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Review article

# Edible mushrooms trending in food: Nutrigenomics, bibliometric, from bench to valuable applications

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ABSTRACT

The worldwide consumption, health-promoting and nutritional properties of mushrooms have been extensively researched over a decade. Although, wide range of edible mushrooms is still unexplored, which can be a valuable source of bioactive compounds in dietary supplements and biopharma industry. Mushrooms represent as dynamic source of nutrients lacking in food from plant or animal origin thus, considered as vital functional food utilized for prevention of numerous diseases. The unique bioactive compounds in mushroom and their anti-inflammatory, anti-tumour and other health attributes have been discussed. The preventive action of mushroom on maintaining the gut health and their property to act as pro, pre or symbiotic is also elucidated. The direct prebiotic activity of mushroom affects gut haemostasis and enhances the gut microbiota. Recent reports on role in improving the brain health and neurological impact by mushroom are mentioned. The role of bioactive components in mushroom with relation to nutrigenomics have been explored. The nutrigenomics has become a crucial tool to assess individuals' diet according its genetic make-up and thus, cure of several diseases. Undeniably, mushroom in present time is regarded as next-generation wonder food, playing crucial role in sustaining health, thus, an active ingredient of food and nutraceutical industries.

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## 1. Introduction

Mushrooms are cultivated and consumed for centuries owing to their nutritional and sensory properties, easy and manageable growing conditions, and health attributes. The mostly used edible mushrooms are *Pleurotus ostreatus*, *Lentinula edodes*, *Agaricus bisporus*, *Flammulina velutipes* and *Auricularia auricular*, whereas medicinal ones include *Ganoderma lucidum*, *Cordyceps sinensis* and *Poria Cocos* [1]. According to the global mushroom market report, the global market for mushrooms is estimated to grow from US$48.8 to 83.5 billion over the period from 2022 to 2030 at a compound annual growth rate (CAGR) of 7 %, with China, India and Japan as leading mushroom countries. The market of button mushrooms is expected to show a 6.9 % CAGR and reach US$51.7 billion by the end of 2030. Considering the ongoing post-pandemic recovery, Shiitake segment growth has been updated to a 7.4 % CAGR for the next eight years. The geographic markets, like Japan and Canada, are each forecast to grow at 2.7 % and 7.2 %, respectively, over the 2022–2030 period. Inside Europe, Germany is predicted to record a growth of approximately 4.1 % CAGR. Led by countries like Australia, India, and South Korea, the market in Asia-Pacific is estimated to reach US$11.6 billion by the year 2030 (https://www.researchandmarkets.com).

Recently in the past few decades, the mushroom has been given special attention as dietary supplements as they contain bioactive compounds which are generally not found in food from plant or animal origin, support health plus well-being, and are utilized as prophylactics for numerous human diseases [2]. Mushrooms are known to affect gut microbiota by acting as direct prebiotics, indirect probiotics or synbiotics, which further influence inflammation and β-glycans, enzymes, and secondary metabolites content in the gut [3]. Currently, mushrooms are recognised as a source of nutraceuticals in nutritional balancing, immune system strengthening, natural body resistance, and illness prevention. Moreover, mushrooms have also been shown to have the ability to reduce the health risks caused by obesity, hypertension, hypolipidemic and age-related impaired functions [4].

Nutrigenomics is an interdisciplinary segment that combines knowledge from physiology, pathology, genetics, molecular biology,

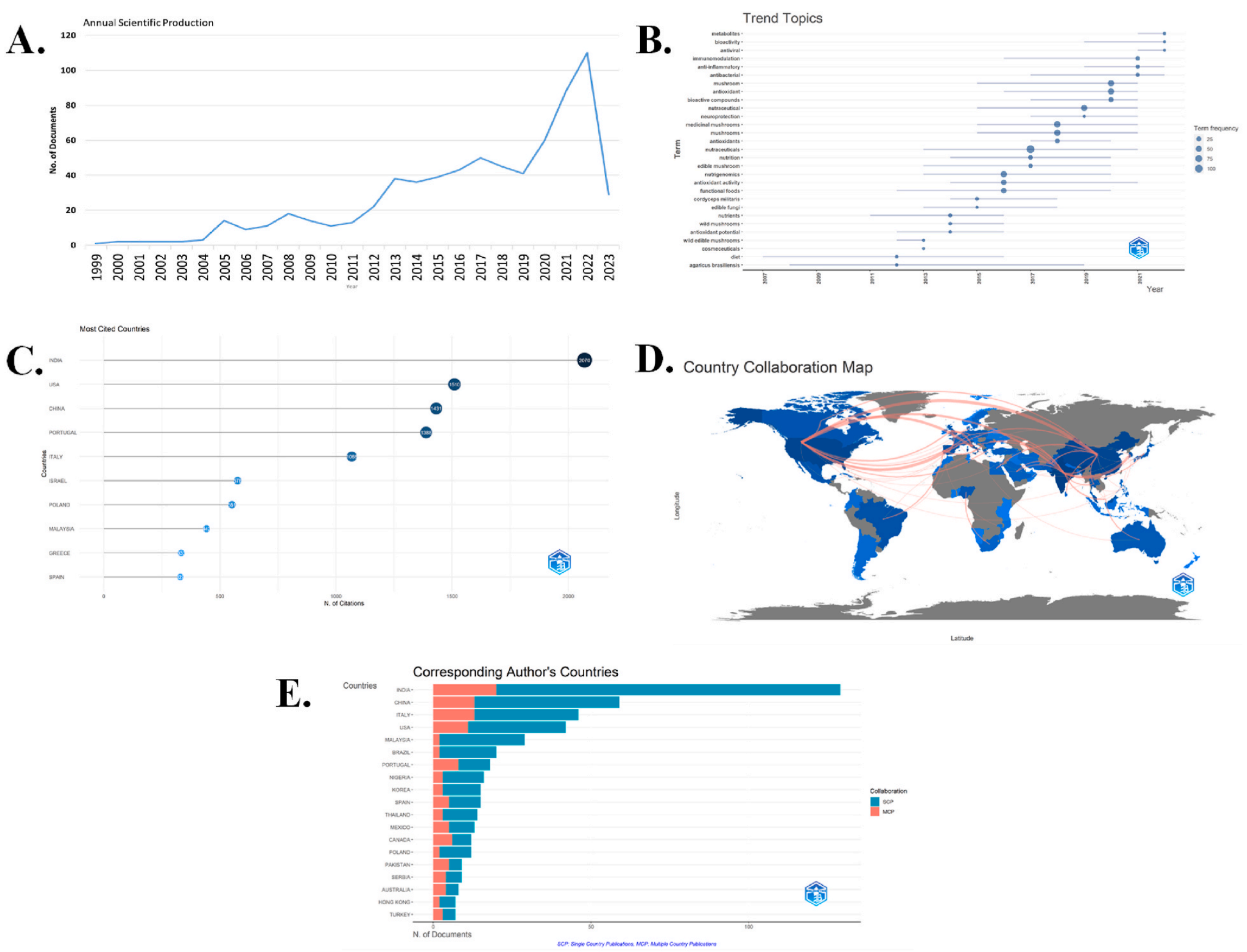


**Fig. 1.** Bibliometric analysis: The present figure can visualize bibliometric data, such as publication trends over time, top contributing countries or institutions, co-authorship networks, and keyword analysis related to edible mushrooms and food trends. (A) Year-wise publication of articles; (B) Trends in topics during the period of study; (C) Most cited countries; (D) Country collaboration network map; (E) SCP and MCP of collaborating nations; (F) Word cloud map of authors' keywords.

and nutrition to determine the effects of nutrients on gene expression and regulation [5]. Bioactives in food act as dietary signals. From the nutrigenomics perceptive, cellular sensor systems such as peroxisome proliferated activated and retinoid X receptors recognize these dietary signals regulate gene expression, protein synthesis, and metabolite production. This necessitates a fundamental understanding of the influence of nutrients at the molecular level, nutrient-related interactions at the genome, proteome, and metabolome levels of individual's, resulting in a revolution in nutrition research from physiology to molecular biology and genetics [6]. Since so many studies have been devoted to examining new and effective products based on the bioactivities of mushrooms, the relation of mushroom bioactives with nutrigenomics has not been explored yet. Thus, this review covers the potential of edible mushrooms as a wonder food, relates the effect of bioactive components present in mushroom with a nutrigenomics lens.

## 2. Bibliometric overview of mushroom research

A bibliometric analysis was conducted to investigate the trends in publications on the theme of study. The 'Dimensions' database was utilized to retrieve relevant literature on the keywords "nutraceuticals AND Mushroom OR nutrigenomics" search engine. Nutraceuticals, an emerging topic with significant implications for our consumption patterns, was the focus of this study. The bibliometric analysis aimed to gain insights into the direction of research on this theme. Bibliometric is valuable for depicting scientific advancements and outlining the main research guidelines [7]. This method is also useful for identifying and uncovering new research insights based on current trends. Moreover, it allows for synthesizing existing research and mapping current knowledge on a specific topic [8,9].

For this study, the Scopus database was accessed on May 10, 2023, using the "nutraceuticals AND Mushroom OR nutrigenomics" search engine. The data retrieval period was selected from 1999 to the present day. A total of 800 research articles were obtained, and unwanted articles were removed during the data-cleaning process. The retrieved and cleaned data were then analyzed using Biblioshiny software to identify trends. Biblioshiny is an open-source tool commonly used for quantitative research in scientometrics and enables visual analysis.

The results of the analysis of the data retrieved from the Scopus database are presented in this section. Fig. 1A illustrates the growth rate of scientific production in the study theme. It can be observed from Fig. 1A that the number of research articles on this theme has been increasing over time, with a slight dip in 2019 followed by a peak in 2022. In recent years, there has been a growing demand for mushroom-based nutraceuticals and functional foods, driven by significant lifestyle changes toward healthier choices and the increased preference for immunity-enhancing supplements, particularly during the COVID-19 pandemic (10). The emerging trend of research on the theme is supported by Fig. 1B, which illustrates the trend in topics related to the study theme. We analyzed the retrieved data using Biblioshiny, which provided us with the results of the trending topics. The frequency of a word indicates the most commonly used keywords by the authors.

From Fig. 1, it is evident that the trending topics in this field of study include nutraceuticals, antioxidants, medicinal mushrooms, and more. These aspects are the focus of researchers when exploring the relationship between nutrition and mushrooms. Bibliometric analysis helps us understand which countries and authors have the most impact in their respective research fields. Therefore, we conducted an analysis in Biblioshiny to identify the most impactful countries based on their citations in the theme of study. Fig. 1C shows that India has the highest impact and received the most citations, with nearly 2070 citations in research related to edible mushrooms and nutraceuticals. Other countries, such as the United States of America and China, followed India in terms of citations. Based on the retrieved data, we also conducted an analysis of global collaborations to understand which countries collaborate the most. Collaboration facilitates the exchange of resources among countries and helps researchers identify prolific authors in specific regions. The country collaboration map is depicted in Fig. 1D.

Collaboration practices vary greatly across scientific areas and disciplines, and they influence scientific performance and scholarly communication. Collaboration is not only evident in solving public problems but can also be observed in publications involving authors, institutions, and countries. In this study, the authors only present collaborations between countries with which they are affiliated. We also analyzed the extent of publications within each country in terms of single-country publications and multiple-country publications. The results are presented in Fig. 1E. The figure indicates that single-country publications (SCP) are more prevalent compared to multiple-country publications (MCP), suggesting that there is still potential for collaboration on this theme. The results reveal that India has the highest SCP-to-MCP ratio, followed by China and Italy.

## 3. Nutritional properties of mushroom

Mushrooms have been consumed by humans since time immemorial with delicacy due to their pleasing flavour and texture [10]. Mushrooms can accumulate trace elements and heavy metals such as Zn, Cu, Mn, Fe, Se, Cd, Pb etc., and act as cofactors of enzymes that have antioxidant functions [11,12]. High amount of potassium and phosphorus is beneficial for patients suffering with musculoskeletal issues [13]. Mushrooms also have very low sodium concentrations, which is important in hypertension [14].

Several selenium compounds such as selenomethionine, selenocysteine, Se-methyl selenocysteine, selenite and seleno-polysaccharides have been reported in mushrooms and reduce the cytotoxic effect of reactive oxygen species (ROS) [15]. Mushrooms are good sources of several vitamins, particularly riboflavin, niacin, and folates. In addition to this, mushrooms also contain small amounts of vitamins C, thiamine (B1) and traces of vitamins $B_{12}$ and $D_2$ [16,17]. The vitamin content of mushrooms varies from species to species. The riboflavin content and bioavailability in edible commercialized mushrooms (*A. bisporus*, *L. edodes* and *P. ostreatus*) are higher than in vegetables. Mushrooms possess desirable nutritional composition with high protein content, low levels of fat, low-calorie value and the high proportion of polyunsaturated fatty acids (PUFA), which make them suitable for heart patients.

They are ideal for diabetic patients due to the absence of starch, low glycaemic index and high amount of mannitol [18].

### 3.1. Vitamin D

Vitamin D is responsible for enhancing the intestinal absorption of minerals such as Ca, Fe, P, and Zn. Vitamin $D_3$ is generally present in animal sources, while vitamin $D_2$ is predominantly present in mushrooms and yeast [19]. Vitamin $D_2$ amount varies significantly within and between species and dependent on developmental stage [20,21]. External environmental factors like climate, habitat, and latitude also influence the vitamin $D_2$ content of mushrooms. The vitamin $D_2$ content of mushrooms can also be increased artificially by treatment with UV irradiation. During treatment, the existing ergosterol is converted into vitamin D2, which inhibits iron-dependent liposomal peroxidation and the growth of cancer cells [22].

### 3.2. Vitamin A

Carotenoids are natural antioxidant compounds present in food in several forms. Among these specifically, β-carotene and lutein were reported in several mushroom species. Canthaxanthin carotenoid compound is found in *Cantharellus cinnabarinus* and *Cantharellus friesii* were used by Chinese herbalists for the treatment of night blindness [18,23].

### 3.3. Antioxidants

Imbalance metabolism and ROS are the main cause of oxidative stress in the human body, leading to several health disorders such as metabolic diseases, heart diseases, severe neural diseases and different types of cancers. To cope with oxidative stress, endogenous antioxidant defense mechanisms and dietary intake of antioxidants play a very important role and helps in regulating the oxidative homeostasis of our body. In the last few years, mushrooms have gained attention as a commercial source of antioxidants [18]. Mushrooms have been reported to possess a wide array of antioxidant compounds and their dietary supplements help to strengthen the antioxidant defense mechanism [24]. Natural antioxidant compounds like ascorbic acid, carotenoids, ergosterol [25], ergothioneine, flavonoids, ergothioneine, phenolics [26,27], polysaccharides [28], tocopherols [29] etc. are found in mushroom fruit bodies, mycelium, and culture broth. The preventive medicine and food industry recently showed increased interest in natural antioxidants due to the restricted use of synthetic antioxidants in food. Mushrooms have an additional advantage because of the shorter time to produce fruiting bodies and mycelium [30]. In order to prevent harm from oxidation in the human body, antioxidant compounds may be extracted and used as functional additives, or mushrooms may be integrated into our diet as an alternative source of food [10].

### 3.4. Phenolic compounds

Phenolic compounds are present in all mushrooms including phenolic acids, flavonoids, lignans, tannins, stilbenes. The oxidized polyphenols act as free radical inhibitors, peroxide decomposers, metal in-activators or oxygen scavengers [31]. Mushrooms contain large amounts of polyphenols at concentrations in the range of 6.25–3.62 mg/mL [32]. Flavonoids assist in direct scavenging of reactive species, chelating the trace metal ion involved in reactive species formation and regeneration of α tocopherol. Various types of flavonoids were reported in different edible mushrooms, e.g., biochanin, catechin chrysin, formononetin, hesperetin, kaempferol, myricetin, naringenin, naringin, pyrogallol, resveratrol, rutin, quercetin and form the major part of total phenol content in *Cantharellus cibarius* [18].

### 3.5. Polysaccharides

A glucan is a homopolysaccharide made of D-glucose units and linked together by glycosidic bonds. Glucans are categorized as α- or β-glucans based on the glycosidic bond type. β-glucan is one of the principal components of the mushroom cell wall, which imparts antioxidant properties to mushrooms. Many mushrooms have fungal β-glucan that differs greatly in length and branching patterns and has a wide spectrum of biological activity [33]. Several polysaccharides from mushrooms are isolated from developing functional foods such as calocyban from *Calocybe indica*, ganoderan from *Ganoderma lucidum*, pleuran from *Pleurotus* species, lentinan from *Lentinus edodes*, and schizophyllan from *Schizophyllum commune*. Polysaccharides exhibits anti-inflammatory, antitumour, and immunomodulatory activities [24].

### 3.6. Tocopherols

Vitamin E is a common term for tocopherols and tocotrienols. Among them, α-tocopherol is the most biologically active and fat-soluble. This compound is present in the cell membrane and has been detected in most mushrooms [18].

### 3.7. β-carotene and lycopene

β-carotene and lycopene are natural pigments present in mushrooms and are not synthesized by animals. β-carotene is the precursor for vitamin A while, lycopene is an acyclic isomer of β-carotene [34]. Hussein et al. (2015) [35] reported that the amount of β-carotene and lycopene found in *Lentinus squarrolosus* was significantly higher than the levels found in other foods such as carrot, persimmon, and tomato.

### 3.8. *Ergosterol*

Ergosterol is found in some mushrooms and is the precursor of vitamin D. When mushrooms are exposed to UV radiation, it is converted to vitamin $D_2$ (ergocalciferol). Vitamin $D_2$ is the only source of vitamin D for vegetarians. Ergothioneine is a sulphur-containing derivative of histidine amino acid, plays an important role in the protection of mitochondrial components, found in commonly cultivated mushroom species such as *Agaricus bisporus*, *Pleurotus* spp. as well as in medicinal mushrooms [36,37].

## 4. Role of nutrigenomics in food selection

The clinical or direct-to-consumer applications of nutrigenomics involve utilizing a genetic predisposition to illness which might be minimized or modified with dietary treatments. Nutrigenomics, the study of the relationships between different types of food and the genome, can be useful in the selection of health-promoting meals [38]. The prospect of nutrigenomics for the food business is to create tasty goods that are scientifically designed. Consumers have come to anticipate sensory delight from foods, including health foods. There are already products in the market that are enhanced with different nutrients and functional foods for disease prevention or treatment. One may foresee beverages and foods being developed as precautionary agents or as treatments for people, families, or subgroups who are susceptible to a certain ailment. There is precedent in the field of pediatrics, where supplements are used to treat individuals with uncontrollable epilepsy [39].

Nutritional science spent the 20th century concentrating on identifying nutrients such as vitamins and minerals, defining their uses, and preventing the diseases brought on by nutrient deficiencies. The focus of contemporary medicine and nutritional science altered when the nutrition-related health issues of the developed world switched to overnutrition, obesity, and type-2 diabetes [40]. Even though there are now only a few workable concepts, nutrigenomics is undoubtedly predicted to be the next big thing in the food sector. One business notion is the development of customised nutraceuticals based on specific genetic profiles. The food industry is aware of the importance of nutrigenomics research as a foundation for the idea of "personalised diets," for locating molecular biomarkers or novel bioactive food ingredients, and for confirming the efficacy of these active substances as functional food ingredients or nutraceuticals [41]. Studying the genome-wide effects of diet is a major goal of nutrigenomics research, with a particular emphasis on the role of metabolic stress in the development of metabolic syndrome, a group of phenotypes that combines inflammation, metabolic stress, insulin resistance, and diabetes. This objective may seem overly ambitious, but it is founded on the notion that food should be supplementary to pharmacological treatment, which focuses on the pathophysiological components of disease, and ought to be primarily focused on maintaining health and preventing disease. This understanding is helpful for treating and preventing chronic illnesses as well as promoting wellness [42]. In terms of health, certain chronic noncommunicable degenerative diseases are on the rise throughout the world. We must concentrate more on nutritional research in order to treat or prevent these illnesses. This field of science is still in its infancy since more research is required to validate the benefits it has brought to human health and illness

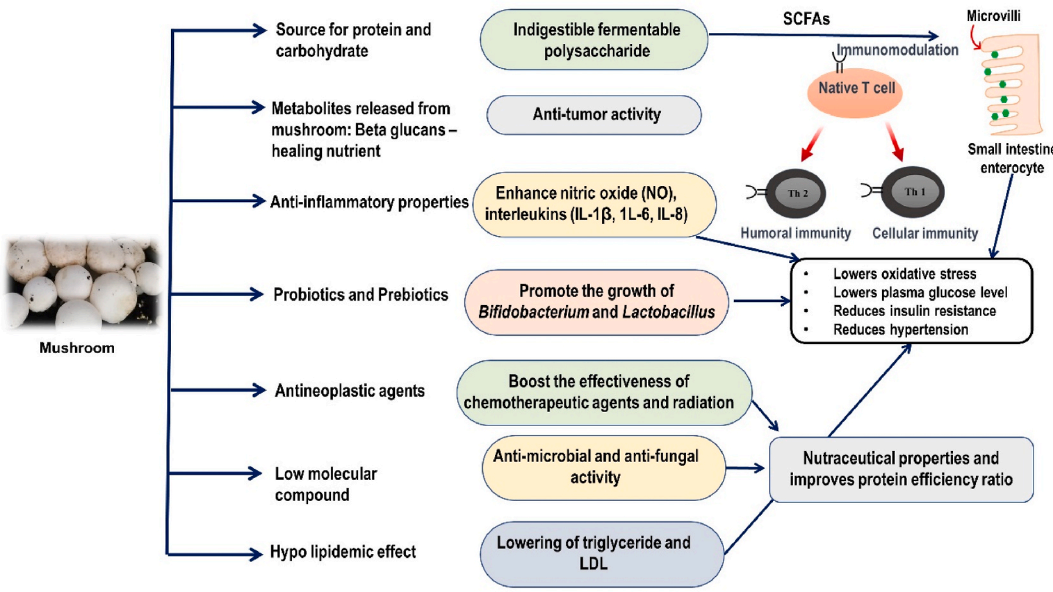


**Fig. 2.** Nutrigenomics - Exploring the Relationship between Edible Mushrooms and Human Health This figure can depict various aspects of nutrigenomics research, such as genetic interactions between edible mushrooms and human genes, molecular pathways influenced by mushroom consumption, and potential health benefits.

prevention.

## 5. Mushroom- a wonder food from the perspective of nutrigenomics

As an edible fungus, mushrooms have long been utilized in China, Japan, and Korea as medicines. Dietary supplements have only recently received attention in other nations as a means of enhancing health and fitness. The impact of mushroom products' -glucans, enzymes, and secondary metabolites on the inflammatory process and the gut microbiota justifies their nutritional significance as indirect probiotics, direct prebiotics, or synbiotics [3,43] (Fig. 2). Several bioactive chemicals found in fungi are recognised to enhance good health and well-being and are utilized as preventatives for a variety of human ailments. Mushrooms are now acknowledged as a source of nutraceuticals useful in nutritional balancing, boosting natural body resistance, boosting human immunity, and reducing disease susceptibility [2].

Over the past several years, information about the bioactive components and nutritional benefits of various mushrooms has grown significantly, and as a result, mushrooms have been identified as a potential functional food with a high concentration of dietary fibres and a lower level of fats, essential amino acids as well as a richness of vitamins and minerals [44]. Besides this, it has been demonstrated that mushrooms have the ability to mitigate the health risks brought on by obesity, hypertension, and hypolipedema, as well as the diminished functions brought by ageing [45]. In accordance with the revealed pharmacological medicinal benefits, which aided in the early intervention, mushrooms were not just being consumed as dietary food but were additionally regarded as a significant and valuable resource for the development of functional food. The development of novel functional foods and health-protecting medications using fruit bodies, mycelia, and extracts from various mushroom preparation techniques has become a popular and fruitful research field. Cereal grains and *Cordyceps militaris* were combined by Zhong et al. (2017) [46] to create a novel extruded product and when compared to the product made from cereal grains, the novel extruded product significantly improved its anti-fatigue property.

In the treatment of neurological degenerative alterations, such as the Alzheimer disorders, functional foods derived from *Hericium erinaceus* (*H. erinaceus*) have been widely used. The expression of neurotrophic factors, including nerve growth factor, was significantly reduced in hericenones made from fruit bodies and erinancines made from *H. erinaceus* mycelium [47]. *Reishi, shiitake, Judas's ear,* and *almond mushrooms* are used as traditional medicines in China and the Philippines as they have anti-aging properties and inhibit tumour cell growth. Culture media supplemented with these mushroom extracts prolong the lifespan of male and female flies (*Drosophila*). This longevity-enhancing effect of edible mushroom extracts on *Drosophila* flies may be attributed to their ability to enhance antioxidant mechanisms by modifying nutrient signalling pathways [48].

## 6. Health benefits of mushroom from the perspective of nutrigenomics

### 6.1. Anti-inflammatory properties

Many chronic diseases associated with ageing usually have inflammation as one of their contributing factors. Due to their abundance in bioactive chemicals, edible mushrooms are becoming more and more popular as functional foods. Numerous studies have documented the anti-inflammatory properties of wild, edible, and medicinal mushrooms, including their crude extracts and bioactive metabolites. Mushrooms have anti-inflammatory potential due to their capacity to decrease the production of inflammatory mediators such nitric oxide (NO), interleukins (IL-1β, 1L-6, IL-8), tumour necrosis factor (TNF-α), and prostaglandin $E_2$ ($PEG_2$) [49,50] (Table 1). The anti-inflammatory activity of mushrooms has been attributed to a number of bioactive substances, including polysaccharides [51], terpenes [49], phenolic compounds [50], sterols [52], fatty acids [53], polysaccharide-protein complexes [54], and other bioactive metabolites [55](Table 1). Mushrooms bioactive compounds with anti-inflammatory effect, making them a natural, safe, and controlled alternative to conventional medicines for the reduction of inflammation [56]. The compounds found in mushrooms, namely colossolactone VIII, colossolactone E colossolactone G, ergosterol, heliantriol F and velutin are potential alternative or complementary medicine for COVID-19 treatment [57] (Table 1) (Fig. 3). Ergosterol (ERG), which is found in many mushrooms and is reported to have anti-inflammatory properties, is reported to alleviate the inflammation caused by diabetic nephropathy in mice by lowering fasting blood glucose levels, inflammatory cytokine levels, and kidney damage. Mechanically, ERG therapy significantly reduced the NF-κB signalling pathway [58]. Moreover, ERG reduces inflammatory, oxidative, and apoptotic stress in Chronic Obstructive Pulmonary Disease through the NF-κB/p65 pathway [59]. Most popular commercial edible mushroom species i.e., shiitake (*Lentinus edodes*), Enoki (*Flammulina velutipes*) and oyster mushroom (*Pleurotus ostreatus*) showed potent anti-inflammatory activity by inhibition of NO and TNF-α production. However, the bioactivity of fresh mushrooms is also noticeably higher than that of cooked mushrooms, demonstrating the heat sensitivity of the anti-inflammatory compounds. Some mushrooms are more likely to deliver higher levels of anti-inflammatory compounds when consumed raw, but doing so carries some health risks [60]. L-ergothionine showed anti-inflammatory properties by inhibit $H_2O_2$ and TNF-α mediated activation of NF-κB [61]. Although, mushrooms have the ability to lower inflammation, it's still not understood how much or how frequently consumption is needed to obtain this benefit [50]. Medicinal mushrooms, specifically *Agaricus blazei* Murill, *H. erinaceus*, and *Grifola frondosa*, have been demonstrated to reduce bacteraemia and prolong survival in mice with *Pneumococcal* sepsis and improved the quality of life in inflammatory bowel disease patients through an anti-inflammatory effect. The severe lung inflammation could be prevented or treated using extracts from these mushrooms [62] (Table 1). Cordycepin, a low-molecular-weight nucleoside substance present in *Cordyceps* species, particularly *C. sinensis* and *C. militaris*, exhibits anti-inflammatory effects *via* inducing the production of IL-10 [63]. The polysaccharide "polysaccharidum" found in *Poria cocos* mushrooms is recognised as a medicine in China for the treatment of hepatitis and cancer [64].

**Table 1**
Health benefits of mushrooms.

| Study | Type | Assays | Pathways | Key conclusions | Reference |
|---|---|---|---|---|---|
| Anti-inflammatory | | | | | |
| To study the anti-inflammatory and heme oxygenase-1 inducing activities of lanostane triterpenes isolated from mushroom *Ganoderma lucidum* | *In vitro* | Cell viability, Western blotting, Immunofluorescence | PI3K/AKT-Nrf2 | The lanostane triterpenes from the medicinal mushroom *G. lucidum* induced HO-1 protein expression which in turn considerably associated with the anti-inflammatory responses of triterpenes in RAW264.7 cells. Additionally, GT-2 induced HO-1 expression at the transcription level *via* the PI3K/AKT-Nrf2 pathway. | (50) |
| To access *in vivo* and *in vitro* anti-inflammatory activity of *Lentinus polychrous* extract | *In vitro*, *in vivo* | Cytotoxicity assay, NO, ROS, TNF-α, Carrageenan-induced rat paw edema assay | iNOS, IL-1β, IL-6, TNF-α, COX-2 | LPME exhibited cytotoxicity $IC_{50}$ of 280.25710.10 μg/ml and significantly suppressed the productions of NO and intracellular $O^{2-}$ in a dose-dependent approach. The extract suppressed iNOS, IL-1β, IL-6, TNF-α and COX-2 expressions and significantly reduced the TNF-α production in LPS-activated macrophage. *In vivo* studies reported a suppressive effect on paw edema in rats. | (129) |
| To evaluate the anti-inflammatory effects of commercially available mushroom species in lipopolysaccharide and interferon-γ activated murine macrophages | *In vitro* | Anti-inflammatory assay | NO | Shiitake ($IC_{50}$-0.047 mg/ml) and Enoki mushrooms ($IC_{50}$-0.099 mg/ml) showed also potent inhibition of TNFα production. | (61) |
| An in-silico approach to evaluate Mushroom-derived bioactive compounds potentially serving as inhibitors of SARS-CoV-2 main protease | *In silico* | | | The study revealed that 25 of 36 candidate compounds have the potential to inhibit the main viral protease based on their binding affinity against the enzyme's active site in comparison to the standard drugs. ADMET analysis and toxicity prediction revealed that 6 out of 25 compounds are the best drug-like property candidates, including colossolactone VIII, E, G, ergosterol, heliantriol F and velutin. | (58) |
| To study renal inflammatory responses of ergosterol in mice model of diabetic nephropathy | *In vivo* | Biochemical assay, Elisa, Western blot | NF-κB | In mice, ERG treatment greatly lowered the fasting blood glucose and inflammatory cytokine levels as well as renal injury, while it increased the insulin level. ERG treatment dramatically decreased NF-κB signaling pathway. | (130) |
| To investigate the effects of ergosterol on anti- inflammatory and anti-oxidative stress in a cigarette smoke extract (CSE)-induced COPD model | *In vitro*, *in vivo* | NO, H&E staining, TUNEL assay, Cell apoptosis assay | NF-κB/p65 | Treatment of 16HBE cells and Balb/c mice with ergosterol inhibited CSE-induced inflammatory, oxidative stress and apoptosis by inhibiting the activation of NF-κB/p65. | (60) |
| To study the anti-inflammatory potential of ethanolic extracts of fourteen edible mushrooms in lipopolysaccharide activated RAW 264.7 macrophages | *In vitro* | NO | Inhibited NO production | The extracts of *Pleurotus ostreatus*, *Macrolepiota procera*, *Boletus impolitus*, *Agaricus bisporus* revealed the strongest anti-inflammatory potential and highest concentration of cinnamic acid (656-156 μg/g), was individual compound with the highest anti-inflammatory activity. The derivatives of p-coumaric acid revealed the strongest properties, especially the derivative methylated in the carboxylic group. | (51) |
| Comparison of wild and domesticated basidiocarps of *A. rugosum* for antioxidant and anti-inflammatory | *In vitro* | NO, Elisa | Inhibited NO production, suppressed TNF-α release | Both WB and DB scavenged NO radicals, suppressed NO production in LPS-stimulated RAW264.7 cells and mediated *via* the down-regulation of inducible nitric oxide synthase (iNOS) | (131) |

(*continued on next page*)

**Table 1** (*continued*)

| Study | Type | Assays | Pathways | Key conclusions | Reference |
|---|---|---|---|---|---|
| effects in LPS-stimulated RAW264.7 cells | | | | gene, down-regulation of the inflammatory gene TNF-α, up-regulation of anti-inflammatory gene IL-10. | |
| Anti-inflammatory effects of extract from *Haliotis discus hannai* fermented with *Cordyceps militaris* mycelia in RAW264.7 macrophages | *In vitro* | NO, Elisa | Inhibited NO production, IL-6 and TNF-α inhibition, TRIF signaling pathway | The extracts of *H. discus hannai* fermented with *C. militaris* mycelia (HFCM-5) showed higher NO inhibitory effects, decreased pro-inflammatory cytokines, TNF-a and IL6 and decreased phosphorylation of IRF3 and STAT1 involved in TRIF-dependent pathway | (132) |
| ***β-Glucan*** | | | | | |
| Anti-inflammatory, anti-angiogenetic and antioxidant activities of polysaccharide-rich extract from fungi *Caripia montagnei* | *In vivo* | Cell viability, Myeloperoxidase (MPO) assay, Chorioallantoic membrane assay | Inhibited NO production, edema inhibition | The animal model, carrageenan-induced pleurisy, revealed that glucan displayed an anti-inflammatory effect. Severe reductions occur in leukocyte migration, modest nitric oxide production. -glucan content from *Caripia montagnei* showed pharmacological activity in inflammation models, angiogenesis, and free radicals' inhibition. | (133) |
| To study the anti-inflammatory properties of the medicinal mushroom *Cordyceps militaris* related to linear (1R3)-b-D-Glucan | *In vivo* | MPO assay | Inhibited IL-1β, TNF-α, COX-2 release | b-(1R3)-D-glucan showed the higher anti-inflammatory effect by the inhibition of IL-1b, TNF-a, and COX-2 expression indicating polymer is the most potent anti-inflammatory compound present in the polysaccharide extracts of *C. militari*. | (134) |
| To study the anti-inflammatory activity of Exopolysaccrides produced by *Pleurotus sajor-caju* | *In vivo* | Paw edema induced by carrageenan, writhing and formalin assays | | The treatment of mice with the purified mannogalactan resulted in reduction of nociception caused by acetic acid and formalin and reduced paw edema induced by carrageenan in mice suggesting *P. sajor-caju* mannogalactan exhibits anti-inflammatory activity. | (52) |
| Polysaccharides from the fungus *Scleroderma nitidum* with anti-inflammatory potential | *In vivo* | Dot-blot assay for NF-kappa B, NO, cell viability | Reduced level of NO, IFN-γ, IL-2, IL-10, suppressed paw edema | Analysis of pro- and anti-inflammatory cytokines showed that polysaccharides treated groups from *S. nitidum* reported an increase in cytokines like IL-1ra, IL-10, and MIP-1β with the decrease in INF-γ, IL-2 *via* modulation of the expression of nuclear factor κB. | (135) |
| Glucans from the edible mushroom *Pleurotus pulmonarius* inhibit colitis-associated colon carcinogenesis in mice | *In vitro*, *in vivo* | Immunoblotting analysis, NF-jB activity assay | Inhibited TNF-α released from cells | *In vitro*, Fruiting body extract (FBE) and mycelia extract (ME) induced apoptosis, modulated the expression of Bcl-2, Bax, and cytochrome *c*, and blocked TNF. *In vivo*, dietary administration of FBE and ME significantly reduced the formation of aberrant crypt foci, which precedes colorectal cancer. The treatments reduced the expression of proliferating cell nuclear antigen and enhanced apoptosis in the colon. | (136) |
| ***Prebiotics*** | | | | | |
| To study the effect of *Ganoderma lucidum* on obesity in mice by modulating the composition of the gut microbiota | *In vivo* | Flow cytometry, Western blot | modulation of lipogenic gene expression | Water extract *Ganoderma* (WEGL) reverses HFD-induced gut dysbiosis which is as indicated by the decreased *Firmicutes*-to-*Bacteroidetes* ratios and endotoxin bearing Proteobacteria levels, maintains intestinal barrier integrity and diminishes metabolic endotoxemia. | (76) |

(*continued on next page*)

**Table 1** (*continued*)

| Study | Type | Assays | Pathways | Key conclusions | Reference |
|---|---|---|---|---|---|
| To evaluate the effects of polysaccharopeptide from *Trametes versicolor* and amoxicillin on the gut microbiome of healthy volunteers. | Clinical | Microbiome analysis | | Polysaccharopeptide from *Trametes versicolor* regulates the gut microbiota to maintain the host health. | (137) |
| To investigate the role of *Lentinula edodes*-derived polysaccharide on mice in terms of immune responses and gut microbiota | *In vivo* | Cytotoxicity assay, Mitogenic and co-mitogenic assay | decreased TNF-α, IL-1α, IL-2; elevated IL-6 | L2 reverses gut microbiota structure, such as a lower ratio of *Firmicutes/ Bacteroidetes*, an increase in *Bacteroidia*, a decrease in *Bacilli* and Betaproteobacteria, an increase in *Bacteroidaceae*, a decrease in *Lactobacillaceae*, and an increase in *Alcaligenaceae*. | (138) |
| Effect of White Button Mushrooms on microbial diversity and resolution of *Citrobacter rodentium* infection in mice | *In vivo* | Metabolomics analysis | | White button mushrooms boost microbial diversity and hasten the clearance of a *Citrobacter rodentium* infection in mice. | (139) |
| ***Mental health*** | | | | | |
| To access the role of *Hericium erinaceus* on mood and sleep disorders in patients affected by overweight or obesity | Clinical | Seventy-seven volunteers (62 females and 15 males), body mass index ≥25 Kg/m2 (age 53.2 ± 0.7 years old) | | *H. erinaceus* treatment improved depression, anxiety, sleep, and binge eating disorders after 8 weeks of supplementation in subjects affected by overweight or obesity under a low-calorie diet regimen. *H. erinaceus* increased circulating pro-BDNF levels without any significant change in BDNF circulating levels. | (140) |
| The effects of *Hericium erinaceus* (Amyloban® 3399) on sleep quality and subjective well-being among female undergraduate students | Clinical | Eight female undergraduate students, (mean age: 21.7 ± 0.4 years) | | The effects of 4 weeks of administration of Amyloban® 3399 resulted in an increase in salivary free-MHPG, corresponded to an improvement in anxiety and quality of sleep. | (141) |
| Mushroom intake and depression: A population-based study (2005–2016) | Clinical | 24,699 participants (mean age: 45.5 (0.3) years) | | Compared with the lowest tertile of mushroom intake, participants in the middle tertile had lower odds of depression however, the highest tertile did not differ. Mushroom consumers had a lower odd of depression without observing any dose-response relationship. | (142) |

### *6.2. Beta glucans – the healing nutrients in mushrooms*

A class of substances known as beta-glucans is thought to be one of the main contributors to mushrooms' immune-stimulating characteristics. These polysaccharides are present in the cell walls of mushrooms and provide antiviral and immunity-booster qualities, support the function of immune cells and feed the gut flora. According to human research, consuming beta glucans shortens the severity of upper respiratory tract illnesses like the flu and the common cold. Although, our bodies do not produce them, beta-glucans have the power to activate both innate and adaptive immune responses (Table 1). White blood cells have receptors that beta-glucans connect to, boosting the body's response to infection [65].

### *6.3. Mushrooms-strong immunomodulators*

Mushrooms have a wide range of impacts, and one of those is their capacity to increase cytokine production. Th1 is the cytokine pattern linked to an effective immune response against cancer. IFN, the predominant Th1 cytokine, is the in charge of triggering the cellular immune response. Th2 cytokines are frequently downregulated by the *Agaricus*, Maitake, Reishi, *Cordyceps*, chaga, oyster, and turkey tail mushrooms, which again shows a benefit in the treatment of cancer. By reducing inflammatory cytokines, mushrooms that reduce inflammation may also have the added advantage of reducing fatigue, anxiety, and other symptoms. Since NK and $CD8^+$ T cells and tumor macrophages eradicate tumour cells, cellular immunity is crucial in an anticancer response. Mushrooms' immune-stimulating actions on NK-cells, macrophages, and T cells may also protect against chemotherapeutic myelosuppression, one of chemotherapy's most harmful side effects [66].

tert-Butyl hydroperoxide is used as model substance for induction of oxidative stress which takes place *via* two pathways; firstly, production of peroxyl and alkoxyl radicals by P450 cytochrome which in turn leads to initiation of lipoperoxidation of membrane phospholipids altering membrane fluidity and permeability. Secondly, lipoperoxidation, depletion of glutathione, and mitochondrial

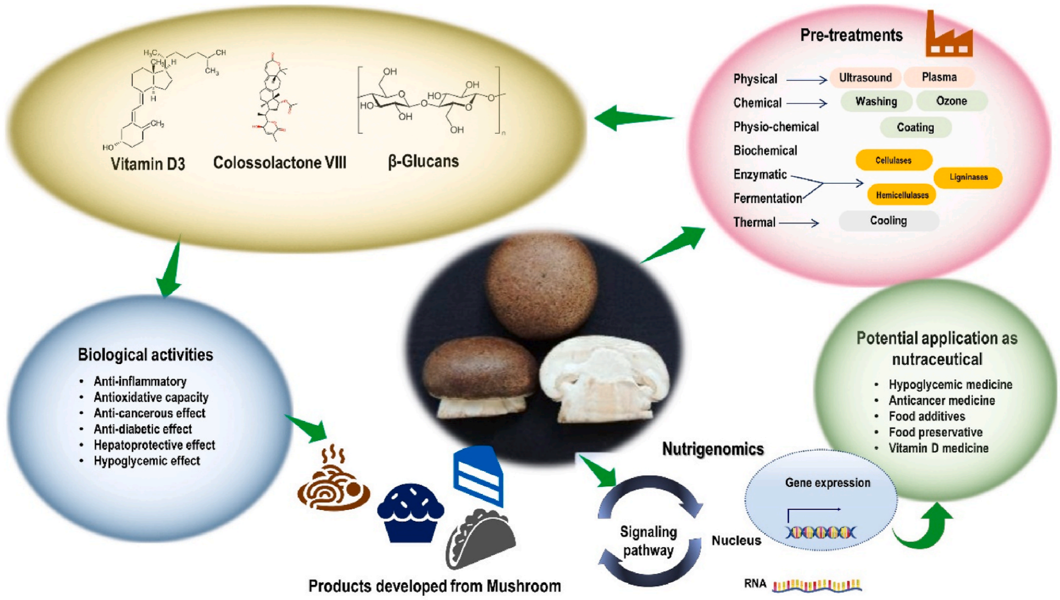


**Fig. 3.** Conceptual model illustrates various processing techniques used to transform edible mushrooms into value-added products, such as drying, canning, fermenting, or extraction, illustrating the diversity of mushroom-based products. Furthermore, edible mushrooms are used in various product formulations, such as functional foods, dietary supplements, and ingredient additions, emphasizing their role in promoting health and wellness.

permeability transition onset result in oxidative stress [67]. Chaga mushrooms have protective effects against the oxidative stress in the liver caused by tert-butyl hydroperoxide and prevent the leakage of liver marker enzymes because of liver damage [68]. According to research by Ref. [69], ergosterol peroxide from *I. obliquus* exhibits anti-cancer activity by inhibiting the β-catenin pathway in colorectal cancer.

### 6.4. Antineoplastic agents with mushrooms

Studies have indicated that medicinal mushrooms can be used in conjunction with antineoplastic medicines to boost the effectiveness of chemotherapeutic agents and radiation, in addition to treating chemotherapeutic myelosuppression [70]. The efficiency of the medication was enhanced when an *Agaricus* extract rich in β-glucan is combined with the chemotherapy medicine doxorubicin [71]. By reducing vascular endothelial growth factor (VEGF) and basic fibro growth factor (bFGF), *Cordyceps* can reduce the blood supply to the cancer cell and increase the ability of cisplatin to exert lethal effects [72]. Ergothioneine was suggested as a potential therapy to lessen the severity of and mortality from coronavirus infectious disease (COVID-19) and cancer [11] (Fig. 3).

### 6.5. Mushrooms for improved gut microbiota

Two primary phyla, *Bacteroidetes* and *Firmicutes*, make up the typical human gut microbiota, which aids in digestion of foods that are indigestible by stomach and intestine enzymes and significantly impacts the immune system by acting as a barrier. Similar to reishi and chaga, *Lentinula edodes*, turkey tail polysaccharide and maitake mushrooms encourage the formation of healthy microorganisms *via* the production of short-chain fatty acids, support the growth of *Lactobacillus* and *Bifidobacterium* strains, and prevent the growth of dysbiotic bacteria. Additionally, maitake mushrooms contain proteoglycans, which have immuno-stimulating effects and enhance the gut barrier and immune system [73].

### 6.6. Mushrooms as prebiotics

Prebiotics are chemicals that stimulate the development or activity of microorganisms that benefit their host. Mushrooms contain various polysaccharides such chitin, hemicellulose, mannans, glucans, galactans, and xylans, thus, are regarded as a potential source of prebiotics [74]. β-glucan polysaccharides present in reishi exhibit prebiotic properties due to its capacity to promote the growth of *Bifidobacterium* and *Lactobacillus* species in the gut [3]. *Ganoderma lucidium* mushroom lowers body weight and insulin resistance, reduces endotoxemia, reverses gut dysbiosis, and alters the intestinal barrier's probity [75] (Table 1). *H. erinaceus* preserves the integrity of the intestinal barrier, boosts the variety and abundance of the gut microbiota, and prevents the growth of *Helicobacter pylori*, a bacteria linked to stomach ulcers [76].

### 6.7. Adaptogenic mushrooms

A substance or food known as an adaptogen aids the body in maintaining or regaining balance during periods of internal or external stress. Adaptogenic potentials are found in various mushrooms, including reishi, chaga, *Cordyceps*, lion's mane, and turkey tail. The hypothalamic-pituitary-adrenal (HPA) axis, a crucial part of the stress response system, is a pathway that reacts to adaptogenic mushrooms [77]. The active ingredients in mushrooms work with the HPA axis to promote memory while regulating stress and mood. Lower brain functionality and psychiatric illnesses have been linked to Nerve Growth Factors (NGFs) abnormalities. Particularly, lion's mane mushrooms and Reishi have important neuroprotective effects on NGFs "hericenones" and "erinacines" and guard against oxidative stress, lowering the incidence of Parkinson's and Alzheimer's diseases [78].

### 6.8. Mushrooms for sound mind

Mushrooms have recently gained attention for their positive effects on both physical and mental health. Mushrooms are used as a supplemental medicine to help with traditional therapies for anxiety, depression, and other mental health issues. Ergothioneine, which protects cells and tissues in the body, including the brain (preventing cognitive decline), is most abundantly found in mushrooms [79]. Reishi mushrooms have been utilized for mental clarity and improves the quality of sleep when taken frequently. Researchers examined the effects of psilocybin, a hallucinogenic substance found in mushrooms, and discovered that depression levels stayed low following the psilocybin therapy [80].

## 7. Technological and sensory properties of potential food products supplemented with mushrooms

Mushroom is a wonderful healthy and nutritious food with biologically active compounds like beta-glucans and has been used in bakery. Fortified mushrooms have the potential to improve nutritional benefits through customer acceptance and profitable predilection for manufacturers [81]. Several researchers have focused quality improvement of the products through fortification with high nutritional values, beneficial health effects, desirable eating properties as well as their cost-effectiveness [82]. As consumer demand for healthy nutrition grows, the creation of novel food products with health-promoting qualities is essential.

### 7.1. Noodles, cheese spreads and soups fortified with mushrooms

Parvin et al. (2020) [82] in their study evaluated sensory and nutritional analysis of noodles fortified with different concentrations of mushroom powder. Sensory analysis has revealed the 5 % fortified concentration was with better taste and improved flavour. Nutritional studies shown that standardized noodles are comprised of protein (14.4 %), fat (1.08 %), energy (366.2 kcal) along with significant mineral content. Overall, mushroom fortified noodles were higher in protein, iron, calcium, fibre and lower in carbohydrate, fats and sodium compared to locally available noodles in Bangladesh depicting beneficial health attributes of mushroom fortified noodles (Table 2).

The effects of addition mushrooms (*Pleurotus ostreatus*) to instant noodles to enhance their nutritional, sensory, and textural qualities were investigated. The optimized product (4 % fortification) was with improved protein (17.3 %), fibre (8.89 %), ash content with good acceptability index. Increase in DPPH inhibition (70 %) was recorded at 2 % mushroom fortification. The product is a nutritive, beneficial and acceptable option for the children and adults with convenience in cooking [83](Table 2).

Spreadable cheese is a good protein, fat and water source and supplemented with mushroom powder to enhance its nutritive characteristics. The fortified cheese spread could be a splendid product with enhanced moisture content with properties of mushroom particularly higher protein and amino acid content with high acceptability index in sensory assessment [84]. Khider et al. (2017) [85] supplemented processed cheese spread with fresh and dried mushrooms (*Pleurotus ostreatus* Hk 35) with good functional, compositional, sensorial and microbiological potentials. The fortified cheese spread was higher in organoleptic properties supplemented with 1 and 1.5 % mushroom powder. Higher moisture, protein, calcium, phosphorus, magnesium and zinc content were recorded in supplemented processed cheese spread. Microbiological investigations suggested lower spore forming bacteria, increase in lipolytic and proteolytic bacteria with enhanced shelf life. The added mushroom enhanced processed cheese's texture, nutrition, flavour and hygiene properties. β-Glucan is a functional molecule that is gaining popularity due to its ability to boost health. Fresh spreadable cheese from ovine milk fortified with β-Glucan (0.4 % w/w) revealed 75.26 % moisture content, 10.30 % fat, 8.50 % protein, and 1.71 % salt without having any profound effect on proteolysis and sensory characteristics of the cheese with high acceptance by the sensory panellists [86]. Süfer & Bozok (2021) [87] formulated gluten-free tarhana soup with edible mushroom, *Lactarius deliciosus* in varying fortification ratios (0–100 %) instead of rice flour. The fortification resulted in enhanced ash, protein, fat, mineral, acidity, phenolics and antioxidant activities of tarhana soup. The sample supplemented with 25 % *L. deliciosus* powder revealed high sensory property with respect to colour, taste, mouthfeel with overall acceptance index. Mushroom lyophilisates can be a good raw material for fortification with good matrix with known biological properties. White bread *Agaricus bisporus* powder supplementation showed higher antioxidant activity, total phenolics and vitamin D2 content with acceptable sensory analysis [88] (Table 2).

Kuppamuthu et al. (2022) [89] fortified soymilk with β-glucans extracted from *Pleurotus ostreatus* and *Agaricus bisporus* to produce value-added beverage with significant health benefits and left over after extraction was utilized as awesome value-addition for food items like mayonnaise. Verma & Singh (2017) [90] fortified potato pudding with oyster mushroom powder and evaluated quality parameters of the product. Nutritional analysis showed that fortified product (5 %) retained high protein, fibre, fat and carbohydrates content and was good in taste as well.

**Table 2**
Studies assessing the impact of mushroom powder addition to food products.

| Study | Matrices | Formulation | Interference | References |
|---|---|---|---|---|
| Effect of fortification of soy milk with β-glucan derived from edible mushrooms | Edible mushrooms (*Pleurotus ostreatus*, *Agaricus bisporus*) | β-glucan: soy milk (1:40) | Soy milk fortified with β-glucan was beneficial to alleviate obesity and related diseases caused by high calorific carbonated beverages. | (90) |
| Effect of Fortification with mushroom β-Glucan on the quality of soft spreadable cheese | *Pleurotus ostreatus* | β-Glucan (0.4 %) | After 21 days of storage, cheese fortified with β-glucan had 75.26 % moisture content, 10.30 % fat, 1.71 % salt, 8.50 % protein. The major free fatty acid was acetic acid and its concentration was higher in cheese with β-glucan. | (87) |
| Study on optimization and standardization of spreadable cheese fortified with mushroom powder | Edible/button mushroom | Mushroom powder (45 g), fortified cheese (260 g) | Moisture, fat, and protein content were higher in fortified cheese. The moisture content of fortified cheese was 58.66 %, protein 29.08 %, fat 32.2 %, ash 3.95 % to that in control cheese 52.36, 29.08 %, 28.8 % and 2.72 %, respectively. | (85) |
| To evaluate the effect on wheat bread supplemented with *Agaricus bisporus* powder | *Agaricus bisporus* | *Agaricus bisporus* (2.5,5 %) | The addition of dried mushrooms significantly increased the content of bioactive compounds (total polyphenols, vitamin D2) and antioxidant properties of bread. A small addition of mushrooms caused a significant change in the basic technological quality of breads. | (89) |
| Gluten-free tarhana fortified with edible mushroom *Lactarius deliciosus* | Edible mushroom *Lactarius deliciosus* | Mushroom powder(0,25,50, 75, and 100 %) | Crude ash, protein, fat, mineral, acidity, total phenolics, antioxidant activities of tarhana samples increased with the fortification of *L. deliciosus* in a dose-dependent manner. Gluten-free tarhana fortified with 25 % *L. deliciosus* powder had the highest sensory scores with respect to colour, taste, and overall acceptability. | (88) |
| Study on fortification with mushroom flour (*Pleurotus ostreatus* (Jacq.) P. Kumm) and cassava four in bread-making | *Pleurotus ostreatus* (Jacq.) P. Kumm | Oyster mushroom flour (2.5–10 %) | The mushroom–cassava–wheat composite, 5–15–80 % and 10–10–80 % had better bakery results, good consistency, high protein and energy contents. The concentration 0–10 % mushroom flour increased bread protein from 19.63 to 22.66 %, calories from 311.8 to 354.5 kcal, dry matter from 77.33 to 87.86 %. The wheat substitution for cassava fortified with mushroom flour negatively affected the bread volume, color and taste. | (94) |
| Evaluation of quality improvement of noodles fortified with mushroom | Oyster mushroom (*Pleurotus ostreatus*) | Mushroom powder (0, 5, 8, 10 %), | Mushroom powder 5 % was better than other mushroom fortified noodles with good taste containing moisture (7.4 %), ash (1.75 %), protein (14.40 %), fat (1.08 %), fibre (0.65 %), carbohydrate (74.72 %) and energy (366.2 kcal). | (83) |
| Fortification of yogurt with β-glucans from oyster mushroom | Oyster mushroom (*Pleurotus ostreatus*) | Submerged biomass of *P. ostreatus*; *Streptococcus thermophilus*, *Lactobacillus delbuckii* subsp. *bulgaricus* cultures | No effect on fermentation process by the addition of preparations; Sensory evaluation revealed that experimental samples differed from the control sample and from each other. | (143) |
| Effect on nutritional and quality characteristics of instant noodles supplemented with oyster mushroom | Oyster mushroom (*Pleurotus ostreatus*) | Mushroom powder (0, 2, 4, 6, 8, 10 %) | Protein content increased with progressing mushroom powder fortification. Significant increase in percent DPPH inhibition (70.11 %) with 2 % mushroom powder addition was observed. Mushroom fortified noodles with enhanced protein (11.32 %) and fibre (1.96 %) content were successfully produced and sensory characteristics at 4 % level of addition of mushroom powder. The optimized product had 17.3 and 8.89 % more protein and fibre compared to control. | (84) |
| Formulation and quality evaluation of mushroom (Oyster mushroom) powder fortified potato pudding | Oyster mushroom | Oyster mushroom (5, 10, 15, 20 %) | Fortified 5 % mushroom powder in potato pudding retained high amount of protein (2.28g), fibre (0.26g), fat (1.36g) and carbohydrate (18.93g) than control sample. | (91) |
| To analyse fortification of pasta with White Button Mushroom | White Button Mushroom | White button mushroom (10–30 %) | The mushroom fortified pasta reported higher antioxidant activity 11.14 % as compared to 5.61 %, phenolics varying from 0.559 to 0.660 % with increased mushroom fortification. The ratio of 80:20 was optimized for development of nutritionally enriched macaroni. | (144) |

(*continued on next page*)

**Table 2** (*continued*)

| Study | Matrices | Formulation | Interference | References |
|---|---|---|---|---|
| Supplementation of composite gluten-free flour with mushroom powder and inulin. | Button mushroom (*Agaricus bisporus*) | Button mushroom (*Agaricus bisporus*): Inulin (86.5:10:3, 83.5:10:6, 80.5:10:9) | Addition of mushroom powder increased ash (1.23–2.34 g/100 g), protein (5.24–11.74 g/100 g), fat (0.15–0.93 g/100 g), energy (345.71–350.77 kcal/100 g), total dietary fibres (3.97–8.61 g/100 g), while moisture and carbohydrate contents declined (12.53–11.13 g/100 g; 80.85 to 73.86 g/100 g). Fortification of inulin reduced moisture (12.53–11.07 g/100 g), ash (1.23–0.11 g/100 g) contents, whereas carbohydrate, energy, and soluble dietary fibers increased. Essential and non-essential amino acids of samples comprising mushroom powder were higher than samples with inulin. | (102) |
| Incorporation of dietary fibre-rich oyster mushroom (*Pleurotus sajor-caju*) powder in biscuits | Oyster mushroom (*Pleurotus sajor-caju*) | *Pleurotus sajor-caju* (PSC) powder 4, 8, 12 % | Elevated incorporation levels of PSC powder increased the dietary fibre (DF) content and reduced the pasting viscosities and starch gelatinisation enthalpy value of biscuits. The addition of DF-rich PSC powder also interfered with the integrity of the starch granules by reducing the sizes and inducing the uneven spherical shapes of the starch granules resulted in reduced starch susceptibility to digestive enzymes. The incorporation of 8 % PSC powder in biscuits (GI = 49) could be an effective way of developing a nutritious and low-GI biscuit with desirable sensorial properties. | (99) |
| To analyse the nutrient composition and sensory properties of biscuit from mushroom-wheat composite flours | *Pleurotus sajur-caju* | Mushroom powder (0, 5, 10, 20, 30 %) | The protein content increased from 13.04 % in the control range of 13.41–15.55 % in the biscuits; crude fibre increased from 2.10 to 2.16–2.93 %, ash content increased from 1.52 %. The protein content increased from 13.04 % in the control to 13.41–15.55 %; crude fibre increased from 2.10 to 2.16–2.93 %; ash content enhanced from 1.52 % to 1.87–3.85 %, crude fat and carbohydrate reduced from 21.71 to 19.05–20.58 % and 61.63 to 58.62–61.58 %, respectively. The result of the mineral analysis revealed that the sodium and potassium were the predominant mineral elements in the biscuit samples and the mineral composition increases with level of mushroom addition. There was no significant difference in the overall acceptability of the control and 5 % mushroom substitution samples. | (101) |
| Improvement of quality attributes of sponge cake using infrared dried button mushroom | Button mushroom | Sponge cake supplemented with button mushroom powder (0, 5, 10, 15 %) | Increasing substitution from 5 % to 15 % button mushroom powder increased the protein and ash. The apparent viscosity in cake batter, volume, springiness, and cohesiveness values of baked cakes uprise with increasing mushroom powder. The density, consistency, hardness, gumminess, chewiness and crumb showed a reverse trend. Sensory evaluation results held that cake with 10 % button mushroom powder was the most acceptable. | (96) |
| Formulation, organoleptic and nutritional evaluation of value-added baked product incorporating oyster mushrooms (*Pleurotus ostearus*) powder | Oyster mushrooms (*Pleurotus ostearus*) | Mushroom powder (0, 5, 10, 15, 20 %) | Mushroom powder at 15 % addition significantly improved colour, flavour and texture and overall acceptability of cake with equal to the control cake. | (145) |
| To study the development and evaluation of value-added biscuits from dehydrated shiitake (*Lentinus edodes*) mushroom | Shiitake mushroom (*Lentinus edodes*) | Mushroom powder (10 g) | Crude protein content in biscuits (10.55 % and 9.61 %) was significantly higher as compared to control (5.74 %). HCl extractability for iron, zinc, phosphorus and calcium (70.53, 72.21, 85.83, 53.69 %) were also significantly higher in treated mushroom biscuits. The developed products could be successfully stored for a period of 30 days. | (100) |
| To study effect on yoghurt fortified with mushroom | *Agaricus bisporus* | *Agaricus bisporus* (0, 5, 10 %) | Yoghurt fortified with mushroom powder (10 %) had higher values of protein, ash, fiber, pH, curd | (146) |

(*continued on next page*)

**Table 2** (*continued*)

| Study | Matrices | Formulation | Interference | References |
|---|---|---|---|---|
| | | | tension, viscosity, amino acids, vitamins (riboflavin, niacin, B12, biotin, B1 and folate), minerals (Mg, K, Fe, Zn, P, Cu, Mn), organoleptic properties and daily nutritional values. | |
| Effect on nutritional and sensory properties of biscuits on wheat flour replacement with mushroom powder and sweet potato flour | Edible mushroom (*Pleurotus plumonarius*) | Mushroom powder (MP), sweet potato flour (SPF) at equal rates (1:1 w: w) | Biscuits supplemented by 10 or 20 % of MP/SPF mixture exhibited a good sensory properties and better acceptability compared to 30 % MP/SPF had less scores for the tested organoleptic properties with less acceptability. Incorporation of MP/SPF into biscuits led to increase the protein, fiber, ash, Fe, Ca, K, P and indispensable amino acids. | (98) |
| The effect of addition of oyster mushroom on nutrient composition and sensory acceptation of wheat- and rice-based products | Dried *Pleurotus sajor-caju* (PSC) powder | Mushroom powder (0, 2, 4, 6 %), rice-porridge (RP), paratha bread (PB), conventional cakes (CC) | Mushroom based RP had significantly higher value of odour attribute, RP added with 6 % PSC powder had the highest score. Mushroom-based PB received better score on textural attribute. In CC, panellists prefer the cake added with 4 % PSC powder with higher scores for softness and flavour attributes. | (92) |
| Utilization of dried mushroom powder for development of mushroom fortified biscuits | *Pleurotus florida* | Mushroom powder (0, 5, 10, 15 %) | Mushroom powder (10 %) with 0.2 % vanilla flavour showed highest scores for organoleptic parameters like colour and appearance, flavour, crispness, taste and overall acceptability even up to 30 days of storage. | (147) |
| Evaluation of quality characteristics of bread made from wheat and Nigerian oyster mushroom (*Pleurotus plumonarius*) powder | Oyster Mushroom (*Pleurotus plumonarius*) | Mushroom powder (0, 5, 15, 20, 25 %) | Supplementation with mushroom powder from 0 to 25 % increased crude protein content 7.96–14.62 %, ash 0.90–2.64 %, crude fiber 0.51–2.48 %. Mushroom powder up to 10 % did not have any detrimental effect on bread sensory properties. | (148) |
| To analyse the quality characteristics of sponge cakes with addition of *Pleurotus eryngii* mushroom powders | *Pleurotus eryngii* | Mushroom powder (3, 5, 7 %) | The specific gravity and viscosity increased with the addition of mushroom powder. The height and specific volume were decreased. Substituting mushroom powder for flour resulted in decreased yellowness and lightness and increased redness of the cake crust. The hardness of cakes containing mushroom powders was higher than that of control. Sensory evaluation comparison of two different drying methods showed that overall acceptability of sponge cakes containing 3 % and 5 % mushroom power were higher than that of control. | (149) |

### *7.2. Bakery products supplemented with mushroom powder*

The addition of mushroom powder in bakery products is a cost-effective way to enhance nutritional value, protein, mineral and fat contents. Additionally, mushroom fortified products find good in scores regarding overall textural and sensory investigations. Aishah & Wan Ishak (2013) [91] formulated paratha bread with dried mushroom powder resulted in increased moisture, protein and ash content of the fortified bread. Replacement of 5 % mushroom mycelia with wheat flour for bread making showed high umami intensity, the presence of significant volume of ergothioneine and amino acids γ-aminobutyric acid with no effect on bread texture [92]. Irakiza et al. (2021) [93] used mushroom four (*Pleurotus ostreatus* (Jacq.) P. Kumm) and cassava flour in bread making in non-wheat growing countries like Democratic Republic of Congo. The authors recommended mushroom–cassava–wheat composite four combination from 5 to 15–80 % and 10–10–80 % for best consistency, high protein content and better bakery outcomes (Table 2).

Supplementation of natural fibres enhances firmness, sensorial characteristics and acceptance of food products. The addition of 4–10 % mushroom powder to bakery items reported best sensory properties. Variation in fibre content affects the firmness and volume of the cakes. Sheikh et al. (2013) [94] reported that 15 % supplementation of mushroom powder is best for quality of the cake with best acceptability. Salehi et al. (2016) [95] found that protein and ash content of cake increased with the increase in mushroom powder content. Rheological properties of cake batter like viscosity, volume, springiness, and cohesiveness values of baked cake increase parallelly with the increase in concentration of mushroom powder however, density, gumminess, and crumb colour indexes (L* and b* values) of cake followed a reverse trend. Following another study by Salehi & Kashaninezhad (2018) [96] evaluated the effect of mushroom powder on viscoelastic property of sponge cake employing stress relaxation test. The results revealed a fall in initial and balance forces with rise in mushroom powder content. The decline in $k_1$ and $k_2$ parameters of Peleg-Normand model depicts decreased elasticity of cake over the time.

Ibrahium & Hegazy (2014) [97] analyzed the partial replacement of wheat flour with mixture of mushroom powder (*Pleurotus plumonarius*) and sweet potato flour (*Ipomoea batatas*) in biscuits. Biscuits processed with 10 or 20 % mushroom and sweet potato flour exhibited better sensory analysis and acceptability. Processed biscuits were higher in protein, fibre, ash iron, calcium, potassium content with increased concentration of indispensable amino acids than the reference protein pattern of FAO/WHO. The authors concluded that 20 % incorporation of mushroom powder and sweet potato flour in wheat biscuits overall enhanced fortified biscuits' nutritional and sensory quality characteristics. The current research is focusing on employing mushroom powder as a source of nutritional fibre in wheat-based food items. Effect of fortification of mushroom powder on biscuits on rheological as well as sensory properties like nutritional values, pasting properties, thermal features, microstructure, *in-vitro* starch digestibility, *in-vivo* glycaemic index were studied. Increased addition of mushroom powder lowered the pasting viscosities and starch gelatinisation enthalpy value of biscuits with noticeable uprise in protein, ash, total dietary fibre and β-glucan content. The inhibition of starch hydrolysis decreased the glycaemic index of biscuits [98]. Singh et al. (2016) [99] used shitake mushroom powder to enhance the overall properties of the biscuits and reported an increase in protein content from 5.74 to 10.55 % *via* incorporation. The nutritional value of biscuits can be improved through fortification with mushroom powder as biscuits are low in protein content and high in calorie, carbohydrates and fats. Bello et al. (2017) [100] reported that biscuits containing mushroom powder were higher in protein content from 13 (control) to 13.4–15.5 %, ash content from 1.5 (control) to 1.9–3.8 %, and fibre content from 2.1 (control) to 2.2–2.9 %. Incorporating mushroom powder increased mineral concentration, i.e., calcium, potassium, magnesium, phosphorus, iron, and zinc. Sulieman et al. (2019) [101] studied the effect of addition of fermented and unfermented mushroom polysaccharide flour on rheological and sensory characteristics of gluten-free dough and biscuits. The authors concluded that fermented and unfermented mushroom polysaccharide flour containing biscuits were high in protein, dietary fibres, minerals and amino acids.

## 8. Mushroom as a source of functional compounds: exploring the pathway of vitamin D in mushroom

Vitamin D, a fat-soluble secosteroid, popularly referred to as "sunshine vitamin," plays a significant role in various physiological and metabolic functions such as skeletal homeostasis, neuromuscular activities in human body, aids in synthesis of calcium transport proteins, decreasing the risk of rickets and osteomalacia in children and adults, respectively. Adequate amount of vitamin D efficiently protects human beings from many diseases like cancer, cardiovascular diseases, diabetes, respiratory and neurodegenerative diseases in humans [102]. Recent reports have also highlighted the pivotal role of vitamin D and some bioactive compounds in mushrooms, which act as a potential nutraceutical against the deadly virus causing COVID-19 [103].

The major dietary forms of vitamin D are vitamin $D_2$ (Ergocalciferol), $D_3$ (Cholecalciferol) and $D_4$. Vitamin $D_2$ is found in fungi, yeast and plants, while vitamin $D_3$ is animal derived. Fungi have very little vitamin $D_3$ and $D_4$ content [104]. Due to the enrichment of wide nutrients and the unique delicious taste of mushrooms, they are directly included in the human diet to enhance the health benefits and reduce the risk of various diseases [105]. Upon exposure to sun and ultraviolet (UV) radiation, the content of dietary vitamin D, specifically vitamin $D_2$ increases appreciably which further protects cartilage and bone health, act as an immunostimulant and immunomodulator [103]. Mushrooms fortified with vitamin D are non-animal derived, naturally obtained from food products packed with substantial amounts of other nutrients and bioactive compounds, which are potential primary sources for vegans and vegetarians [106].

### 8.1. Polysaccharides and beta-glucans

Bioactive polysaccharides are mostly found from a diverse range of edible medicinal mushrooms such as *Schizophyllum commune, Lentinus edodes, Grifola frondose* etc, having anticancer and immunoregulatory activity [107]. Similarly, β-glucans, the most popular and versatile metabolite are best known for its various biological activities [105]. Polysaccharides and glucans are extensively present as a major component in mushrooms, having prebiotic, immunomodulator and antitumoral effects [108]. Glucans, present in fruiting bodies of mushroom are lineal polysaccharides and linked with glucose by β(1–3) in main structure, β(1–6) as branching linkage or α(1–3) linkage [109]. Non-starch polysaccharides and glucans are mainly present in the stem and pilei region of mushroom. Hence, the mushroom stem can be used to develop and produce food supplements enriched with bioactive polysaccharides, glucans and insoluble dietary fiber. The mushroom family *Basidiomycete* and *Ascomycete* consist of Chitin-β-glucans and Chitin-mannan-β-glucans, respectively [110].

### 8.2. Ergosterols and other compounds

Mushroom sterols are constituted with a triple cyclohexane core coupled with cyclopentane and an aliphatic extension. Although cultivated mushrooms lack vitamin D throughout the growth stage due to the absence of sunlight but, they are high in ergosterol, a vitamin $D_2$ precursor that is transformed into vitamin $D_2$ on exposure to ultraviolet light and heat. Through a sequence of photochemical and thermal processes, ultraviolet light from the sun or artificial light catalyzes this conversion process, similar to human skin's production of vitamin $D_3$ on exposure to UV light. However, the function of ergosterol completely depends upon the fungal hyphae formation, growth and sporulation [111]. Fresh mushrooms have limited shelf-life owing to high water activity and generally, different post-harvest drying methods are employed which enhance vitamin D content in mushrooms. Moreover, vitamin D in mushrooms can be fortified by employing various appropriate drying approaches like sun drying, hot air drying, and so on. Dried mushrooms are rich in more intense flavor and found application as a precious ingredient in a variety of recipes. Additionally, lower amounts of sterols like methylene cholesterol, ergosta-7,22-dienol, ergosta-5,7-dienol and ergosta-7-enol are also reported in the fresh mushrooms [19].

### 8.3. How do these compounds work in the human body?

All edible mushrooms are known to be a potential source of vitamin $D_4$ [112]. Exposure of mushroom to sunlight or UV radiation directly transforms the ergosterol to pro-vitamin $D_2$ and then again converted to ergocalciferol or vitamin $D_2$ through a temperature-dependent manner. Similarly, pro-vitamin $D_4$ is converted to vitamin $D_4$ in a similar process. In a report it was shown that the high concentration of ergosterol was reported to be present in gills. When the oyster mushroom is exposed to UV, more than double amount of vitamin $D_2$ is produced as compared to shiitake mushroom [113].

## 9. The importance of mushroom diversity for vitamin $D_2$ and ergosterol contents

### 9.1. Different species of mushrooms have different health benefits

The Phylum Basidiomycota includes approximately 30,000 species of fungi, including puffballs, mushrooms, bracket and club fungi. Under this phylum, the class *Hymenomycetes* has different orders, but the orders *Agaricales*, *Auriculariales*, *Gasteromycetes* and *Aphyllophorales* include the mushrooms having medicinal importance [102].

There is a diversity of edible mushrooms, including *Agaricus* spp. (Button mushrooms), *Phalloides* spp. (Stink horns), *Lycoperdon* spp. (Puff Balls) and other beneficial mushrooms which have nutraceutical effects. Several biotechnological innovations such as strain improvement, mass cultivation, standardized protocol for spawn production, modification of growth conditions etc. are quite beneficial to improving the nutraceutical properties of mushrooms or the development of bio-fortified mushrooms [114].

The content of vitamin $D_2$ varies from species to species. The wild edible Finnish mushrooms, the funnel chanterelle (Cantharellus tubaeformis (Bulliard), collected in late summer and early autumn contained 3–30 μg $D_2$/100 g fresh weight (FW) vitamin $D_2$, as compared to less than 1 μg $D_2$/100 g FW in the button mushroom. The higher amounts of vitamin $D_2$ have been found in wild funnel chanterelles (21.1 μg $D_2$/100 g FW), Cantharellus cibarius (10.7 μg $D_2$/100 g FW), Boletus edulis (58.7 μg $D_2$/100 g FW) and 1.5 μg/100 g FW in wild Agaricus species (103). Exposure of fresh mushrooms to sunlight resulted in an increase in vitamin $D_2$ content to 10 μg/100 g FW (105). Different drying approaches have been employed to enhance the shelf-life and vitamin D2 content. The sun-dried mushrooms sold in China of 35 species contained appreciable amounts of average of 16.9 μg/g DM vitamin $D_2$ content [115]. Hot dried shitake mushroom comprised of 25 μg/g DM vitamin $D_2$ content [112].

### 9.2. How the choice of mushroom can impact the outcomes of nutrigenomics?

The diversity of mushroom species is regarded as a potential yet unexploited treasure which protects humans from a wide range of diseases and the complicacy of consuming unhealthy diet. Due to their functional and prebiotic activities, it is popularly referred as next-generation food and a promising therapeutic and nutraceutical agent [4]. Adding mushroom species such as *Agaricus, Cordyceps, Coriolus* and *Pleurotus* can reduce inflammation in the human body. The bioactive compounds of mushrooms directly target the major transcription factor and regulate the expression of cytokines, adhesion molecules and chemokines by suppressing NF-κB signaling pathway. Similarly, the presence of Biological Response Modifiers, (1,3)-beta glucan activate the cytokines production to enhance the immune system. Mushrooms are a rich source of ergothioneine, a distinctive antioxidant which humans cannot produce. This compound could act against inflammation, various diseases and increase RBCs in blood [4]. Chitin in mushroom is decomposed into glucosamine, reducing the risk of joint inflammation, kidney disease, and cardiovascular and neurodegenerative disease [116].

## 10. Mushroom in the pharmaceutical industry and cancer treatment

Devising anticancer treatments by exploiting unique metabolites from nature is gaining popularity, and in this, mushrooms play a key role *via* production of anticancer components. Research on mushrooms for anticancer compounds is flexible, feasible, and cost-effective, offering promising approaches for developing new drugs in clinical oncology. The scientific and medical research of 3 decades by China, Japan, Korea and USA have confirmed the properties of remarkable unique metabolites from mushrooms capable of preventing and treating several serious cancers [117]. Due to tremendous traits, mushrooms are a booming boon to the pharma industry, possessing various active metabolites which give remarkable outcomes.

### 10.1. Anticancer mechanism of medicinal mushrooms

#### 10.1.1. Overcoming Pgp-mediated multi drug resistance using mushrooms

The major obstacle in chemotherapy is drug resistance. The immune system or acquired drug resistance leads to the development of resistance in tumor cells to drugs and is regarded as multi drug resistance. The overexpression of ATP-biding cassette transporters, efflux pumps and P-glycoprotein (Pgp) are major forms that leads to multi drug resistance encoded by MDR1 gene. *Ganoderma* species promoted apoptosis in drug-sensitive and multidrug-resistant human small-cell lung cancer cells that were resistant to etoposide and doxorubicin. Zhankuic acids isolated from Taiwanofungus camphoratus showed inhibitory effects against Pgp and reversed the drug resistance against doxorubicin, vincritine, and paclitaxel in human cancer cells [118]. Cantharellus cibarius and Russula emetica enhanced the cytotoxic activity of TAX *via* blockage of Pgp-mediated drug efflux in Pgp-positive HCT15 and MES-SA/dX5 cancer cells [119].

#### 10.1.2. Suppression of Wnt/β-catenin pathway in cancer using mushrooms

Several groups of mushrooms were found to be effective in anti-oncogenic activities by holding Wnt–CTNNB1 signalling. The antroquinonol and 4-acetylantroquinonol by *Antrodia camphorate* had an inhibitory effect on colon cancer by suppressing Wnt/β-catenin pathway by uplifting in arresting of G0/G1 phase and induce apoptosis *via* reducing catenin signalling [120]. Tumor growths, invasions and angiogenesis are found to be inhibited by *Phellinus linteus* down-regulating the genes (cyclin $D_1$ and TCF/LEF) of the Wnt signalling pathway in human colon cancer *in vivo* [121].

#### 10.1.3. Target on PI3K/AKT signalling pathway in cancer by using mushrooms

Various mushroom-derived compounds exhibit antitumour and antimetastatic effects *via* blocking molecules in PI3K/AKT signalling pathway. Ganoderic acid from Ganoderma lucidum inhibited human glioblastoma through the inactivation of PI3K/AKT pathway resulted in induction of apoptosis and autophagy [122]. Another compound, hispolon derived from Phellinus linteus blocked the invasion and motility of metastatic liver cancer cell line by downregulation of MMP-2,-9, uPa, and suppressed the ERK1/2, PI3K/AKT, and FAK pathways activation [123]. Proteoglycan from Phellinus linteus reported antiproliferative activity in multiple human cancer cells by significantly decreasing AKT, Reg IV, EGFR, and plasma PGE2 levels [116].

#### 10.1.4. Target on NF-kB pathway in cancer using mushrooms

The antitumour properties of mushroom-derived compounds has highlighted by targeting NF-kB pathway. Antroquinonol and 4-acetylantroquinonol B from *Antrodia camphorate* depicted inhibition NF-B signaling in MCF-7 breast cancer cells [124]. According to research by Kadomatsu et al., cordycepin, a key component of *Cordyceps militaris*, made cells more susceptible to TNF-mediated apoptosis, which inhibits pro-survival NF-κB. *Ganoderma* prevented constitutively active AP-1 and NF-B signalling from promoting metastasis in highly invasive breast and prostate cancer cells [125]. Phellinus linteus produced caffeic acid phenethyl ester, which specifically blocked NF-κB binding to DNA [126].

## 11. Conclusion

The current trends of the world's projected data pertaining to nutrition indicated that most countries are considerably facing the challenge of undernutrition which may turn into over nutrition as the growth of the world population is at a prodigious rate. The land is being degraded by human activities such as mining, urbanization, and industrialization, which is indirectly imposing adverse effects to human health. Based on all these contexts, this review, "Mushroom a wonder food: A perspective from the point of nutrigenomics," projected a pathway that can improve the lifestyle of nutrition and health. Mushrooms may evolve as an impeccable source of daily needs. Convincing evidences of genetic variations, nutrient interactions and health implications are not certain. Focusing on mushroom nutrigenomics makes sense to enhance one's health.

Mushrooms are an exemplary source of functional foods, rich source of essential vitamins, minerals, they harbor less calories and fat content. Convincing evidence elucidated that mushrooms act as antioxidant, antifungal, antibacterial, antiviral, anti-inflammatory, immuno-stimulative, antihypertensive, hepatoprotective, antidiabetic, and anti-allergic properties. To aggravate the specificity of each trait of mushrooms, keen studies on various speculative factors, bioactive compounds and other factors should be immensely carried out on diverse group of mushrooms. Novel toxicological studies need to be advanced to evaluate mushrooms that positively impact tumor cells. Indeed, new efforts should be devised to identify various bioactive compounds of mushrooms to ensure the safety and promotion of pre-clinical and clinical studies. The active metabolic component of mushroom study can be greatly enhanced by genomics, proteomics, and metabolomics.

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## CRediT authorship contribution statement

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## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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