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Bioavailability and Health Benefits of Vitamin D in Mushrooms: A Review

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Abstract

Vitamin D deficiency has been widely reported across the world and linked to several chronic diseases especially among elderly people. Mushrooms are considered to be valuable nutritional foods with recognized bioactive properties when exposed to ultra violet (UV) irradiation they can generate significant amounts of the vitamin D precursor, provitamin D_2 with lesser amounts of vitamin D_3 and vitamin D_4 which is more common in animal foods. The worldwide mushroom industry has shown a spectacular expansion in the last few decades, and mushrooms are the only non-animal, unfortified food source of vitamin D which can provide a substantial amount of vitamin D_2. In general, vitamin D deficiency is mostly due to reduced UV exposure especially during winter months it has an impact on bone and muscle health, cancer disease, cardiovascular diseases, liver function, atopic dermatitis, obesity, depression, and diabetes. Cultivated mushrooms contain certain beneficial chemical components and along with their biological effects, these components can show significant anti-carcinogenic, anti-diabetic, anti-microbial, antioxidant and anti-depression effects and, they help in maintaining healthy bones and muscles. This review examines the current information on bioavailability and clinical studies evidencing the health benefits of consuming mushrooms rich in vitamin D_2.

Keywords

Vitamin D; Mushroom; UV irradiation; Vitamin D deficiency; Bioavailability; Health benefits

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INTRODUCTION

Vitamin D, also popularly known as ˝sunshine vitamin˝ that boosts the immune system and plays an important role in several human metabolic processes such as phosphorus and calcium metabolism, and neuromuscular and skeletal homeostasis (1). During summer, the human body can synthesize their own vitamin D when exposed to sunlight and store it for winter. This naturally intelligent process of the body is important as vitamin D is essential for bone health and immune system functions and low levels of it can cause osteoporosis and osteomalacia. The mushrooms are the only non-animal food that can make vitamin D precursor, vitamin D_2 with substantial amounts of bioavailability (2) and, as such, have the potential to be a primary source of dietary vitamin D for vegans and vegetarians and their levels can be naturally multiplied by exposing them to sunlight and can be significantly increased by exposing them to UV light. The UV irradiated mushrooms of *Agaricus, Pleurotus* species and *Lentinula edodes* have shown to produce

a significant amount of vitamin D content (3) and its content in different mushrooms varies significantly from mushroom to mushroom as well as from tissue to tissue. The two major physiological forms of active vitamin D for humans are ergocalciferol (D_2) and cholecalciferol (D_3). The current recommended Adequate Intake (AI) for Vitamin D for most adults is 5 µg (200 IU). Fortification of foods with vitamin D_2 or vitamin D_3 has been shown to be a safe and effective way to increase 25-hydroxyvitamin D levels in children and adults (4). The deficiency of vitamin D can be a serious medical pre-condition and in extreme cases, it can cause diseases such as rickets. Therefore, the present review will address topics such as bioavailability and health benefits of vitamin D and the identified health problems related to its deficiency.

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SYMPTOMS OF VITAMIN D DEFICIENCY:

The major symptoms of Vitamin D deficiencies are osteomalacia and rickets due to poor calcium and phosphorous mineralization. Other diseases also reported to be associated with lack of vitamin D such as rheumatoid arthritis, multiple sclerosis, cardiovascular disease, cancer, hypertension, stroke, diabetes, mental illness, chronic pain, inflammatory bowel disease, periodontal disease, muscular degeneration and liver diseases (5).

It was reported that the vitamin D insufficiency in patients with Parkinson's disease (PD). However, further studies are required on Vitamin D receptor (VDR) and its interaction with Vitamin D levels (6). Several signs and symptoms of bone disease, namely, muscle weakness, growth retardation, skeletal deformities, bowed legs and stunted growth have been associated with vitamin D a deficiency, (7). Studies have reported that deficiency of vitamin D is involved in Atopic dermatitis (AD) development which is a chronic inflammatory disorder characterized mainly by itchy and dry skin (8). Epidemiological studies have pointed out the chance of low vitamin D levels in obese individuals due to their low appetence to participate in outdoor activities (9).

It was observed that an inadequate supply of vitamin D has a variety of skeletal and non-skeletal effects. There is ample evidence that various non-communicable diseases (hypertension, diabetes, CVD, metabolic syndrome) are associated with low vitamin D plasma levels. These comorbidities, together with the often-concomitant vitamin D deficiency, increase the risk of severe COVID-19 events. Much more attention should be paid to the importance of vitamin D status in the development and course of the disease (10).

BIOAVAILABILITY OF VITAMIN D FROM UV IRRADIATED MUSHROOMS:

Bioavailability is defined as 'that fraction of an oral dose from a particular preparation that reaches the systemic circulation (11). The concentration of 25(OH)D in serum is the barometer of vitamin D status (12), and therefore this measurement can be used in bioavailability studies of vitamin D. Therefore, the measurement of vitamin D in serum is the barometer which can be used in bioavailability studies. Irradiated mushrooms contain high concentrations of vitamin D_2, which is bioavailable and relatively stable during storage and cooking. One of the earliest studies in the 1990s to determine the bioavailability of vitamin D_2 from wild chanterelles showed increased serum 25(OH)D concentrations (13). Since then, the bioavailability of vitamin D_2 from

mushrooms has been demonstrated in both rats and humans.

The increase in serum 25(OH)D in individuals consumed UV light treated edible mushrooms has been reported (14). Human studies were conducted on 30 years old man by administering stir-fried UVB irradiated mushrooms in order to evaluate its potential to increase serum 25(OH)D levels. The increased 25(OH)D level up to 129 % and an increase in calcium levels were observed in the blood samples (15). Vitamin D_2 from UVB irradiated *Agaricus bisporus* of dried mushrooms was fed on female rats, and after 15 weeks they had significant amounts of vitamin D level in its serum and plasma levels of inflammatory mediators were greatly reduced which can suppress the incidence of inflammation. Control was fed with a vitamin D deficient diet (16). Studies on the effect of vitamin D on bone density were conducted by Chen *et al.,* 2015 (17). The mice fed with UV irradiated mushrooms showed an increase in bone density when compared with the control mice fed with non-irradiated mushrooms. Further, studies showed that increased vitamin D levels can stimulate calcium and phosphorus absorption necessary for bone mineralization and femur density (18).

It was reported that vitamin D_2 from UV-irradiated mushrooms is well absorbed and metabolized in the model animal system and the presence of vitamin D_2 can significantly increase the femur bone mineralization (19). A study by on the bioavailability of vitamin D_2 in mushrooms revealed that ingestion of vitamin D_2 in mushrooms was as effective as ingesting vitamin D_2 or vitamin D_3 in a supplement in raising and maintaining 25(OH)D in the serum which is a marker of a person's vitamin D status (20). The potential of UVC fortified *A. bisporus* was evaluated to maintain vitamin D level by exploiting it's in-vivo potential to prevent memory impairment and the incidence of neurological disorders (21).

Natri *et al.,* found that vitamin D_3 fortified bread effectively increased total serum 25(OH)D levels in women (22). Studies were conducted on forty-three prediabetic, D-deficient adults. They were randomized to four groups consuming daily entrees containing 100 g fresh sliced cooked mushrooms for 16 weeks. Two groups were fed UVB-treated mushrooms and two control groups were fed untreated mushrooms (23).

Bioavailability and bone loss inhibitory effects of vitamin D_2 derived from UV-irradiated shiitake mushrooms were determined *in vivo*. The bioavailability of vitamin D_2 and bone structure was investigated to analyze the effect of absences of ovaries. The increased bone mineral density and trabecular bone structure of femur bone, as well as its bioavailability, found increased by the vitamin D_2 from shiitake mushroom. Also, vitamin D_2-fortified shiitake mushroom might help postmenopausal women increase vitamin D_2 bioavailability and retard trabecular bone loss (24).

Himanshi Rathore *et al*., (2020) found that when *Calocybe indica* mushroom was exposed under natural and artificial UVB light to enhance vitamin D_2 contents in the fruit bodies. The rate of conversion of ergosterol into vitamin D_2 at different time intervals (0, 15, 45, 60 and 90 min), it was found that the conversion was linear with time. The estimated antioxidant activities, viz., free radical DPPH scavenging activity and ferric reducing antioxidant power was also found to significantly ($p < 0.05$) increase after 60 min of UVB exposure (25).

VITAMIN D AND ITS HEALTH BENEFITS:

Vitamin D deficiency is seen more among elderly people, and over 50 % of them are lacking from vitamin D (26). In general, the people living at higher latitudes experience low 25(OH)D serum concentrations due to reduced UV exposure especially during winter months and this has an impact on bone and muscle health, cancer disease, cardiovascular diseases, liver function, atopic dermatitis, obesity, depression, and diabetes (27). The mushroom *A. bisporus* became the first UV irradiated mushroom species to be approved as a source of vitamin D (1). Petre Cristian Ilie *et al*., (2020) found significant crude relationships between vitamin D levels and the number COVID-19 cases and especially the mortality caused by this infection. The most vulnerable group of population for COVID-19, the aging population, is also the one that has the most deficit Vitamin D levels. Vitamin D has already been shown to protect against acute respiratory infections and it was shown to be safe (28).

Cultivated mushrooms contain a plant sterol called ergosterol, which is the precursor of Vitamin D_2. The White/Brown mushrooms showed the increased level of Vitamin D_2 by exposure to ultraviolet light for a few minutes, either pre-harvest or post-harvest. The possible health benefits of eating mushrooms packed with vitamin D_2 has been reviewed here.

Bone health:

Vitamin D has the potential to provide adequate levels of calcium and phosphate which prevents the fracture upon fall (29). Studies showed that increased vitamin D levels can stimulate calcium and phosphorus absorption necessary for bone mineralization and femur density (18). A recent report vitamin D_2 from shiitake mushroom showed increased bone mineral density and trabecular bone

structure of femur bone and retard trabecular bone loss (24). Amrein *et al*., found that the Vitamin D deficiency (serum 25-hydroxyvitamin D [25(OH)D] < 50 nmol/L or 20 ng/ml) is associated with unfavorable skeletal outcomes, including fractures and bone loss. A 25(OH)D level of >50 nmol/L or 20 ng/ml is, therefore, the primary treatment goal, although some data suggest a benefit for a higher threshold. Severe vitamin D deficiency with a 25(OH)D concentration below <30 nmol/L (or 12 ng/ml) dramatically increases the risk of excess mortality, infections, and many other diseases, and should be avoided whenever possible. The data on a benefit for mortality and prevention of infections, at least in severely deficient individuals, appear convincing. Vitamin D is clearly not a panacea and is most likely efficient only in deficiency (30).

Antidiabetic substances and effects:

The fruiting bodies of white button mushroom (*A. bisporus*) showed a significant anti-glycaemic effect when ingested by diabetic rats (31). *Pleurotus ostreatus* extracts, polysaccharides of Ganoderma and polymer produced by submerged mycelial culture of shiitake reduced blood glucose level in hyperglycaemic rats (32). Some clinical studies conducted in individuals with pre-diabetes showed that a vitamin D fortified diet improves and prevents the development of diabetes (29).

Anticarcinogenic substances and effects:

The mortality of cancer appeared being significantly reduced among the population working in an agricultural sector characterized by constant exposure to sunlight which can boost the immune system against some cancer forms (33). The cancer therapy applied in the summer season has shown better results when compared to the winter, a fact mainly attributed to the decreased levels of vitamin D in winter seasonal issues (34). Some specific kinases can be activated by vitamin D which are involved in showing antitumor properties by keeping the cell cycle in the G1/S phase and avoiding the growth of malignant cells (35). Kao *et al*. (2013) reported that *Ganoderma lucidum* sensulato fruiting bodies possess anticarcinogenic substances like triterpenes and some glucan molecules and some clinical studies suggest that these compounds can be used as an adjunct therapy for improvement of the immune system of cancer patients (36, 37). Possible therapy for colon carcinogenesis was reported by Stajic *et al.* (2009) (38) by feeding mice with *Pleurotus ostreatus* powder and suppression of the enzyme activities were demonstrated in mice.

Antioxidant substances and effects:

The antioxidant capacity of mushrooms can be characterized approximately by the contents of phenolics or there are different methods for estimation of the actual "capacity" of this system. The total phenolic content of certain cultivated mushrooms was reported to show the antioxidant properties in different ways. The antioxidant property of *Coprinus comatus, Agaricus subrufescens, Pleurotus eryngii* and *Lentinula edodes* is provided by their naturally occurring components as ascorbic acid, total tocopherol content and total phenolics (39).

Suppression of cardiovascular diseases:

Vitamin D plays a major role in suppressing the severity of cardiovascular diseases by reducing the expression of genes responsible for renin production, thus reducing the blood pressure (Papandreou and Hamid, 2015) and by suppressing Rheumatic Heart Disease (RHD) (40) and by activating several cell signal transduction pathways responsible for cell survival and migration, endothelial cell proliferation and vascular permeability (41,42). Some studies showed that vitamin D supplementation can reduce serum total cholesterol levels, thereby contributing to a better cardiovascular function.

Antimicrobial substances and effects:

Studies have reported that the reduction of Atopic dermatitis (AD) severity has also been linked to the potential of vitamin D to induce expression of antimicrobial peptides, which can prevent skin infections (8,43). The *in vitro* studies on the alcohol extract of white button mushrooms showed strong inhibition on the growth of some Gram-positive bacteria (44). The laccase enzyme isolated and purified from the fruiting bodies of *P. ostreatus* have shown certain antiviral effects by inhibiting the entry and replication hepatitis C virus and the laccase from *P. cornucopiae* can decrease the activity of HIV-1 reverse transcriptase (45). William B. Grant (2020) analyzed the roles of vitamin D in reducing the risk of respiratory tract infections, such as the epidemiology of influenza and COVID-19, and the role of vitamin D supplementation might be a useful measure to reduce risk (46). Through several mechanisms, vitamin D can reduce the risk of infections. Those mechanisms include inducing cathelicidins and defensins that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines that produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increasing concentrations of anti-inflammatory cytokines.

Antidepression effects:

Some studies have shown that daily intake of vitamin D supplemented food shows antidepressant effects and responsible for addressing mood disorders and furthermore clinical studies are required to better

understand the physiological function of vitamin D in the brain (47).

Liver protection:

The polysaccharide components obtained during canned mushroom production have been fed to a mouse model of CCl_4-induced hepatic injury and these compounds were shown to reduce and aspartate aminotransferase and alanine aminotransferase concentrations in the serum and reduce hepatocellular degeneration (48). Lee *et al*. (2012) also examined stalk residue of the edible portion of *P. eryngii*, and showed that it contains abundant crude soluble polysaccharide and β-glucan and the inclusion this stalk residue in the diet significantly elevates the antioxidative enzyme activity levels in the serum, liver, and spleen of broiler chickens when compared to those of the control group (49).

CONCLUDING REMARKS AND FUTURE PERSPECTIVES

The consumption of D_2 enriched irradiated mushrooms is maybe an exclusive case since they are the only non-animal, unfortified food source of vitamin D which has got potential health benefits. Most research studies have shown a substantial amount of vitamin D content in UV irradiated mushrooms and their efficacy to increase serum 25(OH)D levels. This report shows that irradiated mushrooms are an alternative source of vitamin D_2, whose large-scale production is commercially viable at a low cost. The dynamic increase of the cultivation of certain mushrooms is interpretable by the existence of medicinal compounds. The vitamin D_2 enhancement of mushrooms boosts their nutraceutical value, with anti-carcinogenic, anti-diabetic, anti-microbial and antioxidant and anti-depression effects and of these mushrooms have outstanding importance and also can strengthen different components of the immune system, bones, and muscles. The bioavailability of vitamin D_2 was determined *in vivo* and the reports showed raised 25(OH)D in the serum which is a marker of a person's vitamin D status and has been demonstrated in both rats and humans. Further studies still need to be conducted to optimize the recovery of vitamin D_2 from an irradiated mushroom with minimal cost and high purity and to find solutions for making such vitamin D_2-enhanced mushrooms commercially available in a safe and affordable manner. Certain cultivated mushrooms have anti-diabetic effects, which can improve glucose metabolism mainly for patients of diabetes type 2. Extracts of many cultivated mushrooms have antimicrobial effects against Gram-negative and Gram-positive bacteria and certain viruses (HIV-1, hepatitis C, vesicular stomatitis virus, encephalitis virus).

Conflict of Interest:

Conflict of interest declared none.

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