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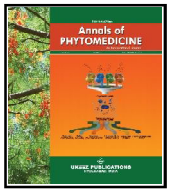

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Role of vitamin D beyond bone health: A systematic review

Yogesh and Sonika Sharma◆

Department of Food and Nutrition, Punjab Agricultural University, Ludhiana-141004, Punjab, India

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Abstract

The deficiency of vitamin D is highly prevalent but one of the most misdiagnosed nutrient deficiencies in the world. It has been shown for decades that vitamin D has a primary role in maintaining optimum bone health. Nowadays, studies related to the non-skeletal effect of vitamin D has gained the attention of scientists and professionals working in the field of nutrition and related fields. Vitamin D plays a crucial role in bone health and the immune system of the human body, maintenance of glucose homeostasis, regulation of body weight and maintaining insulin level with adjusting cardiovascular risk factors. These functions show the importance of vitamin D and its implications on human health, so correction of the deficient condition of the nutrient can improve the nutritional status of the population of the country. In a tropical country like India where most of the region gets sufficient exposure to sunlight still a great percentage of the population is suffering from vitamin D deficiency. Serum levels of vitamin D can be increased by sun exposure and by consuming foods rich in vitamin D such as oily fish (salmon and mackerel), mushrooms and dairy products. Also, the fortification of vitamin D in certain staple foods and supplementation have been seen to improve vitamin D levels. In the present review, we have focused on the need for vitamin D beyond bone health and food-based strategies to overcome its deficiency.

1. Introduction

Vitamin D, also known as calciferol and sunshine vitamin is a fat-soluble vitamin that was discovered in 1930 by the Nobel Prize laureate Adolf Otto Reinhold Windaus (Wolf, 2004). Vitamin D has two forms, D2 (ergocalciferol) and D3 (cholecalciferol). Vitamin D plays a very crucial role in maintaining calcium and bone metabolism, so most of the observational and placebo-controlled trials have focused on the skeletal effects of vitamin D, but now the nonskeletal effects, which are associated with many chronic diseases like atherosclerosis, hypertension, cardiovascular diseases, diabetes, obesity, myocardial infarction and stroke, are also gaining the interest of nutrition scientist and other professionals (Gupta, 2014).

Vitamin D3 synthesis starts in the skin when sunlight exposure helps the conversion of provitamin D3 to previtamin D3 by thermal isomerization. Vitamin D3 is obtained when previtamin D3 is isomerized in the epidermal basal layers, which binds to vitamin D binding protein and is transported to the liver. Vitamin D2 and D3 are hydroxylated in the liver with the help of hepatic 25-hydroxylases. In the kidney, the 25-hydroxycholecalciferol is 1-hydroxylated in the presence of 1α-hydroxylase and converts into 1,25-dihydroxycholecalciferol (DeLuca, 2004).

Sun exposure is a major source of vitamin D, there is wide variation in the concentration of the circulating form of vitamin D which is 25 dihydroxy vitamin D in different seasons (Brot *et al*., 2001). Some food also contains vitamin D in good quantity like oily fish such as salmon and mackerel, mushrooms, dairy products, *etc*. Although exposure to sunlight and consumption of certain food aids in achieving optimum serum vitamin D levels, the deficiency of vitamin D is widespread all over the world. Vitamin D deficiency is prevailing in both sunshine sufficient as well as sunshine insufficient countries. In spite a tropical country, India has a high prevalence rate from 50% to 94% as indicated by community-based studies and 37% to 99% based on hospital-based studies in a review study by Aparna *et al.* (2018). Indian diet generally fails to provide sufficient vitamin D [vitamin D2 from vegetarian sources and D3 from animal sources] which has led to the need to encourage the intake of supplements and fortified food. Nutrient requirement guidelines by the Indian Council of Medical Research (ICMR) in 2020 recommended a daily allowance of 600 IU and an estimated average requirement (EAR) of 400 IU for all age groups (ICMR, 2020).

2. Prevalence of vitamin D deficiency

The deficiency of vitamin D is diagnosed all over the world. The deficiency of vitamin D was seen mainly in the Middle East countries, China, Mongolia and India where levels less than 25 nmol/l were considered deficient (Van Schoor and Lips, 2018). About 70 per cent of the population of South Asia has vitamin D levels of less than 50 nmol/l (Nimitphong and Holick, 2013). In India, a community-based study showed that the prevalence of 25-hydroxyvitamin D deficiency ranged from 50 per cent to 94 per cent when the cut-off was considered less than 20 nmol/l (Aparna *et al*., 2018). Although, India is a tropical country with sufficient sunshine available throughout the year, the prevalence of vitamin D deficiency is higher owing to many factors such as dark skin color, high pollution, use of sunscreens with higher SPF, consumption of a diet rich in phytates and lower availability of vitamin D fortified food in the market and cultural practices like staying indoor (Aparna *et al*., 2018).

Corresponding author: Dr. Sonika Sharma

Department of Food and Nutrition, Punjab Agricultural University, Ludhiana-141004, Punjab, India

E-mail: drsonika@pau.edu

Tel.: +91-8146122277

3. Vitamin D in bone health

Bones provide strength and shape to the body. Bone remodeling is a process of mineralization and demineralization of bone which involves many complex reactions. It happens throughout the lifespan. Remodeling of bone is dependent on the status of micronutrients such as vitamin D, calcium and phosphate. The relationship between vitamin D, calcium and bones is most widely studied. Adequate calcitriol (the form of vitamin D which is active) status promotes the absorption of calcium which further helps in the formation of bony tissue. Low levels of calcium in the blood stimulate the production of the parathyroid hormone, which is secreted from the thyroid gland and helps in the conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol, also known as calcitriol, up-regulates transcription factors in vitamin D response element (VDRE) to increase the protein like calbindin (found in the intestine and kidney), calmodulins and calcium channel transporter. Moreover, it interacts with osteoblast to increase the expression of the receptor activator of nuclear factor kappa-k ligand (RANKL) which stimulates the catabolization of bone and releases calcium in the blood. This function of vitamin D helps in the maintenance of calcium levels at 4-5.6 mg/dl.

In the elderly population, there is a high prevalence of bone-related diseases (Giaze *et al.*, 2017) which is due to a decrease in the enzymes, transporters, proteins and hormones related to the metabolism of the vitamin. According to a study published in the Journal of Osteoporosis; osteoporosis is more common in old women due to the loss of estrogen production after menopause which leads to bone loss (Bhattarai *et al.*, 2020). Vitamin D and calcium are involved in preventing bone-related complications, but a recent study did not show any improvement in the bone mineral density or decrease in fracture risk when these nutrients were supplemented solely (Aspray *et al.*, 2019). Although, the supplementation of vitamin D with calcium has shown an improvement in bone mineral density. It is concluded by last decade's studies that about 800 IU of vitamin D and 1-1.2 g of calcium could prevent the risk of fractures and bone mineral density loss (Kärkkäinen *et al.*, 2010; Tang *et al.*, 2007). A recent study on older adults considered the vitamin D metabolites ratio (ratio of 24,25-dihydroxyvitamin D to 25-dihydroxy vitamin D) as a marker of vitamin D status and provided more accurate results. According to this study, a 50 per cent reduction in vitamin D metabolites ratio was associated with 49 per cent more fracture risk during the 10 years period (Ginsberg *et al.*, 2021). Higher than normal serum levels of calcitriol, an active form of vitamin D, decrease the incidence of non-vertebral and hip fractures (Brincat *et al.*, 2015). In contrast, in a study done on 311 participants, there are no significant benefits of taking higher doses of vitamin D (Burt *et al.*, 2019). Apart from chemical supplements, natural herbs such as *Maranto despumilum*is gaining attention owing to its osteo-protective activities (Giaze *et al.*, 2017).

It was observed that a high dose of vitamin D or vitamin D in association with calcium could lead to kidney stones (Letavernier and Daudo, 2018), while other studies did not show any risk of kidney stones in typical amounts (Ferraro *et al.*, 2017) and for the amount up to 100,000 IU per month (Malihi *et al.*, 2019).

Vitamin D is activated in the kidneys. The decrease in the function of the kidney due to any acute or chronic diseases could lead to a decrease in the levels of serum 25(OH)D. Hence, reduction in kidney function leads to osteoporotic fractures. Supplementation of vitamin D could prevent the deficiency. A higher than 800 IU of vitamin D could prevent osteoporotic fractures in chronic kidney diseases patients (Lips *et al.*, 2017).

4. Vitamin D and metabolic syndrome

Apart from mineral regulation and bone remodeling, vitamin D is involved in the normal functioning of other cells like pancreatic beta-cell, malpighian layer cells, brain cells, adipocytes and mammary glands. The deficiency of vitamin D in blood could impact the function of these tissues and could lead to metabolic syndrome. Metabolic syndrome (MeS) is a cluster of disorders including insulin resistance, hypertension, central obesity and atherogenic dyslipidemia. There is an inverse relationship between vitamin D and MeS (Melguizo-Rodriguez *et al.*, 2021). A study was done on 107 patients with high BMI of which 61 had metabolic syndrome and 46 were without metabolic syndrome. It was seen that serum vitamin D levels were significantly lower in MeS obese patients than in non-obese patients (Barchetta *et al.*, 2013). An observational study showed that vitamin D deficient groups had high triglycerides and low HDL (Barchettav *et al.*, 2013) which in the future could lead to obesity. Whereas, opposing results were shown by a study of 1,017 consecutive morbidity obese women and men patients in which it was concluded that parathyroid levels were an independent predictor of a metabolic syndrome rather than vitamin D. According to a study neither vitamin D nor PTH is associated with MeS (Sotunde *et al.*, 2017).

5. Vitamin D and obesity

According to the World Health Organization, obesity is an excessive or abnormal accumulation of fat that presents a health risk. There is an equivocal relation between vitamin D deficiency and obesity as it is not clear whether obesity causes vitamin D deficiency or vitamin D deficiency causes obesity.

Obesity could be the major cause of the deficiency of vitamin D. This is explained by volumetric dilution of 25(OH)D which states that vitamin D is distributed in fat, muscles, serum and liver and the volume of these compartments increases in obesity which leads to the volumetric dilution effect (Walsh *et al.*, 2017), and hence reduces the circulating vitamin D. A study has shown that BMI, waist circumference, and waist-to-height ratio had a negative relation to vitamin D levels in puerto rican adults (Gonzalez *et al.*, 2015). Obese children and adolescents showed a greater risk of vitamin D deficiency (Fiamenghi and Mello, 2021), as increasing weight is related to vitamin D deficiency, a reduction in fat mass increases serum vitamin D levels. A study performed on women for a year had shown that the females who lost weight above 15 per cent had a mean rise in 25(OH)D of 7.7 ng/ml (Mason *et al.*, 2011). Another recent study involving 31 individuals also showed an increase in vitamin D levels after losing weight (Buscemi *et al.*, 2021).

Low vitamin D serum levels could also promote obesity. There is a common hypothesis that suggests that a fall in serum vitamin D, due to less sunlight exposure or other factors, could trigger winter metabolism in individuals. The body adapts to slow metabolism in the winter which leads to the accumulation of fat mass and metabolic syndrome (Foss, 2009). Studies of the past decade showed that vitamin D deficiency is linked to obesity and it could be due to vitamin D involvement in the pathogenesis of obesity. According to a recent study, the deficiency of vitamin D could increase parathyroid

hormone levels which promotes lipogenesis in adipocytes (Karampela *et al.,* 2021). Moreover, there is evidence that an active form of vitamin D could inhibit adipogenesis hence, decreasing obesity (Dix *et al.,* 2018). A study conducted on 171 participants has shown that the combination of vitamin D and calcium supplements could decrease visceral body fat (Rosenblum *et al*., 2012). But, a recent study showed no effect of consuming vitamin D on body fat mass (Golzarand*et al.,* 2018).

6. Vitamin D and type 2 diabetes mellitus

India ranks second in terms of diabetic cases (Mounika and Hymavathi, 2021). The prevalence of diabetes was 463 million in 2019 and in the future, it is estimated that it would climb up to 578 million in 2030, 642 million in 2040 and 700 million in 2045 (Ogurtsova *et al.*,2017). Diabetes, a metabolic disorder, occurs when blood sugar levels are very high. According to the American Diabetes Association (2020), a higher than 126 mg/dl level of fasting blood sugar is marked as diabetes.

A few studies have shown an inverse relationship between serum vitamin D levels and insulin resistance. A recent study composed of 2,008 patients has shown that low vitamin D levels or hypovitaminosis D could cause insulin resistance (Nur-Eke *et al*., 2019). Another study, involving 157 prediabetic patients, also showed an inverse relationship between the extent of insulin resistance and vitamin D (Dutta *et al*., 2013). It is found that vitamin D is higher in non-diabetic patients than in diabetic patients (Nasr *et al.,* 2022).

The relationship between serum vitamin D and diabetes mellitus 2 is explained by several mechanisms. An optimum status of vitamin D could reduce inflammation, reactive oxygen species (ROS) and maintain the normal levels of calcium in beta cells of the pancreas. Vitamin D is also able to prevent hypermethylation and other epigenetic alteration in the beta cells (Vondra and Hampl, 2021). Vitamin D could also aid in the stimulation of insulin. Animal studies have shown that 1,25-OHD3, the active form of vitamin D, stimulates the production of insulin from pancreatic cells (Lips *et al.,* 2017).

Studies related to vitamin D supplements and improvement in insulin sensitivity have shown equivocal results. In a study, when a higher-than-normal dose of vitamin D supplement was given to 162 pre-diabetic patients, an improvement in insulin sensitivity and decreased risk of diabetes were observed (Niroomand *et al*., 2019). Another study showed that vitamin D could improve insulin sensitivity, but only for a short period when high doses are given (Li *et al.,* 2018). A reduction in fasting plasma glucose and HbA1c is seen when vitamin D is given to diabetic patients (Mirhosseini *et al.,* 2017). A recent six-month study on 96 high-risk or newly diabetic patients showed that vitamin D supplements could have a beneficial effect on insulin sensitivity and pancreatic cells (Lemieux *et al*., 2019). There are a few studies that do not show the positive effect of supplementing vitamin D to diabetic or pre-diabetic patients. A weekly dose of 28000 IU given to 71 pre-diabetic patients, does not show any improvement in the glucose tolerance or marker of glucose status (Moreira-Lucas *et al.,* 2017). In another study, supplementation of vitamin D has not shown a positive effect on insulin sensitivity (Poolsup*et al.,* 2016) and beta-cell function (Oosterwerff*et al.,* 2014).

7. Vitamin D and type 1 diabetes mellitus

Type I diabetes (IDDM) is caused by an autoimmune reaction that leads to the deficiency of insulin production. A recent study has shown that the autoimmune disorder is widespread in approximately 97,700 children in India and about 490,000 children worldwide (Desai and Deshmukh, 2020). The low serum levels of 25-OHD3 have been related to type I diabetes mellitus (D'Aurizio *et al.,* 2015). Vitamin D levels in serum could modulate the risk of IDDM by genetic or immunomodulatory functions (Infante *et al.,* 2019). Studies have demonstrated appropriate supplementation with vitamin D could reduce the risk of IDDM as vitamin D is connected with adaptive immunity, decrease auto-aggression-related inflammation and induce immunological tolerance (Rakand Bronkowska, 2018). Controversial results were shown by the Mendelian randomization study suggested that calcidiol levels are unlikely to have a significant effect on the risk of IDDM. (Manousaki *et al.,* 2021). Although there is not enough evidence that vitamin D could prevent immunological diseases in humans, *in vitro* and animal studies have shown that vitamin D could decrease systemic inflammation and prevent autoimmune disease (Kriegel *et al.,* 2011).

8. Vitamin D and hypertension

According to WHO, hypertension is defined as systolic blood pressure above or equal to 140 mm of Hg and diastolic blood pressure above or or equal to 90 mm of Hg. It is estimated that about 1.27 billion people had hypertension in 2019 (Zhou *et al.,* 2021). High blood pressure is related to vitamin D deficiency. As vitamin D receptors and enzymes related to activation of vitamin D are found in endothelial and vascular muscle cells, it depicts the role of the vitamin in cardiovascular ailments (Latic and Erben, 2020). Moreover, there is a linkage between vitamin D status in the body and RAAS (renin-angiotensin-aldosterone system) activity. Low amounts of vitamin D could lead to the overactivation of the RAAS (Gimenez *et al.,* 2020). Studies on mice have shown that vitamin D is linked to vasodilator nitric oxide and its deficiency could cause arterial stiffness, remodeling of the aorta, and impaired heart function at later ages (Andrukhova*et al.,* 2014) but there is no such evidence that vitamin D supplements could ameliorate hypertension in humans (Zhang, 2020).

Vitamin D supplementation may improve high blood pressure (Mirhosseini *et al.,* 2018). A study on 4,744 participants observed that the supplementation of vitamin D does not affect systolic blood pressure (SBP) and diastolic blood pressure (DBP) in young adults, whereas a drop in SBP and DBP was shown in the old population when above 800 IU of supplementation of vitamin D was given for less than half-year of the period (Golzarand *et al*., 2016). A positive effect of vitamin D supplements on hypertension was shown in healthy subjects but not in overweight subjects (Golzarand *et al.,* 2016). A monthly high dose of 100,000 IU of vitamin D for 1 year lowered central blood pressure parameters in some adults with vitamin D deficiency (Sluyter *et al*., 2017). Several studies have shown no effect of vitamin D supplements in decreasing hypertension. A study that involved 200 participants with hypertension and low serum 25(OH)D (less than 30 ng/ml) had shown no significant effect of vitamin D supplementation (2800 IU/day) on blood pressure (Pilz *et al.,* 2015). Vitamin D long-term supplementation of about 200,000 IU for 2 months, followed by half of the former dose monthly up to 18 months did not affect SBP and DBP in healthy white adults (Scragg *et al.,* 2014).

9. Vitamin D and breast cancer

Breast cancer is the world's most prevalent cancer. According to WHO, around 685,000 deaths and 2.3 million women were diagnosed with breast cancer in 2020 and it is estimated that incidents of breast cancer would grow to about 3.2 million by 2050 (Tao *et al.*, 2015). Low vitamin D status in patients with breast cancer suggests that vitamin D could be linked with breast cancer (Welsh, 2018). A negative relation has been shown between serum levels of vitamin D and breast cancer (Hossain *et al.*, 2019).

A decrease in the availability of vitamin D in tissue could lead to cancer. The concentration of vitamin D in the breast cells is determined by two enzymes: CYP27B1 and CYP24A1. CYP27B1 is involved in the conversion of calcidiol to calcitriol, and hence activates the vitamin in the cell. Whereas, CYP24A1 is involved in the degradation of vitamin D from the cell, and hence aids in the excretion of vitamin D. The ratio of the enzymes CYP27B1 and CYP24A1 found in the breast tissue is important for the optimum growth of cells as emerging evidence suggests that the altered ratio of these enzymes is shown during cancer development (Voutsadakis, 2020). The CYP27B1 expression is slightly decreased while CYP24A1 expression is augmented in carcinomas resulting in less synthesis of calcitriol while increasing the ability to degrade this vitamin. When vitamin D is adequately available in the breast tissue, it is involved in the induction of apoptosis, cell differentiation, and anti-inflammatory and anti-proliferative effects (Miriam *et al.*, 2018). These functions of vitamin D are possible due to nuclear vitamin D receptors which interact with ligand 1k,25(OH)2D3.

Vitamin D supplements might have a chemopreventive effect against breast cancer as well as it is an affordable and safe way to reduce cancer incidence. Another study proved that women with less than 10.5 mg/dl calcium serum levels and 20 ng/ml of calcidiol serum levels had higher risk of having breast cancer (Sofi *et al.*, 2018), while a Mendelian randomization analysis comprising 15,748 breast cancer cases had shown no evidence to support the relation between calcidiol and risk of breast cancer. (Jiang *et al.*, 2019)

10. Vitamin D and prostate cancer

The second most common cancer among men is prostate cancer. According to 2018 statistics, 1,600,000 men are diagnosed with and about 366,000 men die of prostate cancer (Pernar *et al.*, 2018).

As vitamin D has a crucial role in antiproliferative, apoptosis and differentiation-inducing, G1/S cell cycle arrest and immuno-suppressive effects in cancer (Vanhevel *et al.*, 2022). It could be linked to prostate cancer. Several androgen and vitamin D metabolism enzymes are found in the prostate and alteration in expression patterns of these enzymes could lead to the development of cancer (Maksymchuk and Kashuba, 2020). Just like in the case of breast cancer, the overexpression of one of the enzymes called CYP24A1, involved in vitamin D degradation, is seen in prostate cancer (Ahn *et al.*, 2016). Another study showed that levels of about 85 nmol/l of vitamin D may increase the rate of survival in prostate cancer patients (Brandstedt *et al.*, 2016). Epidemiological studies suggest that diets higher in calcium could increase the risk of prostate cancer while the risk is reduced by vitamin D (Capiod *et al.*, 2018). A recent meta-analysis showed high serum vitamin D could decrease prostate cancer-related deaths (Song *et al.*, 2018).

11. Vitamin D and immunity

Vitamin D has a role in the immunity (Abdussalam *et al.*, 2021) of an individual as vitamin D-related enzymes and receptors are present in the immune cells, and hence it controls the activity of both innate and adaptive immunity (Del, 2022). Vitamin D suppresses autoimmunity, an anti-inflammatory effect promoting differentiation and reducing inflammatory cytokines (Sassi *et al.*, 2018). Poor status of vitamin D could lead to viral or bacterial infections (Ismailova *et al.*, 2021; Charoenngam and Holick, 2020). The coronavirus disease (COVID-19) has spread all through the world owing to its high rate of spread (Palai *et al.*, 2021). Recent studies have shown that vitamin D receptors are found in immune cells, so the deficiency of vitamin D could lead to the risk of a viral infection such as SARS-CoV-2 infection (Bellik *et al.*, 2020).

12. Vitamin D supplementation

An amount of 800-1000 IU/day is recommended safe. A recent safety upper limit of 4000 IU/day could have adverse effects on the system other than minerals homeostasis (Rizzoli, 2021). As shown in a meta-analysis that a higher than high supplementation dose (2800 IU/day) of vitamin D for one or more years could lead to hyper-calcemia and hypercalciuria (Malihi *et al.*, 2019). Other studies have shown conflicting results proving no adverse effect of higher doses of vitamin D in the long term.

13. Food fortified with vitamin D

A deficiency of vitamin D is prevalent all over the world. Food fortification is a primary solution for combating vitamin D deficiency among vegetation vitamin D deficient populations. Vegetarian food has a low content of vitamin D which leads to very low availability of foods rich in vitamin D for the general or vegan population. The only option left to provide food rich in vitamin D to the masses is the fortification of vitamin D in various foodstuffs.

Fortification of staple food like bread could ensure the adequate status of vitamin D levels and decreased parathyroid hormone in the population (Souza *et al.*, 2022). It has been shown in an 8-week randomized-controlled trial in healthy middle-aged women that ergocalciferol-D2 is less potent than cholecalciferol-D3 in increasing the serum levels of vitamin D (Itkonen *et al.*, 2016). When supplementation of vitamin D, about 25000 IU, was given to two groups in supplementation form and fortified bread form, no statistical difference in serum vitamin D was seen between the two groups (Iossifidis *et al.*, 2021). Another study involving 96 healthy people showed increased serum vitamin D levels after incorporating fortified bread into their diet (Nikooyeh *et al.*, 2016).

Vitamin D fortified cooking oil is also effective in increasing serum vitamin D levels. It could be an effective way of mass fortification to combat vitamin D deficiency, and it could also decrease the risk factors related to cardiovascular diseases like weight, waist girth, serum total cholesterol and LDL-C (Nikooyeh *et al.*, 2020).

Milk is fortified either mandatory or voluntarily in many countries. Studies showed a positive relation between fortified milk and serum levels of vitamin D in the population (Itkonen *et al.*, 2018). In countries like Finland, Canada and the United States, where milk fortification is mandatory, milk consumption contributed to about 28-63 percent of vitamin D intake. While countries like Sweden and Norway the contribution of milk toward serum vitamin D was low

or negligible (Itkonen *et al.*, 2018). In Northern Ireland, milk fortification is an effective method to help people achieve desired levels of vitamin D (Weir *et al.*, 2021). About 70 per cent of Irish adults, daily requirement is meant by fortification of commonly consumed products like bread and milk (McCourt *et al.*, 2020).

Mushrooms are rich sources of vitamin D as they contain high ergocalciferol (Vitamin D2). New methods are developed to increase the vitamin D2 content in mushrooms. *Calocybe indica*, a species of edible mushroom when exposed to artificial UVB light, synthesized 140.58 ug/g of ergocalciferol in 60 min while only synthesizing 78.33 ug/g under natural light. Moreover, it was observed that the antioxidant activity was also increased (Rathore *et al.*, 2020). Although, the levels of vitamin D2 in mushrooms may decrease while in storage, it is likely to remain above 10 mg/100g fresh weight, if consumed before the "best before" date (Cardwell *et al.*, 2018).

Vitamin D is a very crucial micronutrient whose deficiency can cause many chronic diseases like cardiovascular disease, bone health, insulin resistance, cancer and other death-causing diseases. Different dietary approaches should be initiated at the grass-root level to prevent this condition. Thus, consumption of food fortified with vitamin D increases vitamin D intake and improves the status of the vitamin in the body.

14. Conclusion

Vitamin D deficiency is prevalent worldwide. The indispensable function of vitamin D in bone metabolism is proven and myriad studies have shown the positive effect of supplements of vitamin D on bone health. In recent studies, although the mechanisms behind the role of vitamin D in metabolic syndrome, hypertension, obesity, diabetes type 2, autoimmune diseases and a certain type of cancer have been observed, the supplementation of vitamin D to treat the disorders has not shown any significant results. More research in this area is required to find the efficiency of vitamin D supplementation in treating these metabolic disorders. Supplementation and fortification have been the best way to obtain optimum serum vitamin D levels.

Conflict of interest

The authors declare no conflict of interest relevant to this article.

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