxidant and antihyperglycimic activities (Lu et al. 2020).

The addition of shiitake mushroom *(Lentinula edodes)* powder containing phenolic content (176 ± 29 mg GAE/g DW) as an ingredient in cereal bars production resulted in increasing of phenolic content of fortified product and improving its functional and nutritional characteristics besides promoting the use of these product as functional foods (Spim et al. 2021).

Furthermore, Olawuyi and Lee (2019) stated that the use of some mushroom species such as shiitake mushroom which containing a significant level of phenolic content in production of muffins (wheat-based product) improved the phenolic content and enhanced the antioxidant properties and sensory characteristics of the fortified muffins products.

Mushroom phenols as cosmeceutical agents

There are increasing interests with production of cosmeceuticals and skin care agents containing extracts of mushrooms, or their active components (Abd Razak et al. 2019).

Some mushroom bioactive compounds can be used as cosmeceutical ingredients through the cosmeceutical formulations production, these mushroom cosmeceutical ingredients have significant effects for dermal problems such as pigmentation, ageing and wrinkles (Taofiq et al. 2016; Wu et al. 2016). Extracts rich in phenolic compounds of some of the mushroom species, such *Pleurotus ostreatus* and *Ganoderma lucidum* were tested for its skin care activity, and displayed a good dermatological activity. Ethanolic extract of *Ganoderma lucidum* mushroom species were used to produce formulation for skin care, the formulation showed a good activity and the dermal penetration of phenolic acids was recorded (Taofiq et al. 2019).

Also, the scavenging activity of natural polyphenols against ROS, make these compounds as important candidates for anti-aging lotions or creams production in the cosmetical industries (Soto, Falqué, and Domínguez 2015). *Volvariella volvacea* mushroom extracts also showed anti-collagenase activity and can be used as cosmeceutical agents (Dandapat and Sinha 2015; Ruksiriwanich et al. 2014). Moreover, the anti-collagenase activity of some mushroom phenolic compounds, including ellagic acid (Bae et al. 2010) and *p*-coumaric acid (Seok and Boo 2015), was also observed in many previous studies.

The challenges of using mushroom phenols in industrial applications

Stability, solubility, bioavailability and bioactivity of polyphenols are effected during storage period and different processing, thus limiting their industrial applications in food and

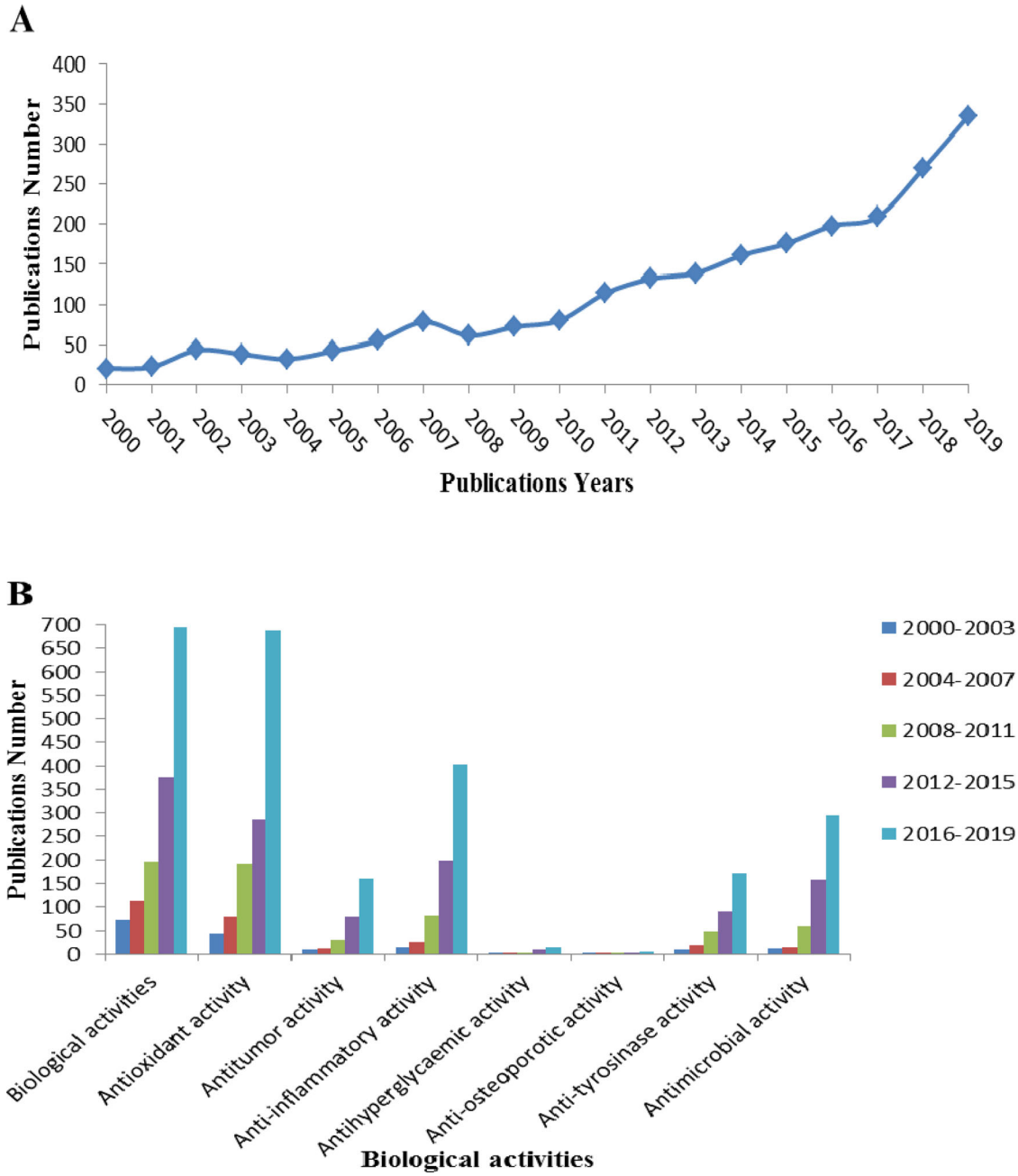

Figure 4. (A) Publications of mushroom polyphenols (2000–2019). (B) Publications of biological activity mushroom polyphenols (2000–2019). (By Science direct database, December 31, 2019).

medicines (Khoshnoudi-Nia, Sharif, and Jafari 2020). Moreover, Anu Bhushani and Anandharamakrishnan (2014), Faridi Esfanjani and Jafari (2016) and Singhal et al. (2020) illustrated that phenolic compounds are sensitive to storage conditions (high temperature, oxidation and light), food processing as well as gastrointestinal tract conditions such as pH, interactions with other components and enzymes. These conditions can hamper their combination in dietary supplements industries. Also, mushroom phenolic compounds are very sensitive under alkaline conditions may be because of polymerization and oxidation reactions which lead to formation of different phenolic derivatives possess undesirable characteristics (Chen et al. 2014; Lucas-González et al. 2018; Ucar and Karadag 2019). The unpleasant taste of phenolic compounds is another challenge for their utilization in food products (Bell 2001; Fang and Bhandari 2010).

Trends of mushroom phenolic compounds research

The trends on mushroom polyphenols research in recent years have been consequently increased, with a comparatively higher number of publications from last 3 years (Figure 4(A)). Recently, it has been observed that there is a growing interest on the research of mushroom polyphenols as nanoformulated products and their green extraction.

Novel drug delivery systems can improve effectiveness of therapeutic compounds and decreased toxicity, doses and side effects of these compounds (Soleymani et al. 2019). In

this context, Wang et al. (2018) displayed that, bioactive compounds of mushroom species have been produced as nanoparticles materials to add in food industries as active ingredients. The natural nanopolyphenols production from mushroom extracts by encapsulation with ultrasonic may be used for some chronic diseases control such different types of cancer (Mahmoud et al. 2016). Furthermore, Taofiq et al. (2018) illustrated that the encapsulated forms of mushroom extracts enhance the bioactivity and controlled release.

Also, there are great interests for using of mushroom polyphenols as functional food or mixing with others to make fortified food products. These products have been demonstrated to have many biological properties, including antioxidant, antimicrobial and antitumor activities.

The trend of several research papers on mushroom polyphenols biological activity highlighted that a higher number of studies were carried out against antioxidant activity, anti-inflammatory activity and antimicrobial activity. Also research papers increase in latest years in antitumor activity and anti-tyrosinase activity (Figure 4(B)).

Conclusions

Polyphenols are one of the most effective classes of secondary metabolites with specific importance, as also reported in good numbers from mushroom fruiting bodies with confirmed biological activities. Phenolic acids (*p*-coumaric, cinnamic, *p*-hydroxybenzoic, benzoic, ferulic, and gallic acids) and flavonoids (naringenin, hesperetin, kaempferol, and quercetin) are the main phenolic compounds reported from several mushroom species extracts. Preferable mushroom species for phenolic extraction includes *Agaricus brasiliensis*, *Cantharellus cibarius*, *Inonotus obliquus*, *Lactarius indigo*, and *Melanoleuca cognate*. Phenolic compounds extracted from mushroom or whole extract were found to possess several biological activities such as antioxidant, antitumor, antihyperglycemic, antimicrobial, antiosteoporotic, anti-tyrosinase, and anti-inflammatory activities. Due to these characteristics, mushroom polyphenolic compounds used as functional foods, nutraceutical agents in several available formulations. Also, skin care activity of mushroom phenolic compounds and its use as cosmeceutical agents was observed.

The trends of mushroom phenols showed its increased research from past few years. In recent years, new research on nanoformulations were highlighted in some studies and showed promising results. Supplementary studies need to be concentrated on improving efficiency of phenolic compounds, while maintaining their bioactivity, bioavailability as well as stability through storage, preparation and consummation. Also, novel drug delivery system by nano-formulations or encapsulation to enhance its biological activities and stability need to be searched.

Authors' contributions

Asem Mahmoud Abdelshafy collected data from the published literature, constructed charts and tables, Writing – original draft. Tarun Belwal revise the spelling and grammatical errors and gave advice. Lei Wang helped collect data. Dong Li and Ze Liang gave suggestions and comments. Zisheng Luo gave advice throughout the draft of this manuscript. Li Li Validation and Writing – review & editing.

Disclosure statement

No conflict of interest exists in this paper.

Abbreviations

ABTS:	2,2-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid;
CAE:	catechin equivaent;
CPE:	cytopathic effect;
DE:	dry extract;
DNA:	deoxyribonucleic acid;
DPPH:	1,1-diphenyl-2-picrylhydrazyl;
DW:	dry weight;
E:	Extract;
E2:	estrogen;
ER:	estrogen receptor;
FRAP:	Ferric reducing antioxidant power;
FW:	fresh weight;
GAE:	gallic acid equivalent;
H_2O_2:	hydrogen peroxide;
HepG2:	human liver cancer cell line;
HUVECs:	human umbilical vein endothelial cells;
iNOS:	IL-1β, IL6, proinflammatory cytokines;
L-DOPA:	3,4-dihydroxy-1-phenylalanine;
NADH:	nicotinamide adenine dinucleotide hydrogen;
NFkB:	nuclear factor-kB;
NO:	nitric oxide;
O_2:	superoxide radicals;
OH:	hydroxyl radicals;
QE:	quercetin equivalent;
RAW 264.7:	macrophage-like cell line;
ROS:	reactive oxygen species;
TEAC:	Trolox equivalents antioxidant activity;
T.F.C:	total flavonoids content;
T.P.C:	total phenolic content;
VEGF:	vascular endothelial growth factor

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References

Abaza, M. S., R. Al-Attiyah, R. Bhardwaj, G. Abbadi, M. Koyippally, and M. Afzal. 2013. Syringic acid from Tamarix aucheriana possesses antimitogenic and chemo-sensitizing activities in human

colorectal cancer cells. *Pharmaceutical Biology* 51 (9):1110–24. doi: 10.3109/13880209.2013.781194.

Abd Razak, D. L., N. H. M. Fadzil, A. Jamaluddin, N. Y. Abd Rashid, N. A. Sani, and M. A. Manan. 2019. Effects of different extracting conditions on anti-tyrosinase and antioxidant activities of Schizophyllum commune fruit bodies. *Biocatalysis and Agricultural Biotechnology* 19:101116. doi: 10.1016/j.bcab.2019.101116.

Ahmad, N., F. Mahmood, S. A. Khalil, R. Zamir, H. Fazal, and B. H. Abbasi. 2014. Antioxidant activity via DPPH, gram-positive and gram-negative antimicrobial potential in edible mushrooms. *Toxicology and Industrial Health* 30 (9):826–34. doi: 10.1177/0748233712463775.

Akata, I., G. Zengin, C. Picot, and M. Mahomoodally. 2019. Enzyme inhibitory and antioxidant properties of six mushroom species from the Agaricaceae family. *South African Journal of Botany* 120:95–9. doi: 10.1016/j.sajb.2018.01.008.

Akindahunsi, A. A., and F. L. Oyetayo. 2006. Nutrient and antinutrient distribution of edible mushroom, Pleurotus tuber-regium (fries) singer. *LWT - Food Science and Technology* 39 (5):548–53. doi: 10.1016/j.lwt.2005.04.005.

Alam, N., M. M. Sikder, M. A. Karim, and S. M. R. Amin. 2019. Antioxidant and antityrosinase activities of milky white mushroom. *Bangladesh Journal of Botany* 48 (4):1065–73. doi: 10.3329/bjb.v48i4.49054.

Alam, N., K. N. Yoon, and T. S. Lee. 2011. Evaluation of the antioxidant and antityrosinase activities of three extracts from Pleurotus nebrodensis fruiting bodies. *African Journal of Biotechnology* 10: 2978–86.

Aljadi, A., and M. Kamaruddin. 2004. Evaluation of the phenolic contents and antioxidant capacities of two Malaysian floral honeys. *Food Chemistry* 85 (4):513–8. doi: 10.1016/S0308-8146(02)00596-4.

Alkan, S., A. Uysal, G. Kasik, S. Vlaisavljevic, S. Berežni, and G. Zengin. 2020. Chemical characterization, antioxidant, enzyme inhibition and antimutagenic properties of eight mushroom species: A comparative study. *Journal of Fungi* 6 (3):166. doi: 10.3390/jof6030166.

Alkhatib, A. 2020. Antiviral functional foods and exercise lifestyle prevention of coronavirus. *Nutrients* 12, 1 (9):2633. doi: 10.3390/nu1209.

Altaf, U., P. Lalotra, and Y. Sharma. 2020. Nutritional and mineral composition of four wild edible mushrooms from Jammu and Kashmir, India. *Indian Phytopathology* 73 (2):313–20. doi: 10.1007/s42360-020-00230-1.

Alves, M. J., I. C. Ferreira, H. J. Froufe, R. M. Abreu, A. Martins, and M. Pintado. 2013. Antimicrobial activity of phenolic compounds identified in wild mushrooms, SAR analysis and docking studies. *Journal of Applied Microbiology* 115 (2):346–57. doi: 10.1111/jam.12196.

Angelini, P., R. Venanzoni, G. Angeles Flores, B. Tirillini, G. Orlando, L. Recinella, A. Chiavaroli, L. Brunetti, S. Leone, S. C. Di Simone, et al. 2020. Evaluation of antioxidant, antimicrobial and tyrosinase inhibitory activities of extracts from Tricholosporum goniospermum, an edible wild mushroom. *Antibiotics* 9 (8):513. doi: 10.3390/antibiotics9080513.

Anu Bhushani, J., and C. Anandharamakrishnan. 2014. Electrospinning and electrospraying techniques: Potential food based applications. *Trends in Food Science & Technology* 38 (1):21–33. doi: 10.1016/j.tifs.2014.03.004.

Aprotosoaie, A. C., D. E. Zavastin, C.-T. Mihai, G. Voichita, D. Gherghel, M. Silion, A. Trifan, and A. Miron. 2017. Antioxidant and antigenotoxic potential of Ramaria largentii Marr & D. E. Stuntz, a wild edible mushroom collected from Northeast Romania. *Food and Chemical Toxicology* 108:429–37. doi: 10.1016/j.fct.2017.02.006.

Araujo, J. R., P. Goncalves, and F. Martel. 2011. Chemopreventive effect of dietary polyphenols in colorectal cancer cell lines. *Nutrition Research (New York, N.Y.)* 31 (2):77–87. doi: 10.1016/j.nutres.2011.01.006.

Arora, S., S. Goyal, J. Balani, and S. Tandon. 2013. Enhanced antiproliferative effects of aqueous extracts of some medicinal mushrooms on colon cancer cells. *International Journal of Medicinal Mushrooms* 15 (3):301–14. doi: 10.1615/intjmedmushr.v15.i3.70.

Bach, F., A. A. F. Zielinski, C. V. Helm, G. M. Maciel, A. C. Pedro, A. P. Stafussa, S. Ávila, and C. W. I. Haminiuk. 2019. Bio compounds of edible mushrooms: In vitro antioxidant and antimicrobial activities. *LWT* 107:214–20. doi: 10.1016/j.lwt.2019.03.017.

Bae, J. Y., J. S. Choi, S. W. Kang, Y. J. Lee, J. Park, and Y. H. Kang. 2010. Dietary compound ellagic acid alleviates skin wrinkle and inflammation induced by UV-B irradiation. *Experimental Dermatology* 19 (8):e182–e190. doi: 10.1111/j.1600-0625.2009.01044.x.

Bahadori, M. B., C. Sarikurkcu, O. U. Yalcin, M. Cengiz, and H. Gungor. 2019. Metal concentration, phenolics profiling, and antioxidant activity of two wild edible Melanoleuca mushrooms (M. cognata and M. stridula). *Microchemical Journal* 150:104172. doi: 10.1016/j.microc.2019.104172.

Barros, L., P. Baptista, L. M. Estevinho, and I. C. Ferreira. 2007. Effect of fruiting body maturity stage on chemical composition and antimicrobial activity of Lactarius sp. mushrooms. *Journal of Agricultural and Food Chemistry* 55 (21):8766–71. doi: 10.1021/jf071435+.

Barros, L., D. M. Correia, I. C. F. R. Ferreira, P. Baptista, and C. Santos-Buelga. 2008. Optimization of the determination of tocopherols in Agaricus sp. edible mushrooms by a normal phase liquid chromatographic method. *Food Chemistry* 110 (4):1046–50. doi: 10.1016/j.foodchem.2008.03.016.

Bell, L. N. 2001. Stability testing of nutraceuticals and functional foods. In: *Handbook of Nutraceuticals and Functional Foods*, eds Wildman, R.E.C. New York, NY: CRC Press.

Blade, C., G. Aragones, A. Arola-Arnal, B. Muguerza, F. I. Bravo, M. J. Salvado, L. Arola, and M. Suarez. 2016. Proanthocyanidins in health and disease. *Biofactors* 42:5–12.

Bouzgarrou, C., K. Amara, F. S. Reis, J. C. M. Barreira, F. Skhiri, N. Chatti, A. Martins, L. Barros, and I. Ferreira. 2018. Incorporation of tocopherol-rich extracts from mushroom mycelia into yogurt. *Food & Function* 9 (6):3166–72. doi: 10.1039/c8fo00482j.

Carcelli, M., D. Rogolino, J. Bartoli, N. Pala, C. Compari, N. Ronda, F. Bacciottini, M. Incerti, and E. Fisicaro. 2020. Hydroxyphenyl thiosemicarbazones as inhibitors of mushroom tyrosinase and antibrowning agents. *Food Chemistry* 303:125310 doi:10.1016/j.foodchem.2019.125310. PMC: 31473456

Çayan, F., E. Deveci, G. Tel-Çayan, and M. E. Duru. 2020. Identification and quantification of phenolic acid compounds of twenty-six mushrooms by HPLC–DAD. *Journal of Food Measurement and Characterization* 14 (3):1690–9. doi: 10.1007/s11694-020-00417-0.

Chang, T. S. 2009. An updated review of tyrosinase inhibitors. *International Journal of Molecular Sciences* 10 (6):2440–75. doi: 10.3390/ijms10062440.

Chen, G.-L., S.-G. Chen, Y.-Y. Zhao, C.-X. Luo, J. Li, and Y.-Q. Gao. 2014. Total phenolic contents of 33 fruits and their antioxidant capacities before and after in vitro digestion. *Industrial Crops and Products* 57:150–7. doi: 10.1016/j.indcrop.2014.03.018.

Chen, Y., J. Lv, K. Li, J. Xu, M. Li, W. Zhang, and X. Pang. 2016. Sporoderm-broken spores of Ganoderma lucidum inhibit the growth of lung cancer: Involvement of the Akt/mTOR signaling pathway. *Nutrition and Cancer* 68 (7):1151–60. doi: 10.1080/01635581.2016.1208832.

Circu, M. L., and T. Y. Aw. 2010. Reactive oxygen species, cellular redox systems, and apoptosis. *Free Radical Biology & Medicine* 48 (6):749–62. doi: 10.1016/j.freeradbiomed.2009.12.022.

Ćirić, A., I. Kruljević, D. Stojković, Â. Fernandes, L. Barros, R. C. Calhelha, I. C. Ferreira, M. Soković, and J. Glamočlija. 2019. Comparative investigation on edible mushrooms Macrolepiota mastoidea, M. rhacodes and M. procera: Functional foods with diverse biological activities. *Food & Function* 10 (12):7678–86. doi: 10.1039/C9FO01900F.

Contato, A. G., F. D. Inácio, C. A. V. de Araújo, T. Brugnari, G. M. Maciel, C. W. I. Haminiuk, A. Bracht, R. M. Peralta, and C. G. M. de Souza. 2020. Comparison between the aqueous extracts of

mycelium and basidioma of the edible mushroom Pleurotus pulmonarius: Chemical composition and antioxidant analysis. *Journal of Food Measurement and Characterization* 14 (2):830–7. doi: 10.1007/s11694-019-00331-0.

Dandapat, S., and M. Sinha. 2015. Antioxidant and anti-inflammatory activity of Pleurotus tuber-regium (Rumph. ex Fr.) Singer. *Advances in Biological Research* 9:140–5.

de Souza Campos Junior, F. A., M. H. Petrarca, A. D. Meinhart, M. de Jesus Filho, and H. T. Godoy. 2019. Multivariate optimization of extraction and validation of phenolic acids in edible mushrooms by capillary electrophoresis. *Food Research International* 126:108685. doi: 10.1016/j.foodres.2019.108685.

Dennis, E. A., and P. C. Norris. 2015. Eicosanoid storm in infection and inflammation. *Nature Reviews Immunology* 15 (8):511–23. doi: 10.1038/nri3859.

Ding, X., Y. Hou, and W. Hou. 2012. Structure feature and antitumor activity of a novel polysaccharide isolated from Lactarius deliciosus Gray. *Carbohydrate Polymers* 89 (2):397–402. doi: 10.1016/j.carbpol.2012.03.020.

Elkhateeb, W., G. Daba, P. Thomas, and T.-C. Wen. 2019. Medicinal mushrooms as a new source of natural therapeutic bioactive compounds. *Egyptian Pharmaceutical Journal* 18:88–101.

Elmastas, M., O. Isildak, I. Turkekul, and N. Temur. 2007. Determination of antioxidant activity and antioxidant compounds in wild edible mushrooms. *Journal of Food Composition and Analysis* 20 (3-4):337–45. doi: 10.1016/j.jfca.2006.07.003.

Elsayed, E. A., H. El Enshasy, M. A. Wadaan, and R. Aziz. 2014. Mushrooms: A potential natural source of anti-inflammatory compounds for medical applications. *Mediators of Inflammation* 2014: 805841. doi: 10.1155/2014/805841.

Erjavec, J., M. Ravnikar, J. Brzin, T. Grebenc, A. Blejec, M. Ž. Gosak, J. Sabotič, J. Kos, and T. Dreo. 2016. Antibacterial activity of wild mushroom extracts on bacterial wilt pathogen Ralstonia solanacearum. *Plant Disease* 100 (2):453–64. doi: 10.1094/PDIS-08-14-0812-RE.

Faienza, M. F., A. Ventura, F. Marzano, and L. Cavallo. 2013. Postmenopausal osteoporosis: The role of immune system cells. *Clinical & Developmental Immunology* 2013:575936. doi: 10.1155/2013/575936.

Fang, Z., and B. Bhandari. 2010. Encapsulation of polyphenols–A review. *Trends in Food Science & Technology* 21 (10):510–23. doi: 10.1016/j.tifs.2010.08.003.

Faridi Esfanjani, A., and S. M. Jafari. 2016. Biopolymer nano-particles and natural nano-carriers for nano-encapsulation of phenolic compounds. *Colloids and Surfaces B: Biointerfaces* 146:532–43. doi: 10.1016/j.colsurfb.2016.06.053.

Feeney, M. J., J. Dwyer, C. M. Hasler-Lewis, J. A. Milner, M. Noakes, S. Rowe, M. Wach, R. B. Beelman, J. Caldwell, M. T. Cantorna, et al. 2014. Mushrooms and health summit proceedings. *Journal of Nutrition* 144:8.

Sabino Ferrari, A. B., G. Azevedo De Oliveira, H. Mannochio Russo, L. Carvalho Bertozo, V. Silva Bolzani, D. Cunha Zied, V. Farias Ximenes, and M. L. Zeraik. 2021. Pleurotusostreatus and Agaricus subrufescens : investigation of chemical composition and antioxidant properties of these mushrooms cultivated with different handmade and commercial supplements. *International Journal of Food Science & Technology* 56 (1):452–60. doi:10.1111/ijfs.14660.

Ferreira, I. C., L. Barros, and R. M. Abreu. 2009. Antioxidants in wild mushrooms. *Current Medicinal Chemistry* 16 (12):1543–60. doi: 10.2174/092986709787909587.

Garduno-Diaz, S. D., and S. Khokhar. 2012. Prevalence, risk factors and complications associated with type 2 diabetes in migrant South Asians. *Diabetes/Metabolism Research and Reviews* 28 (1):6–24. doi: 10.1002/dmrr.1219.

Garrab, M., H. Edziri, R. El Mokni, M. Mastouri, H. Mabrouk, and W. Douki. 2019. Phenolic composition, antioxidant and anticholinesterase properties of the three mushrooms Agaricus silvaticus Schaeff., *Hydnum rufescens* Pers. and *Meripilus giganteus* (Pers.) Karst. in Tunisia. *South African Journal of Botany* 124:359–63.

Gąsecka, M., M. Siwulski, and M. Mleczek. 2018. Evaluation of bioactive compounds content and antioxidant properties of soil-growing and wood-growing edible mushrooms. *Journal of Food Processing and Preservation* 42 (1):e13386. doi: 10.1111/jfpp.13386.

Gogoi, P., P. Chutia, P. Singh, and C. L. Mahanta. 2019. Effect of optimized ultrasound-assisted aqueous and ethanolic extraction of Pleurotus citrinopileatus mushroom on total phenol, flavonoids and antioxidant properties. *Journal of Food Process Engineering* 42 (6): e13172. doi: 10.1111/jfpe.13172.

Gonzalez-Vallinas, M., M. Gonzalez-Castejon, A. Rodriguez-Casado, and A. Ramirez de Molina. 2013. Dietary phytochemicals in cancer prevention and therapy: A complementary approach with promising perspectives. *Nutrition Reviews* 71:585–99.

Guillamon, E., A. Garcia-Lafuente, M. Lozano, M. D'Arrigo, M. A. Rostagno, A. Villares, and J. A. Martinez. 2010. Edible mushrooms: Role in the prevention of cardiovascular diseases. *Fitoterapia* 81 (7): 715–23. doi: 10.1016/j.fitote.2010.06.005.

Heleno, S. A., L. Barros, M. J. Sousa, A. Martins, and I. C. F. R. Ferreira. 2010. Tocopherols composition of Portuguese wild mushrooms with antioxidant capacity. *Food Chemistry* 119 (4):1443–50. doi: 10.1016/j.foodchem.2009.09.025.

Hu, Q., and Y. Luo. 2016. Polyphenol-chitosan conjugates: Synthesis, characterization, and applications. *Carbohydrate Polymers* 151: 624–39. doi: 10.1016/j.carbpol.2016.05.109.

Hu, Q., B. Yuan, H. Xiao, L. Zhao, X. Wu, K. Rakariyatham, L. Zhong, Y. Han, B. Muinde Kimatu, and W. Yang. 2018. Polyphenols-rich extract from Pleurotus eryngii with growth inhibitory of HCT116 colon cancer cells and anti-inflammatory function in RAW264.7 cells. *Food & Function* 9 (3):1601–11. doi: 10.1039/c7fo01794d.

Huang, H.-C., T.-F. Hsu, H.-L. Chao, C.-C. Chen, S.-W. Chiu, and T.-M. Chang. 2014. Inhibition of melanogenesis in murine melanoma cells by Agaricus brasiliensis methanol extract and anti-reactive oxygen species (ROS) activity. *African Journal of Microbiology Research* 8:519–24.

Hwang, A. Y., S. C. Yang, J. Kim, T. Lim, H. Cho, and K. T. Hwang. 2019. Effects of non-traditional extraction methods on extracting bioactive compounds from chaga mushroom (Inonotus obliquus) compared with hot water extraction. *LWT* 110:80–4. doi: 10.1016/j.lwt.2019.04.073.

Hwang, B. S., I. K. Lee, H. J. Choi, and B. S. Yun. 2015. Anti-influenza activities of polyphenols from the medicinal mushroom Phellinus baumii. *Bioorganic & Medicinal Chemistry Letters* 25 (16):3256–60. doi: 10.1016/j.bmcl.2015.05.081.

Islam, T., X. Yu, and B. Xu. 2016. Phenolic profiles, antioxidant capacities and metal chelating ability of edible mushrooms commonly consumed in China. *LWT - Food Science and Technology* 72:423–31. doi: 10.1016/j.lwt.2016.05.005.

Jayakumar, T., P. A. Thomas, and P. Geraldine. 2009. In-vitro antioxidant activities of an ethanolic extract of the oyster mushroom, Pleurotus ostreatus. *Innovative Food Science & Emerging Technologies* 10 (2):228–34. doi: 10.1016/j.ifset.2008.07.002.

Jeong, E. M., M. Liu, M. Sturdy, G. Gao, S. T. Varghese, A. A. Sovari, and S. C. Dudley. Jr. 2012. Metabolic stress, reactive oxygen species, and arrhythmia. *Journal of Molecular and Cellular Cardiology* 52 (2): 454–63. doi: 10.1016/j.yjmcc.2011.09.018.

Kaewnarin, K., N. Suwannarach, J. Kumla, and S. Lumyong. 2016. Phenolic profile of various wild edible mushroom extracts from Thailand and their antioxidant properties, anti-tyrosinase and hyperglycaemic inhibitory activities. *Journal of Functional Foods* 27: 352–64. doi: 10.1016/j.jff.2016.09.008.

Kalac, P. 2013. A review of chemical composition and nutritional value of wild-growing and cultivated mushrooms. *Journal of the Science of Food and Agriculture* 93:209–18.

Kato, A., H. Yasuko, H. Goto, J. Hollinshead, R. J. Nash, and I. Adachi. 2009. Inhibitory effect of rhetsinine isolated from Evodia rutaecarpa on aldose reductase activity. *Phytomedicine : international Journal of Phytotherapy and Phytopharmacology* 16 (2-3):258–61. doi: 10.1016/j.phymed.2007.04.008.

Keflie, T. S., and H. K. Biesalski. 2021. Micronutrients and bioactive substances: Their potential roles in combating COVID-19. *Nutrition* 84:111103. doi: 10.1016/j.nut.2020.111103.

Khan, A. A., A. Gani, M. Ahmad, F. A. Masoodi, F. Amin, and S. Kousar. 2016. Mushroom varieties found in the Himalayan regions of India: Antioxidant, antimicrobial, and antiproliferative activities. *Food Science and Biotechnology* 25 (4):1095–100. doi: 10.1007/s10068-016-0176-6.

Khoshnoudi-Nia, S., N. Sharif, and S. M. Jafari. 2020. Loading of phenolic compounds into electrospun nanofibers and electrosprayed nanoparticles. *Trends in Food Science & Technology* 95:59–74. doi: 10.1016/j.tifs.2019.11.013.

Koike, D., K. Yamadera, and E. P. DiMagno. 1995. Effect of a wheat amylase inhibitor on canine carbohydrate digestion, gastrointestinal function, and pancreatic growth. *Gastroenterology* 108 (4):1221–9. doi: 10.1016/0016-5085(95)90223-6.

Kosanić, M., B. Ranković, and M. Dašić. 2012. Mushrooms as possible antioxidant and antimicrobial agents. *Iranian Journal of Pharmaceutical Research: IJPR* 11 (4):1095–102.

Kosanić, M., B. Ranković, A. Rančić, and T. Stanojković. 2016. Evaluation of metal concentration and antioxidant, antimicrobial, and anticancer potentials of two edible mushrooms Lactarius deliciosus and Macrolepiota procera. *Journal of Food and Drug Analysis* 24 (3):477–84. doi: 10.1016/j.jfda.2016.01.008.

Lee, I.-K., S.-J. Seok, W.-G. Kim, and B.-S. Yun. 2006. Diaporthin and orthosporin from the fruiting body of Daldinia concentrica. *Mycobiology* 34 (1):38–40. doi: 10.4489/MYCO.2006.34.1.038.

Lee, S., J. Y. Park, D. Lee, S. Seok, Y. J. Kwon, T. S. Jang, K. S. Kang, and K. H. Kim. 2017. Chemical constituents from the rare mushroom Calvatia nipponica inhibit the promotion of angiogenesis in HUVECs. *Bioorganic & Medicinal Chemistry Letters* 27 (17):4122–7. doi: 10.1016/j.bmcl.2017.07.036.

Lewandowska, H., M. Kalinowska, W. Lewandowski, T. M. Stępkowski, and K. Brzóska. 2016. The role of natural polyphenols in cell signaling and cytoprotection against cancer development. *The Journal of Nutritional Biochemistry* 32:1–19. doi: 10.1016/j.jnutbio.2015.11.006.

Lin, S., L. T. Ching, K. Lam, and P. C. K. Cheung. 2017. Anti-angiogenic effect of water extract from the fruiting body of Agrocybe aegerita. *LWT* 75:155–63. doi: 10.1016/j.lwt.2016.08.044.

Liu, K., X. Xiao, J. Wang, C. Y. O. Chen, and H. Hu. 2017. Polyphenolic composition and antioxidant, antiproliferative, and antimicrobial activities of mushroom Inonotus sanghuang. *LWT - Food Science and Technology* 82:154–61. doi: 10.1016/j.lwt.2017.04.041.

Liu, Y. T., J. Sun, Z. Y. Luo, S. Q. Rao, Y. J. Su, R. R. Xu, and Y. J. Yang. 2012. Chemical composition of five wild edible mushrooms collected from Southwest China and their antihyperglycemic and antioxidant activity. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association* 50 (5):1238–44. doi: 10.1016/j.fct.2012.01.023.

Lu, X., M. A. Brennan, J. Narciso, W. Guan, J. Zhang, L. Yuan, L. Serventi, and C. S. Brennan. 2020. Correlations between the phenolic and fibre composition of mushrooms and the glycaemic and textural characteristics of mushroom enriched extruded products. *LWT* 118:108730. doi: 10.1016/j.lwt.2019.108730.

Lucas-González, R., M. Viuda-Martos, J. A. P. Álvarez, and J. Fernández-López. 2018. Changes in bioaccessibility, polyphenol profile and antioxidant potential of flours obtained from persimmon fruit (Diospyros kaki) co-products during in vitro gastrointestinal digestion. *Food Chemistry* 256:252–8. doi: 10.1016/j.foodchem.2018.02.128.

Ma, G., W. Yang, L. Zhao, F. Pei, D. Fang, and Q. Hu. 2018. A critical review on the health promoting effects of mushrooms nutraceuticals. *Food Science and Human Wellness* 7 (2):125–33. doi: 10.1016/j.fshw.2018.05.002.

Mahmoud, K. F., A. A. Amin, E. I. Seliem, and M. F. Salama. 2016. Nano capsulated polyphenol extracted from oyster mushroom (Pleurotus ostreatus), characterization and stability evaluation. *International Journal of PharmTech Research* 9:2016.

Martinkovich, S., D. Shah, S. L. Planey, and J. A. Arnott. 2014. Selective estrogen receptor modulators: Tissue specificity and clinical utility. *Clinical Interventions in Aging* 9:1437–52. doi: 10.2147/CIA.S66690.

Michalak, A. 2006. Phenolic compounds and their antioxidant activity in plants growing under heavy metal stress. *Polish Journal of Environmental Studies* 15: 523–30.

Miles, P. G., and S.-T. Chang. 2004. *Mushrooms: Cultivation, nutritional value, medicinal effect, and environmental impact*. Washington , DC: CRC Press.

Mingyi, Y., T. Belwal, H. P. Devkota, L. Li, and Z. Luo. 2019. Trends of utilizing mushroom polysaccharides (MPs) as potent nutraceutical components in food and medicine: A comprehensive review. *Trends in Food Science & Technology* 92:94–110. doi: 10.1016/j.tifs.2019.08.009.

Moro, C., I. Palacios, M. Lozano, M. D'Arrigo, E. Guillamón, A. Villares, J. A. Martínez, and A. García-Lafuente. 2012. Anti-inflammatory activity of methanolic extracts from edible mushrooms in LPS activated RAW 264.7 macrophages. *Food Chemistry* 130 (2):350–5. doi: 10.1016/j.foodchem.2011.07.049.

Muszyńska, B., A. Grzywacz-Kisielewska, K. Kała, and J. Gdula-Argasińska. 2018. Anti-inflammatory properties of edible mushrooms: A review. *Food Chemistry* 243:373–81. doi: 10.1016/j.foodchem.2017.09.149.

Muszyńska, B., K. Sułkowska-Ziaja, and H. Ekiert. 2013. Phenolic acids in selected edible Basidiomycota species: Armillaria mellea, Boletus badius, Boletus edulis, Cantharellus cibarius, Lactarius deliciosus and Pleurotus ostreatus. *Acta Scientiarum Polonorum - Hortorum Cultus* 12:107–16.

Mutukwa, I. B., C. A. Hall, III, L. Cihacek, and C. W. Lee. 2019. Evaluation of drying method and pretreatment effects on the nutritional and antioxidant properties of oyster mushroom (Pleurotus ostreatus). *Journal of Food Processing and Preservation* 43 (4):e13910. doi: 10.1111/jfpp.13910.

Nakajima, Y., H. Nishida, S. Matsugo, and T. Konishi. 2009. Cancer cell cytotoxicity of extracts and small phenolic compounds from Chaga [Inonotus obliquus (persoon) Pilat]. *Journal of Medicinal Food* 12 (3):501–7. doi: 10.1089/jmf.2008.1149.

Nowacka-Jechalke, N., M. Olech, and R. Nowak. 2018. Chapter 11 - Mushroom polyphenols as chemopreventive agents. In *Polyphenols: Prevention and treatment of human disease*, ed. R. R. Watson, V. R. Preedy, and S. Zibadi, 2nd ed., 137–50. London: Academic Press.

Nowacka, N., R. Nowak, M. Drozd, M. Olech, R. Los, and A. Malm. 2014. Analysis of phenolic constituents, antiradical and antimicrobial activity of edible mushrooms growing wild in Poland. *LWT - Food Science and Technology* 59 (2):689–94. doi: 10.1016/j.lwt.2014.05.041.

Nowacka, N., R. Nowak, M. Drozd, M. Olech, R. Los, and A. Malm. 2015. Antibacterial, antiradical potential and phenolic compounds of thirty-one polish mushrooms. *PLoS One* 10 (10):e0140355. doi: 10.1371/journal.pone.0140355.

Nukata, M., T. Hashimoto, I. Yamamoto, N. Iwasaki, M. Tanaka, and Y. Asakawa. 2002. Neogrifolin derivatives possessing anti-oxidative activity from the mushroom Albatrellus ovinus. *Phytochemistry* 59 (7):731–7. doi: 10.1016/S0031-9422(02)00050-X.

Okuda, T., and H. Ito. 2011. Tannins of constant structure in medicinal and food plants—Hydrolyzable tannins and polyphenols related to tannins. *Molecules* 16 (3):2191–217. doi: 10.3390/molecules16032191.

Olawuyi, I. F., and W. Y. Lee. 2019. Quality and antioxidant properties of functional rice muffins enriched with shiitake mushroom and carrot pomace. *International Journal of Food Science & Technology* 54 (7):2321–8. doi: 10.1111/ijfs.14155.

Oliveira, D. A., M. Angonese, C. Gomes, and S. R. S. Ferreira. 2016. Valorization of passion fruit (Passiflora edulis sp.) by-products: Sustainable recovery and biological activities. *The Journal of Supercritical Fluids* 111:55–62. doi: 10.1016/j.supflu.2016.01.010.

Orhan, I., and O. Üstün. 2011. Determination of total phenol content, antioxidant activity and acetylcholinesterase inhibition in selected mushrooms from Turkey. *Journal of Food Composition and Analysis* 24 (3):386–90. doi: 10.1016/j.jfca.2010.11.005.

Oyetayo, V. O. 2009. Free radical scavenging and antimicrobial properties of extracts of wild mushrooms. *Brazilian Journal of Microbiology* 40 (2):380–6. doi: 10.1590/S1517-83822009000200031.

Ozen, T., C. Darcan, O. Aktop, and I. Turkekul. 2011. Screening of antioxidant, antimicrobial activities and chemical contents of edible mushrooms wildly grown in the black sea region of Turkey. *Combinatorial Chemistry & High Throughput Screening* 14 (2): 72–84. doi: 10.2174/138620711794474079.

Palacios, I., M. Lozano, C. Moro, M. D'Arrigo, M. A. Rostagno, J. A. Martínez, A. García-Lafuente, E. Guillamón, and A. Villares. 2011. Antioxidant properties of phenolic compounds occurring in edible mushrooms. *Food Chemistry* 128 (3):674–8. doi: 10.1016/j.foodchem.2011.03.085.

Park, I.-H., S.-K. Chung, K.-B. Lee, Y.-C. Yoo, S.-K. Kim, G.-S. Kim, and K.-S. Song. 2004. An antioxidant hispidin from the mycelial cultures of Phellinus linteus. *Archives of Pharmacal Research* 27 (6): 615–8. doi: 10.1007/BF02980159.

Paul, N., P. S. Slathia, A. Vaid, and R. Kumar. 2018. Traditional knowledge of Gucchi, Morchella esculenta (Ascomycetes), in Doda District, Jammu and Kashmir, India. *International Journal of Medicinal Mushrooms* 20 (5):445–50. doi: 10.1615/IntJMedMushrooms.2018025995.

Pavithra, M., K. R. Sridhar, A. A. Greeshma, and K. Tomita-Yokotani. 2016. Bioactive potential of the wild mushroom Astraeus hygrometricus in South-west India. *Mycology* 7 (4):191–202. doi: 10.1080/21501203.2016.1260663.

Perluigi, M., F. De Marco, C. Foppoli, R. Coccia, C. Blarzino, M. Luisa Marcante, and C. Cini. 2003. Tyrosinase protects human melanocytes from ROS-generating compounds. *Biochemical and Biophysical Research Communications* 305 (2):250–6. doi: 10.1016/S0006-291X(03)00751-4.

Quang, D. N., L. Harinantenaina, T. Nishizawa, T. Hashimoto, C. Kohchi, G.-I. Soma, and Y. Asakawa. 2006. Inhibitory activity of nitric oxide production in RAW 264.7 cells of daldinals A–C from the fungus Daldinia childiae and other metabolites isolated from inedible mushrooms. *Journal of Natural Medicines* 60 (4):303–7. doi: 10.1007/s11418-006-0010-1.

Rathore, H., S. Prasad, and S. Sharma. 2017. Mushroom nutraceuticals for improved nutrition and better human health: A review. *PharmaNutrition* 5 (2):35–46. doi: 10.1016/j.phanu.2017.02.001.

Ruksiriwanich, W., J. Sirithunyalug, K. Boonpisuttinant, and P. Jantrawut. 2014. Potent in vitro collagen biosynthesis stimulating and antioxidant activities of edible mushroom Volvariella volvacea aqueous extract. *International Journal of Pharmacy and Pharmaceutical Sciences* 6:406–12.

Sadi, G., A. Kaya, H. A. Yalcin, B. Emsen, A. Kocabas, D. I. Kartal, and A. Altay. 2016. Wild edible mushrooms from turkey as possible anticancer agents on HepG2 cells together with their antioxidant and antimicrobial properties. *International Journal of Medicinal Mushrooms* 18 (1):83–95. doi: 10.1615/IntJMedMushrooms.v18.i1.100.

Saltarelli, R., F. Palma, A. M. Gioacchini, C. Calcabrini, U. Mancini, R. De Bellis, V. Stocchi, and L. Potenza. 2019. Phytochemical composition, antioxidant and antiproliferative activities and effects on nuclear DNA of ethanolic extract from an Italian mycelial isolate of Ganoderma lucidum. *Journal of Ethnopharmacology* 231:464–73. doi: 10.1016/j.jep.2018.11.041.

Seok, J. K., and Y. C. Boo. 2015. p-Coumaric acid attenuates UVB-induced release of stratifin from keratinocytes and indirectly regulates matrix metalloproteinase 1 release from fibroblasts. *The Korean Journal of Physiology & Pharmacology: Official Journal of the Korean Physiological Society and the Korean Society of Pharmacology* 19 (3): 241–7. doi: 10.4196/kjpp.2015.19.3.241.

Sezgin, S., A. Dalar, and Y. Uzun. 2020. Determination of antioxidant activities and chemical composition of sequential fractions of five edible mushrooms from Turkey. *Journal of Food Science and Technology* 57 (5):1866–11. doi: 10.1007/s13197-019-04221-7.

Shahidi, F. 2000. Antioxidants in food and food antioxidants. *Nahrung/Food* 44 (3):158–63. doi: 10.1002/1521-3803(20000501)44:3<158::AID-FOOD158>3.0.CO;2-L.

Shobana, S., Y. N. Sreerama, and N. G. Malleshi. 2009. Composition and enzyme inhibitory properties of finger millet (Eleusine coracana L.) seed coat phenolics: Mode of inhibition of α-glucosidase and pancreatic amylase. *Food Chemistry* 115 (4):1268–73. doi: 10.1016/j.foodchem.2009.01.042.

Singhal, S., P. Rasane, J. Singh, S. Kaur, V. Kumar, K. Dhawan, S. Gurumayum, N. Kaur, N. Gupta, and D. Kaur. 2020. Effect of processing on vital chemical components of button mushroom. *Journal of Food Process Engineering* 43 (1):e13229. doi: 10.1111/jfpe.13229.

Smolskaitė, L., P. R. Venskutonis, and T. Talou. 2015. Comprehensive evaluation of antioxidant and antimicrobial properties of different mushroom species. *LWT - Food Science and Technology* 60 (1): 462–71. doi: 10.1016/j.lwt.2014.08.007.

Soleymani, S., A. Iranpanah, F. Najafi, T. Belwal, S. Ramola, Z. Abbasabadi, S. Momtaz, and M. H. Farzaei. 2019. Implications of grape extract and its nanoformulated bioactive agent resveratrol against skin disorders. *Archives of Dermatological Research* 311 (8): 577–12. doi: 10.1007/s00403-019-01930-z.

Song, J., M. M. Manir, and S. S. Moon. 2009. Cytotoxic grifolin derivatives isolated from the wild mushroom Boletus pseudocalopus (Basidiomycetes). *Chemistry & Biodiversity* 6 (9):1435–42. doi: 10.1002/cbdv.200800217.

Soto, M. L., E. Falqué, and H. Domínguez. 2015. Relevance of natural phenolics from grape and derivative products in the formulation of cosmetics. *Cosmetics* 2 (3):259–76. doi: 10.3390/cosmetics2030259.

Souilem, F., Â. Fernandes, R. C. Calhelha, J. C. M. Barreira, L. Barros, F. Skhiri, A. Martins, and I. C. F. R. Ferreira. 2017. Wild mushrooms and their mycelia as sources of bioactive compounds: Antioxidant, anti-inflammatory and cytotoxic properties. *Food Chemistry* 230:40–8. doi: 10.1016/j.foodchem.2017.03.026.

Spim, S. R. V., N. R. C. M. Castanho, A. M. H. Pistila, A. F. Jozala, J. M. O. Júnior, and D. Grotto. 2021. Lentinula edodes mushroom as an ingredient to enhance the nutritional and functional properties of cereal bars. *Journal of Food Science and Technology*58:1349–57.

Stoffel, F., W. D. O. Santana, R. C. Fontana, J. G. N. Gregolon, T. B. L. Kist, F. G. De Siqueira, S. Mendonça, and M. Camassola. 2019. Chemical features and bioactivity of grain flours colonized by macrofungi as a strategy for nutritional enrichment. *Food Chemistry* 297:124988. doi: 10.1016/j.foodchem.2019.124988.

Stojkovic, D., M. Smiljkovic, A. Ciric, J. Glamoclija, L. Van Griensven, I. C. F. R. Ferreira, and M. Sokovic. 2019. An insight into antidiabetic properties of six medicinal and edible mushrooms: Inhibition of α-amylase and α-glucosidase linked to type-2 diabetes. *South African Journal of Botany* 120:100–3. doi: 10.1016/j.sajb.2018.01.007.

Tanaka, T., N. Kawaguchi, N. Zaima, T. Moriyama, Y. Fukuta, and N. Shirasaka. 2017. Antiosteoporotic activity of a syringic acid diet in ovariectomized mice. *Journal of Natural Medicines* 71 (4):632–41. doi: 10.1007/s11418-017-1105-6.

Tanaka, T., H. Onuma, T. Shigihara, E. Kimura, Y. Fukuta, N. Shirasaka, T. Moriyama, and Y. Homma. 2019. Anti-osteoporotic effects of syringic acid and vanilic acid in the extracts of waste beds after mushroom cultivation. *Journal of Bioscience and Bioengineering* 128 (5):622–9. doi: 10.1016/j.jbiosc.2019.04.021.

Taofiq, O., R. C. Calhelha, S. Heleno, L. Barros, A. Martins, C. Santos-Buelga, M. Queiroz, and I. Ferreira. 2015. The contribution of phenolic acids to the anti-inflammatory activity of mushrooms: Screening in phenolic extracts, individual parent molecules and synthesized glucuronated and methylated derivatives. *Food Research International* 76 (Pt 3):821–7. doi: 10.1016/j.foodres.2015.07.044.

Taofiq, O., A. M. González-Paramás, A. Martins, M. F. Barreiro, and I. C. Ferreira. 2016. Mushrooms extracts and compounds in cosmetics, cosmeceuticals and nutricosmetics—A review. *Industrial Crops and Products* 90:38–48. doi: 10.1016/j.indcrop.2016.06.012.

Taofiq, O., S. A. Heleno, R. C. Calhelha, I. P. Fernandes, M. J. Alves, L. Barros, A. M. González-Paramás, I. C. Ferreira, and M. F. Barreiro. 2018. Mushroom-based cosmeceutical ingredients: Microencapsulation and in vitro release profile. *Industrial Crops and Products* 124:44–52. doi: 10.1016/j.indcrop.2018.07.057.

Taofiq, O., F. Rodrigues, L. Barros, M. F. Barreiro, I. C. F. R. Ferreira, and M. B. P. P. Oliveira. 2019. Mushroom ethanolic extracts as

cosmeceuticals ingredients: Safety and ex vivo skin permeation studies. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association* 127:228–36. doi: 10.1016/j.fct.2019.03.045.

Tella, S. H., and J. C. Gallagher. 2014. Prevention and treatment of postmenopausal osteoporosis. *The Journal of Steroid Biochemistry and Molecular Biology* 142:155–70. doi: 10.1016/j.jsbmb.2013.09.008.

Tepsongkroh, B., K. Jangchud, A. Jangchud, P. Chonpracha, R. Ardoin, and W. Prinyawiwatkul. 2020. Consumer perception of extruded snacks containing brown rice and dried mushroom. *International Journal of Food Science & Technology* 55 (1):46–54. doi: 10.1111/ijfs.14220.

Ucar, T. M., and A. Karadag. 2019. The effects of vacuum and freeze-drying on the physicochemical properties and in vitro digestibility of phenolics in oyster mushroom (Pleurotus ostreatus). *Journal of Food Measurement and Characterization* 13 (3):2298–309. doi: 10.1007/s11694-019-00149-w.

Ukaegbu, C. I., S. R. Shah, H. Abd Hamid, O. R. Alara, and M. Z. I. Sarker. 2020. Phenolic compounds of aqueous and methanol extracts of Hypsizygus tessellatus (brown and white var.) and Flammulina velutipes caps: Antioxidant and antiproliferative activities. *Pharmaceutical Chemistry Journal* 54 (2):170–83. doi: 10.1007/s11094-020-02174-2.

Vaz, J. A., G. M. Almeida, I. C. Ferreira, A. Martins, and M. H. Vasconcelos. 2012. Clitocybe alexandri extract induces cell cycle arrest and apoptosis in a lung cancer cell line: Identification of phenolic acids with cytotoxic potential. *Food Chemistry* 132 (1):482–6. doi: 10.1016/j.foodchem.2011.11.031.

Vaz, J. A., L. Barros, A. Martins, C. Santos-Buelga, M. H. Vasconcelos, and I. C. F. R. Ferreira. 2011. Chemical composition of wild edible mushrooms and antioxidant properties of their water soluble polysaccharidic and ethanolic fractions. *Food Chemistry* 126 (2):610–6. doi: 10.1016/j.foodchem.2010.11.063.

Veljovic, S., M. Veljovic, N. Nikicevic, S. Despotovic, S. Radulovic, M. Niksic, and L. Filipovic. 2017. Chemical composition, antiproliferative and antioxidant activity of differently processed Ganoderma lucidum ethanol extracts. *Journal of Food Science and Technology* 54:1312–20.

Wagay, J. A., G. A. Nayik, S. A. Wani, R. A. Mir, M. A. Ahmad, Q. I. Rahman, and D. Vyas. 2019. Phenolic profiling and antioxidant capacity of Morchella esculenta L. by chemical and electrochemical methods at multiwall carbon nanotube paste electrode. *Journal of Food Measurement and Characterization* 13 (3):1805–19. doi: 10.1007/s11694-019-00099-3.

Wang, W., Z. Wu, X. Wang, C. Li, K. Zhang, J. Zhou, S. Cheng, and F. Lu. 2018. Enzymatic hydrolysis combined with high-pressure homogenisation for the preparation of polysaccharide-based nanoparticles from the by-product of Flammulina velutipes. *International Journal of Food Science & Technology* 53 (10):2422–9. doi: 10.1111/ijfs.13836.

Wieczorek, P. P., D. Witkowska, I. Jasicka-Misiak, A. Poliwoda, M. Oterman, and K. Zielińska. 2015. Chapter 5 - Bioactive alkaloids of hallucinogenic mushrooms. In *Studies in natural products chemistry*, ed. R. Atta ur, 133–68. Cambridge, USA: Elsevier.

Witkowska, A. M., M. E. Zujko, and I. Mirończuk-Chodakowska. 2011. Comparative study of wild edible mushrooms as sources of antioxidants. *International Journal of Medicinal Mushrooms* 13 (4):335–41. doi: 10.1615/intjmedmushr.v13.i4.30.

Wu, T., and B. Xu. 2015. Antidiabetic and antioxidant activities of eight medicinal mushroom species from China. *International Journal of Medicinal Mushrooms* 17 (2):129–40. doi: 10.1615/intjmedmushrooms.v17.i2.40.

Wu, Y., M.-H. Choi, J. Li, H. Yang, and H.-J. Shin. 2016. Mushroom cosmetics: The present and future. *Cosmetics* 3 (3):22. doi: 10.3390/cosmetics3030022.

Wu, Z., and Y. Li. 2017. Grifolin exhibits anti-cancer activity by inhibiting the development and invasion of gastric tumor cells. *Oncotarget* 8 (13):21454–60. doi: 10.18632/oncotarget.15250.

Xiaokang, W., N. P. Brunton, J. G. Lyng, S. M. Harrison, S. T. Carpes, and K. Papoutsis. 2020. Volatile and non-volatile compounds of shiitake mushrooms treated with pulsed light after twenty-four hour storage at different conditions. *Food Bioscience* 36:100619. doi: 10.1016/j.fbio.2020.100619.

Yahia, E. M., F. Gutiérrez-Orozco, and M. A. Moreno-Pérez. 2017. Identification of phenolic compounds by liquid chromatography-mass spectrometry in seventeen species of wild mushrooms in Central Mexico and determination of their antioxidant activity and bioactive compounds. *Food Chemistry* 226:14–22. doi: 10.1016/j.foodchem.2017.01.044.

Yan, H., X. Che, Q. Lv, L. Zhang, S. Dongol, Y. Wang, H. Sun, and J. Jiang. 2017. Grifolin induces apoptosis and promotes cell cycle arrest in the A2780 human ovarian cancer cell line via inactivation of the ERK1/2 and Akt pathways. *Oncology Letters* 13 (6):4806–12. doi: 10.3892/ol.2017.6092.

Yıldız, S., A. Yılmaz, Z. Can, C. Kılıç, and Ü. Yıldız. 2017. Total phenolic, flavonoid, tannin contents and antioxidant properties of Pleurotus ostreatus and Pleurotus citrinopileatus cultivated on various sawdust. *The Journal of Food* 42:315–23.

Yoon, K. N., N. Alam, K. R. Lee, P. G. Shin, J. C. Cheong, Y. B. Yoo, and T. S. Lee. 2011. Antioxidant and antityrosinase activities of various extracts from the fruiting bodies of Lentinus lepideus. *Molecules (Basel, Switzerland)* 16 (3):2334–47. doi: 10.3390/molecules16032334.

Zielinski, A. A. F., C. W. I. Haminiuk, and T. Beta. 2016. Multiresponse optimization of phenolic antioxidants from white tea (Camellia sinensis L. Kuntze) and their identification by LC–DAD–Q-TOF–MS/MS. *LWT - Food Science and Technology* 65:897–907. doi: 10.1016/j.lwt.2015.09.020.

Zolghadri, S., A. Bahrami, M. T. Hassan Khan, J. Munoz-Munoz, F. Garcia-Molina, F. Garcia-Canovas, and A. A. Saboury. 2019. A comprehensive review on tyrosinase inhibitors. *Journal of Enzyme Inhibition and Medicinal Chemistry* 34 (1):279–309. doi: 10.1080/14756366.2018.1545767.