Nutritional potential of biomass and metabolites from filamentous fungi

J.A. Takahashi[1] and S.A. Carvalho[1,2]

[1]Department of Chemistry, Federal University of Minas Gerais, Av. Antonio Carlos, 6627, CEP31270-901, Belo Horizonte, MG, Brazil
[2]Department of Basic and Instrumental Studies, Southeast University of Bahia State, Praça Primavera, 40, CEP 45700-000, Itapetinga, BA, Brazil

Mushrooms are very appreciated as food in several countries and, besides their fine taste, they have great nutritional value as sources of essential fatty acids, minerals, proteins and biologically active metabolites. By the other hand, non-basidiomycete filamentous fungi from several genera such as *Rhizopus* or *Penicillium* are commonly not associated with human diet. Nevertheless, these and other non-basidiomycete filamentous fungi have also been reported to produce several metabolites useful to be added to food for preservation, coloring, flavoring or even aiming at a biological effect such as antioxidants and essential fatty acids. This review will focus on metabolites produced by filamentous fungi (including mushrooms) that have been showing potential for use by food industry such as sources of antioxidant agents (*Rhizopus oligosporus*, *Pennicillium herquei*), flavors (*Ceratocystis fimbriata*), color pigments (*Phycomyces blakesleeanus*, *Blakeslea trispora*), vitamins (*Ashbya gossypii*) and essential fatty acids (*Syncephalastrum racemosum*, *Mucor circinelloides*). Use of filamentous fungi biomasses for human nutrition as sources of proteins and minerals will also be reviewed.

Keywords filamentous fungi; mushrooms; antioxidants; food

1. Introduction

Fungi produce numerous extra cellular enzymes and secondary metabolites, including organic acids, pigments and other food additives nevertheless they usually are more associated to their pharmacological properties, such as antibiotic and immunosuppressant, than to their nutritional value [1, 2].

Mushrooms are probably the most known edible filamentous fungi but species essentially microscopic like those belonging to *Penicillium* genus are also important sources of food additives and edible biomass. For instance, in the production of Roquefort Gorgonzola and blue type cheeses, a key step is the inoculation and development of *Penicillium roqueforti* that generates a peculiar flavor and aroma [3, 4]. *Penicillium camemberti* is another species essential in the maturation of some cheeses, furnishing lipolitic and proteolitic enzymes responsible for the production of volatile compounds, such as 1-octen-3-ol, that confers the characteristic flavor of Camembert and Brie cheeses [5].

2. Nutritional potential of filamentous fungi

2.1 Mushrooms

The number of mushrooms existing species in nature is estimated in around 10,000, from which approximately 10% are likely to be edible [6]. Worldwide, approximately twenty-five species are widely accepted as food, but only a few of them are commercially produced. It is reported that 2.4 million tons of mushrooms were produced in 2002, the major producers being China (708 billion tons), United States (390 thousand tons), The Netherlands and Japan, while main consumer countries where Germany, China, The Netherlands and Japan [7]. Latin America has produced only 1.3% of the world total cultivated mushrooms that year, the largest producers being Mexico (58.6%), Chile (17.6%) and Brazil (10.6%) [8].

Among the edible mushrooms produced worldwide, *Agaricus bisporus* is the most cultivated one (38%), followed by species of the genus *Pleurotus* (25%) and *Lentinula edodes* (10%) [9]. There are clearly two mushrooms markets: one referring to the most commercialized species, champignon (*Agaricus bisporus*), and another that gathers exotic mushrooms, including species such as *L. edodes*, *Pleurotus* sp., *Auricularia* sp., *Flamulina velutipes*, *Grifola frondosa*, *Hypsizygus marmoreus*, *Pholiota nameko*, *Tremella fuciformis* and *Volvariella* sp. [9, 10]. Recently, the species *Agaricus blazei*, known as "sun mushroom" has awakened the interest for consumption, as a food supplement, due to its potential medicinal properties [10, 11].

Ingestion of mushrooms in some countries is contained by the high cost, little knowledge of their nutritional and medicinal properties and lack of expertise to distinguish beneficial from poisoning species. Mushrooms names are sometimes adopted in accordance to their provenience as for shiitake and hiratake, Japanese names adopted for *L. edodes* and *Pleurotus sp.* species, respectively, as well as the French origin of *A. bisporus,* named champignon. Table 1 shows some usual names described in the literature for some species of edible mushrooms.

Table 1 Scientific and common names of some edible mushrooms.

Scientific names	Common names
Agaricus bisporus	Button mushroom/white [12]; Portabella [13]; Crimini mushroom [14, 15]
Pleurotus ostreatus or *Pleurotus ssp.*	Oyster mushroom [13; 16,17]; Hiratake [18]; White oyster mushroom [19]
Hypsizygus marmoreus	Buna-shimeji mushroom [19, 20]; Shimeji [21]
Lentinula edodes	Shiitake [15, 17]; Black forest mushroom or oak mushroom [19]

Mushrooms are good sources of protein, carbohydrates and fibers and, conveniently, they have low lipid content, being considered healthy foods [22]. Kalač [13] compiled nutrition information for fifteen species of edible mushrooms, including the centesimal composition, describing crude protein contents levels between 16.5-59.4% of dry matter (dm), carbohydrates between 30.6-75.0% dm, and lipids between 0.4-9.0% dm. Furlani [23] studied the centesimal composition of shiitake, champignon and oyster mushrooms, acquired in Brazil, that presented average protein levels ranging between 19.0-28.5%, carbohydrates between 54.1-69.6%, lipids between 4.3-5.4% and ash totals between 7.0-12.0%. Shibata and Demiate [24] reported that carbohydrates, proteins, lipids and ashes composition in the sun mushroom varied between 41.9-47.9%, 34.8-39.8%, 0.8-1.2% and 6.9-7.8%, respectively, according to the cultivation form.

General profiles of edible mushrooms show presence of essential aminoacids such as lysine, valine and methionine [22, 25, 26], essential fatty acids like linoleic (C18: 2n-6) and oleic (C18:1n-9) acids [27], and carbohydrates like mannitol and trealoses [13, 28, 29]. Most usual minerals found in mushrooms are calcium, magnesium, potassium, iron, zinc and copper [6, 12, 30, 31], but levels of selenium compounds in the edible species *Albatrellus pes-caprae* and *Boletus edulis* were reported by Slejkovec and collaborators [32].

Presence of vitamin C (ascorbic acid) and niacin was reported for *A. bisporus*, *L. edodes* and *P. ostreatus* [12]. Vitamins B1 and B2 were reported for shiitake, champignon and oyster mushrooms by Furlani and Godoy [33]. Vitamin D was reported in the fruit bodies of *Cantharellus cibarius* (chanterelle), an edible mushroom available in both pigmented and albino forms [34], and in *A. bisporus* [35].

Levels of calcium, magnesium, zinc and iron were described for mushrooms from Finland, Malaysia and Turkey (Table 2). The variation is due to several reasons like species, source (wild or cultivated), climatic variations, maturity level, conservation process, and substrate of cultivation [23, 36]. Level of calcium in *Pleurotus ostreatus* reached up to 126 mg % for a wild species collected in Erzurum province in Turkey [17, 30]. Magnesium levels varied from 130-300 mg while, for zinc, a small variation (8.3-14.9 mg %) was found among all analyzed samples from Finland and Turkey. Iron levels varied greatly, reaching 68.2 mg % for a *P. ostreatus* sample. Malaysian mushrooms showed very low levels of zinc and iron, compared to the samples obtained from other countries. Differences found corroborate the influence of external parameters, including seasonal variations. In fact, Turkish *P. ostreatus* and *P. sajor-caju* as well as Finlandian samples were cultivated; Turkish *P. ostreatus* from Erzurum province was a wild sample, as well as the Malaysian *Pleurotus* specimen. Çağlarırmak [17] evaluating the calcium, magnesium, zinc and iron contents of *L. edodes*, according to the growth period, reported a decrease on their levels with the time.

Table 2 Levels of calcium, magnesium, zinc and iron in mushrooms from Finland, Malaysia and Turkey (mg/100 g of dry material).

Mushroom species	Origin	Ca	Mg	Zn	Fe
Agaricus bisporus/white	Finland	25.0	130.0	6.6	4.8
Agaricus bisporus/brown	Finland	13.0	141.0	4.7	2.8
Pleurotus ostreatus [12]	Finland	1.0	200.0	8.3	5.4
Lentinula edodes [12]	Finland	5.0	155.0	9.2	3.3
Pleurotus sp.[12]	Malasya	41.3	133.6	0.1	0.1
Pleurotus ostreatus [6]	Erzurum/Turkey	126.0	170.0	14.2	68.2
Pleurotus ostreatus [17]	İzmir/Turkey	109.5	300.0	14.9	20.3
P. sajor-caju[17]	İzmir/Turkey	40.7	267.8	15.8	13.4
L. edodes/stage 1*[17]	Kocaeli/Turkey	126.0	355.1	11.3	7.8
*L. edodes/*stage 2*[17]	Kocaeli/Turkey	25.7	164.1	11.7	4.0
*L. edodes/*stage 3*[17]	Kocaeli/Turkey	66.4	162.9	10.7	6.4
*L. edodes/*stage 4*[17]	Kocaeli/Turkey	63.3	145.7	10.1	6.4

* Stage 1 to 4 refers to the age of the sample, stage 1 refers to younger sample.

2.1 Other filamentous fungi

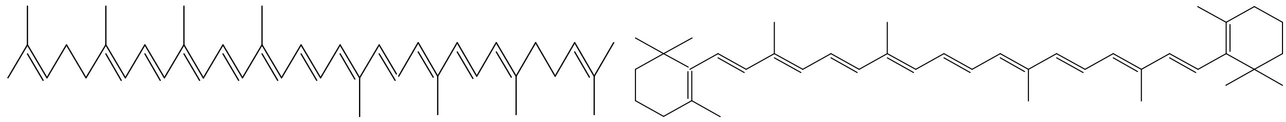
Biomass or dried cells of fungi, as well as of algae, yeasts and bacteria are used as sources of proteins and denominated single cell protein (SCP). In this way, biomass of *Fusarium venenatum* is commercialized being reported to be a good source of zinc and biotin, also having protein content very similar to that found in milk [37, 38]. Anupama and Ravindra [39] compared the amino acid composition of *Aspergillus niger* SCP with FAO casein standard, observing comparable protein levels in the two different sources. The amino acids valine, leucine, lysine and phenylalanine were more abundant in *A. niger* SCP while, in casein, a FAO protein standard, isoleucine was the major amino acid present.

Non-basidiomycete filamentous fungi have been widely used in the production of several compounds used as food additives (Table 3 and Fig. 1).

Table 3 Fungal products used or bearing potential for use in industry as food additives

Industrial use	Product	Fungal species	References
Acidulating agent	Citric acid	*Aspergillus niger*	[40, 41]
Color pigment	Carotenoids	*P. blakesleeanus* and *B. trispora*	[42, 43]
	Monascin	*Monascus* sp.	[44]
	Arpink Red^{TM}	*P. oxalicum*	[45, 46]
Vitamin	Riboflavin (Vitamin B_{12})	*A. gossypii*	[47]
Antioxidant	Phenolic compounds	*R. oligosporus*	[48, 49]
Aroma	Isoamyl and ethyl acetate	*Ceratocystis fimbriata*	[50]
Cocoa butter substitute	Fatty acids	*M. alpina*	[51]
Food enrichment	Biomass	*S. cerevisiae* and *Rhizopus* sp.	[52, 53]
Food formulation	Biomass	*F. graminearum*	[37]

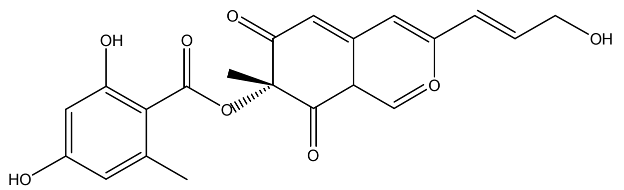
Colored carotenes are used as strong antioxidants and as pigments in food. Microorganisms accumulate several types of carotenoids as a part of their response to various environmental stresses [42]. Some pigment producers, e.g. *Rhodotorula* sp., have been taxonomically classified based on qualitative and quantitative assessments of their carotenoids biosynthesis [42]. Research on carotenoid production has been reported in different fungal classes; zygomycetes (*e.g.*,*Phycomyces blakesleeanus*), ascomycetes (*e.g.*, *Neurospora crassa* and *Gibberella fujikuroi*), and basidiomycetes *Xanthophyllomyces dendrorhous*) [54]. Light, temperature and culture medium composition have direct influence in carotenoids production. Organic compounds like terpenes, ionones, amines, alkaloids and antibiotics have also showed effect on carotene synthesis. Chemical stimulators such as pyridine, imidazole, and methylheptenone stimulate lycopene formation in *Blakeslea trispora* and *Phycomyces blakesleeanus* [42, 43]. The major commercial utility of lycopene is against cardiovascular diseases and prostate cancer, while β-carotene is reported to be an anti cancer drug, acing also as a source of provitamin A, food colorant and photo protecting agent [42]. Structures of lycopene and β-carotene are presented in Figure 1.



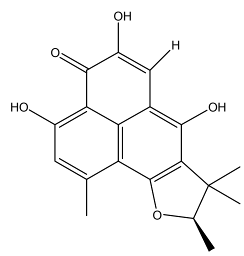
Lycopene (ψ,ψ-carotene) β-carotene (β-β-carotene)

Figure 1 Carotenoid pigments produced by *Blakeslea trispora* and *Phycomyces blakesleeanus*

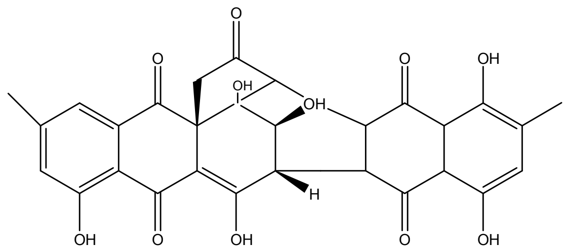
Citric acid is of great importance for the food and beverage industry, being used as acidulating agent, preservative, antioxidant, and flavoring agent [55] but pigments are among the compounds most obtained from filamentous fungi fermentation. For example, Arpink Red^{TM}, a dye pigment produced by *Penicillium oxalicum*, have favorable characteristics for use in foods like water solubility, wide range of colors, and do not require a stabilizing agent to be added to foodstuff. Other extra cellular substances produced by filamentous fungi used as dyes are mitorubrinol and purpurogenone, produced by *Penicillium purpurogenum*. Atrovenetin, produced by *Penicillium herquei* presents double function as a food additive: dye and antioxidant of tocopherol [45], all of them being water soluble. The structural diversity of these substances is represented by some chemical structures compiled in Figure 2.



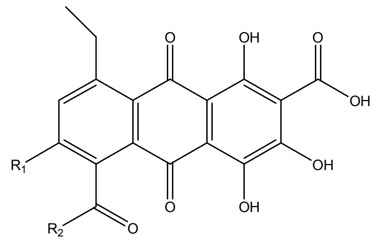
Mitorubrinol, produced by *Penicillium purpurogenum*
Color: orange-red



Atronenetin, produced by *Penicillium herquei*
Color: yellow



Purpurogenone, produced by *Penicillium purpurogenum*
Color: orange-yellow



Basic structure of Arpink red^{TM}, produced by *Penicillium oxalicum* var. *armeniaca.*

Color: dark red

Figure 2 Structures of some non carotenoid pigments produced by filamentous fungi genera *Penicillium*.

The chemical production of riboflavin (vitamin B2) is being replaced by processes using fungal species as *Ashbya gossypii* that offer good yield and low cost of production [47]. *Ceratocystis fimbriata* is reported to have a great potential in the production of compounds bearing ester groups, very useful additives presenting varied flavors such as those of peach, pineapple, bananas, citrus and roses [50]. Single Cell Oil (SCO) produced by microorganisms has been intensively studied in the search for new lipidic matrixes for cacao butter substitution and, alimentary supplementation.

The market of children food formulations consume large amounts of polyunsaturated fatty acids for supplementing, especially arachidonic acid (ARA - C20: 4n3) and docosahexenoic acid (DHA - C22: 6n3). Single cell oil rich in γ-linolenic acid has been early produced by using the fungus *Mucor circinelloides* while the fungal species *Mortierella alpina* produces cells containing up to 40 50% of ARA, being used as supplement in children food formulations [56].

3. Fungi as sources of essential fatty acids

3.1. Metabolic importance of essential fatty acids

The biological importance of fatty acids is related to their role in human metabolism. Saturated fatty acids such as palmitic (C16: 0) and myristic (C14: 0), and *trans* fatty acids are reported to raise blood levels of low density lipoproteins (LDL), better known as bad cholesterol [57] and are associated to coronay diseases. In contrast, essential fatty acids are precursors of important structures such as prostaglandins that participate in a variety of physiological actions such as reproduction, protection of the gastric mucosa increasing of renal blood flow, among other functions. Essential fatty acids such linoleic acid (LA; C18: 2n6), α-linolenic acid (ALA; C18: 3n3), arachidonic acid (ARA; C20: 4n6), eicosapentaenoic acid (EPA; C20: 5n3) and docosahexaenoic acid (DHA; C22: 6n3) are involved in the flexibility, fluidity and selective permeability of cell membranes. The brain is rich in DHA and ARA, DHA being the main component of the grey matter of the brain and the eye retina, and a key component of the heart tissue. EPA has beneficial effects to the cardiovascular system and is a precursor of biosynthesis of eicosanoids, regulators biological cardiovascular system [56, 58].

Linoleic acid (C18: 2n6) is the largest representative of omega-6 (ω-6) family, being the abundantly present in vegetable oils, meat, dairy products, cereals, among others. Linolenic acid (C18: 3n3) is the largest representative of omega-3 (ω-3) family, found, in smaller quantities, in cold water fish (sardines, salmon, tuna), some vegetable oil (colza), nuts and seeds [58, 59]. It is reported that ω-3 fatty acids reduce the risk of diseases in coronary arteries, hypertension, type 2 diabetes, arthritis, rheumatism, autoimmune disorders and cancer. Diets rich in some fatty acids seems to create an inflammatory environment that could increase the risk of diseases, and the literature points that an unbalanced intake of fatty acids belonging to the families ω-6 and ω-3 would increase the risk of various diseases; then only a balanced intake would lead to health benefits [58-60]. Humans can synthesize fatty acids [51, 60, 61], but habits such as smoking, alcohol intake, lack of exercise practice and advanced age make inefficient the conversion of fatty acids systemic enzymatic conversion [51]. Premature children also lacks of an efficient endogenous ARA production. In this way, alternative sources of ARA and other PUFA are sought for human consume.

The distribution of saturated fatty acids (SFA), monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) on a food is an indicative of its nutritional quality, since high levels of PUFA are highly desirable as PUFA contain essential fatty acids. Literature points that the ratio PUFA/SFA below 0.45 indicates non-healthy foods [62-64].

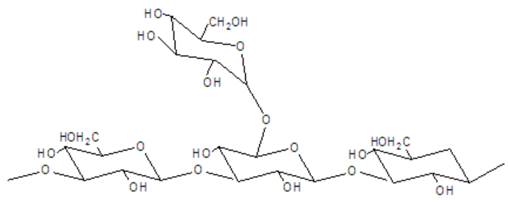
3.2 Essential fatty acids in filamentous fungi

Yilmaz and collaborators [63] reported levels of MUFA above PUFA in wild *Agaricus campestris* and *P. ostreatus*, harvested in Tokat province in Turkey. The levels reached 47% of MUFA and 35% of PUFA of the total quantified in *A. campestris*. By the other hand, the species *P. ostreatus* presented 64% of MUFA and 42% of PUFA. Pedneault and collaborators [64], reported for the same species, the ratio PUFA: SFA: MUFA of 71: 10: 19%, with the unsaturation degree increasing with the decline of temperature (27, 21, 17 and 12 ^{o}C) used for the mushrooms cultivation.

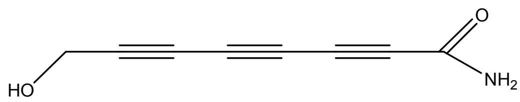
Production of γ-linolenic acid (GLA) by fungi has been extensively used aiming at the development of an economically advantageous process for the industrial production of GLA that is very affected by the culture medium composition. Biomass of *Mortierella isabellina* and *Cunninghamella echinulata* showed low productivity [65, 66], while a screening of forty-eight Mucorales species showed that, when cultivated in sunflower oil, *Mucor mucedo* was the best GLA producer [67]. High GLA production by *Mucor* species was also reported by Mamatha and collaborators [68], while other *Mucor* species like *M. iemalis* and *M. circinelloides* v. Tieghem productivity was studied by Kennedy and collaborators [69]. A careful study of the nitrogen source in the medium led to an optimized production of GLA by *C. echinulata* [70]. Bhatia et al [71] studying the differences in the fatty acids productivity in seven filamentous fungi (*Aspergillus niger*, *A. luchuensis*, *Penicillium crustosum*, *Alternaria tenuis*, *Rhizoctonia solani*, *Mucor* sp. and *Pythium irregulare*) concluded that the best nitrogen source to be used for fatty acids production cannot be generalized, being species-dependent. In order to improve ARA productivity by *M. alpina*, approaches like genetic modifications [72] and glutamate supplementation [73] have been used aiming at to produce highly productive species.

4. Bioactive metabolites from filamentous fungi

Many mushrooms produce molecules that have biological properties like hipoglicemic and hipocolinesterolemic [74, 75]. Antitumor and antiregulatory polysaccharides, such as lentinan (Fig. 3), extracted from *Lentinus edodes* species (Shiitake), which also have antifungal and antibacterial activities is also a good example [76-78]. Agrocibin (Fig. 3), isolated from the ethyl acetate extract of the species *Agrocybe perfecta*, presents imunossupressing, tripanocidal, cytotoxic and antifungal activities [79]. Presence of nicotinic acid, and pyrazole-3(5)-carboxylic acid in *Volvariella volvacea* were related to the beneficial health effects of this edible specimen [80].



(1-3) - β - glican (Lentinan)



Agrocibin

Figure 3 Structure of Lentinan, isolated from *L. edodes,* and structure of Agrocibin, isolated from *Agrocybe perfecta*

Chitosan, a polymer of (1→4) 2-amino-2-deoxy-β-D-glucose is a natural polymer derived from chitin, a polysaccharide found in the exoskeleton of shellfish, and chemically similar to cellulose. Chitosan is less commonly found in living organisms than chitin but it can be found in the cell walls of certain groups of fungi, particularly *Phycomyces blakesleeanus, Cunninghamella* sp., *Gongronella butleri*, and *Absidia coerula*, that are alternative sources of chitosan. A strain of *Syncephalastrum racemosum*, isolated from herbivores feces, was studied for chitosan production using sugar cane substrates, such as juice or molasses, from Northeast Brazil [81]. Surprisingly, when compared to a standard commercial fungicide, Rovral® (iprodione), there was not found a significtive protecting diference among chitosan and iprodione in the berries decay process [82].

4.1 Antioxidant activity

The antioxidant profile of edible beefsteak fungus *Fistulina hepatica* showed that DPPH is inhibited depending on the concentration. This specimen is also able to inhibit superoxide radical, due to its ability as scavenger and xanthine oxidase inhibitor [83]. Compounds like (1'E)-erythro-4-(3',4'-dihydroxypentenyl)oxazole, (1'E,4'S)-4-(3'-oxo-4'-hydroxypentenyl)oxazole and 6-pentyl-pyrone have been pointed as fungal metabolites responsible for inhibition of linoleate auto-oxidation [84]. Work by Barros and collaborators [29] corroborated and broadened the antioxidant activity of mushrooms, as they analyzed seven species *Cantharellus cibarius*, *Hypholoma fasciculare*, *Lepista nuda*, *Lycoperdon molle*, *Lycoperdon perlatum*, *Ramaria botrytis*, and *Tricholoma acerbum*. They performed a deep study on their antioxidant activity by using four methodologies, showing that, besides biosynthesizing natural compounds associated to nutritional features, such as phenolics, tocopherols, ascorbic acid, and carotenoids, they present a broad antioxidant activity besides antimicrobial capacity [29]. *Auricularia auricular*, a mushroom rich in carbohydrates, showed beneficial effects in prevention of hypercholesterolemia; polysaccharides present in A. auricular were able to improve lipoprotein lipase activity and total antioxidant capacity in mice [85]. *Sarcodon imbricatus*, when evaluated as source of nutraceuticals, showed DPPH radical scavenging activity [86]. The *in vitro* and *in vivo* antioxidant activity of *Hypsizygus marmoreus* (Peck) Bigel. (known as bunashimeji in Japan), one of the most popular culinary-medicinal Japanese mushrooms, has been reported by Matsuzawa [20].

5. Food enrichment by fungi

A. bisporus has been tested as a nutritional supplement for bread, since it has been showing to be a good source of selenium, chromium, vitamin and antioxidant agents [35]. Presence of oyster mushroom mycelia powder in semolina flour for pasta preparation is suggested as a good way to increase fiber intake aiming at reducing coronary diseases and diabetes incidence. Addition up to 10% of dried powered mushroom biomass has been accepted by tasters for color, flavor, mouth feel and elasticity [87]. *Rhizopus oligosporus* has been grown in fruit residues (solid state fermentation) aiming at increasing the concentration of free phenol compounds with antioxidant activity, since these compounds are often found in conjugate forms bearing a sugar or lipidic moiety [48].

6. Final remarks

An interesting review by Chye et al [6] brings about the nutritional features of mushrooms as an alternative food source for people in developing countries, mentioning the need for deeper studies on wild mushrooms toxicology, nutrients levels and contents alteration by growth conditions. It is a proper worry, since care must be taken when eating wild mushrooms, as some of them are extremely toxic. Toxic constituents present in *A. blazei* and other toxic mushrooms have been studied [88]. Nutritional requirements for edible mushrooms growing, aiming at production of aroma compounds, pigments, and flavor agents was reviewed by Jacob et al [89]. The action of *Rhizopus* sp. and *A. oryzae* on agroindustrial by-products like deffated rice and wheat bran led to an increase of protein contents, adding value to these residues that are mostly used for animal feed [53]

Ongoing research on newly described biological activities of fungal species and the development of new drugs from fungal metabolites, such as immuno-modulating [90], antitumor [91] drugs will collaborate for a widespread use of fungi as food, including the non-mushroom species.

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