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ULTRAVIOLET IRRADIATION TO ENRICH FOODS WITH VITAMIN D

(review)

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Abstract

Vitamin D deficiency found in 50-90 % of the adult and children's population in Russia (I.N. Zakharova et al., 2015; V.M. Kodentsova et al., 2017, 2018) and caused by inadequate intake and reduced endogenous synthesis in the skin due to insufficient solar irradiation, is associated with many chronic diseases and makes an important problem (A. Hossein-nezhad et al., 2013). One of the options for biofortification, called "bio-addition", is based on the ability of living organisms to form vitamin D from endogenous ergosterol by UV irradiation. Ultraviolet irradiation of animals allows minimizing seasonal variations in the concentration of vitamin D in cow's milk (R.R. Weir et al., 2017). A one-hour exposure of animals for 14-day to insolation at summer noon increased the vitamin D_3 content in pork ($p < 0.001$) to 0.716±0.097 μg/100 g (28.6±3.9 IU/100 g) which significantly exceeded the same indicator in the control animals (0.218±0.024 μg/100 g, or 8.7±1.0 IU per 100 g) (D.E. Larson-Meyer et al., 2017). UV irradiation effectively increased vitamin D level in chicken, from 0.16 to 0.96 μg per 100 g, even at 3000 IU/kg of dietary vitamin D_3 (A. Schutkowski et al., 2013).The amount of vitamin D_2 in shiitake mushrooms (*Lentinula edodes*) can achieve, under optimal conditions of UV irradiation, 29.87±1.38 μg per g dry weight. In the USA, Ireland, the Netherlands and Australia, fresh mushrooms are exposed to UV irradiation, which leads to an increase in the vitamin D_2 content to 10 μg/100 g wet weight (O. Taofiq et al., 2017; G. Cardwell et al., 2018). This is 50-100 % of the recommended daily consumption of the vitamin. The processing of baking yeast *Saccharomyces cerevisiae* by ultraviolet irradiation induces the conversion of ergosterol into vitamin D_2. The average content of vitamin D_2 is 3,065,417 IU/100 g (2,560,000-3,750,000 IU/100 g) or 770 μg/g (640-940 μg/g), which increases its initial concentration (less than 20 IU of vitamin D_2/100 g) almost 30-50-fold (EFSA, 2014). The vitamin D_2-enriched UV-treated yeast is allowed by The European Food Safety Authority (EFSA) for fortification of yeast-leavened bread, rolls and fine pastry at maximum D_2 dose of 5 μg per 100 g of the products. The concentration of vitamins D_2 and D_3 after UV irradiating of the wheat germ oil (1.6 mm oil layer) was 1035 and 37 ng/g, respectively (A.C. Baur et al., 2016). Similarly, there is an increase of the vitamin D content in eggs after exposure of chickens to UV irradiation or natural sunlight (A. Schutkowski et al., 2013; J. Kühn et al., 2014, 2015). In the conditions of the complete absence of the commercial production of vitamins in our country, bio-addition with vitamin D of chicken meat, eggs and dairy products by UV irradiation of animals, mushrooms, yeast, vegetable oils takes on particular significance.

Keywords: vitamin D, вiofortification, bio-addition, poultry, eggs, cows' milk, mushrooms, vitamin D-enriched UV-treated baker's yeast, ultraviolet light irradiation, wheat germ oil

Functional products for healthy lifestyle and prevention of diseases caused by an inadequate and unbalanced diet are one of the main challenges and current global trends. Comparing the people's actual diet and the state of health indicates that the diet adequate for energy expenditure does not meet the needs in macroand micronutrients and minor biologically active substances. The quality of a functional food product (FFP) and the effects of its systematic consumption crucially depend on the food raw materials used. Vitamin value is the most important indicator to characterize the usefulness of food raw materials and the resulting FFPs, which determines the relevance of research aimed at increasing the concentration of vitamins in farm products. To improve vitamin availability, vitamins are added directly to foods or to raw foodstuffs [1]. However, as food fortification is still a voluntary initiative of producers, the portion of such products in the retail network is low. In addition, there is unfortunately a misconception among the public and sometimes in scientific literature that synthetic vitamins are poorly assimilated by the body.

Biofortification is a modern intensively developing technology to improve composition of biologically significant nutrients in foods. In animal and poultry production, this is achieved by adding vitamins, minerals, polyunsaturated fatty acids to feed [2], and in crop production by traditional and marker-assisted selection, biotechnology and agrotechnology [3]. The promising version of biofortification is based on the ability of living organisms to form vitamin D from endogenous ergosterol or 7-dehydrocholesterol under UV radiation. Vitamin D, which is synthesized in animals, mushrooms or yeast, undergoes the stages of biotransformation and is consumed by humans in its natural form.

This overview summarizes the opportunities for increasing the vitamin D content of agricultural products through ultraviolet irradiation (UV irradiation).

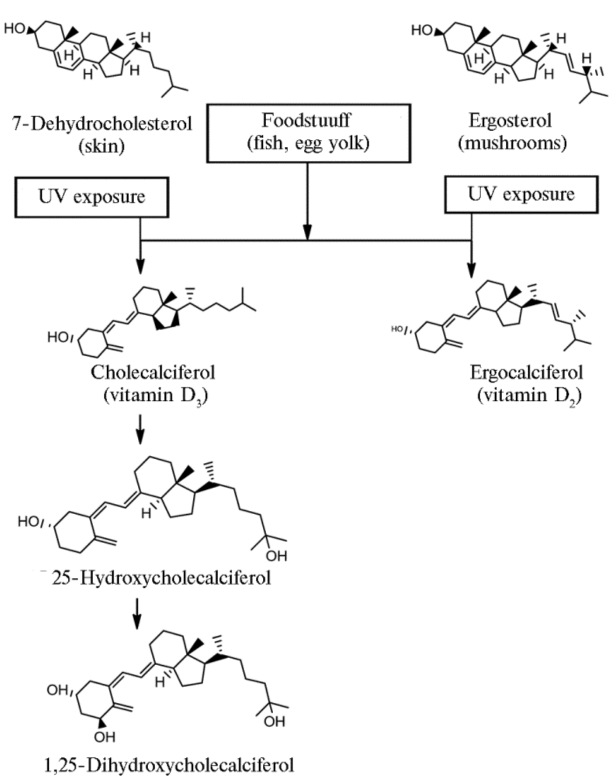
The essentiality of vitamin D (as well as other vitamins) for the human body is beyond doubt. Vitamins D, or calciferols, are represented by two compounds, the cholecalciferol (vitamin D_3) and ergocalciferol (vitamin D_2). The difference between vitamin D and other vitamins is that it not only enters the body with food but can also be formed in the skin due to ultraviolet radiation (Fig.) [4, 5].

The main sources of vitamin D_3 in the human diet (in decreasing order of content) are cod liver, fish, eggs, liver, and butter [6]. In addition to cholecalciferol, 25-hydroxy-cholecalciferol ($25OHD_3$) contributes significantly to the vitamin value of meat and dairy products. In food of plant origin (algae, leaves and fruits of some plants), the vitamin D amounts are extremely low (from 0.03 to 0.67 μg/100 g dry matter) [7]. Vitamin D_2 is present in mushrooms. Vitamin D vitamers have different biological activity for humans. Vitamin D_3 is more effective than D_2 [8, 9]. It was found that in tackling inadequate vitamin D status 10 μg of vitamin D_3 is equivalent to 23 μg of vitamin D_2 or 6.8 μg of $25OHD_3$ [10, 11].

Calciferols are formed due to photo-isomerization of provitamins under UV radiation (see Fig.). Terrestrial animals are able to synthesize 7-dehydrocholesterol, the provitamin of cholecalciferol, from cholesterol; mushrooms and yeasts contain ergosterol, the provitamin of ergocalciferol [5]. Cholecalciferol is formed from 7-dehydrocholesterol when irradiated with sunlight or artificial ultraviolet light (λ = 280-320 nm) as a result of photochemical modification of 7-dehydrocholesterol followed by non-enzymatic isomerization.

It is believed that up to 80% of vitamin D can be synthesized in human skin under the influence of B ultraviolet radiation (λ = 290-315 nm) [12]. However, in Russia, due to insufficient sun exposure, endogenous vitamin D synthesis in the skin does not meet the body's need for this vitamin.

After entering the body, vitamin D is hydroxylated (see Fig.), turning first into 25-hydroxyvitamin D (25OHD) circulating in the blood (blood 25OHD is measured to assess individual vitamin D status) and then into its metabolically active form, the 1,25-dihydroxyvitamin D, possessing hormonal function [12].



UV dependent endogenous vitamin D synthesis and metabolism as adapted from [39].

Vitamin D deficiency in the population, caused by inadequate food intake and/or reduced endogenous synthesis in the skin due to insolation deficiency, has highly undesirable health effects [1, 13, 14], associated not only with skeletal but also with non-skeletal functions [15]. Vitamin D deficiency correlates with many chronic age-borne diseases [16], cardiovascular disorders [17], myocardial infarction, type 2 diabetes, tuberculosis, bronchial asthma, atopic dermatitis, urticaria, cancer of the prostate, breast, intestines, autoimmune diseases [17], and is accompanied by neurocognitive disorders, depressive states, reproductive dysfunction [12, 18, 19].

According to the results of studies of vitamin supply in the Russian population, vitamin D deficiency or insufficient intake occur in 50-90% of the adults and children [4, 14, 20, 21]. This problem is solved in some countries (USA, UK, Germany, Italy, Belgium, Finland) by legally regulated technological food fortification of mass consumption products [22]. As a result, technologically enriched liquid dairy products contribute 28-63% of vitamin D [23] to the total consumption. The effectiveness of such enrichment has been proven. In particular, there are reports on a decrease in the osteoporotic fractures [24, 25] and economic benefits [26, 27]. An alternative way to increase the vitamin D content of agricultural products is to irradiate them with ultraviolet light.

Cow's milk. Vitamin D content in milk depends on the intake of ergocalciferol with mushrooms and cholecalciferol from vitamin supplements, as well as endogenous synthesis in the skin [28]. Experiments using blankets and udder covers have shown that, despite the wool cover of the skin, vitamin D synthesis in cows is carried out evenly over the entire body surface [29]. Seasonal variations in the vitamin D content in cow's milk are well known, which are minimal in winter (0-0.04 µg/g fat) and maximum in summer (up to 0.014 µg/g fat) during intensive insolation at pasture [30]. Natural insolation is more effective in improving the vitamin D status in animals than the addition of vitamin D_3 or D_2 to feed [29, 31]. Artificial UV irradiation of cows for 24 days, imitating 1, 2, 3 or 4 hours of sun exposure in summer at 56° N, resulted in an increase in vitamin D_3 and $25OHD_3$ content in milk [30, 32]. Such irradiation minimizes seasonal variations in vitamin D concentration in cow's milk.

Animal meat. These products have traditionally not been considered an important source of vitamin D for humans, but in recent years there have been reports of the possibility of meat intravital modification.

Wavelength $\lambda = 296$ nm was optimal for the endogenous synthesis of vitamin D_3 in the pig skin. The maximum dose of 20 kJ/m^2 provides 3.5-4.0 μg of vitamin D_3/cm^2 of skin [33]. Exposure to sunlight in pigs has been found to increase the vitamin D content in the sirloin as well [34]. Exposure to sunlight increased ($p = 0.003$) the content of 25OHD, the form more effective for human, in muscle tissue and subcutaneous fat, but did not affect the amount of vitamin D_3 ($p = 0.56$). In pigs, after 14-day stay in the sun for 1 hour in summer afternoon, the content of vitamin D_3 in meat increased ($p < 0.001$) to 0.716±0.097 μg/100 g (28.6±3.9 MU/100 g), significantly exceeding the same indicator in the control group (0.218±0.024 μg/100 g or 8.7±1.0 MU/100 g) [34]. The amount of 25OHD$_3$ reached 0.281±0.014 μg/100 g vs. 0.130±0.016 μg/100 g. The total vitamin D content (D_3 + 25OHD$_3$) in the sirloin of pigs exposed to UV radiation increased 2.9-fold (0.997±0.094 μg/100 g vs. 0.348±0.027 μg/100 g, $p = 0.001$). The fact that the vitamin D_3 content in subcutaneous fat tissue did not change under sun exposure and was the same in pigs exposed to sunlight and in animals in the control group (with a 2-fold increase in the amount of 25OHD$_3$), has not been explained [34]. Sun exposure has led to better vitamin D availability in pigs, as per blood 25OHD$_3$ level, even with sufficient vitamin D content in the diet [35]. Daily UV irradiation of mini pigs (corresponding to sun exposure at noon for 10-20 minutes) stimulated the skin synthesis of vitamin D_3 and resulted in an increase in the amount of vitamin D_3 and 25OHD$_3$ in blood and the carcass. The vitamin D_3 concentration in adipose tissue of mini pigs was 150-260 ng/g if the animals were exposed to UV light, and 90-150 ng/g after D_3 oral administration at a dose of up to 60 μg per day, or 3.7-4.4 μg/kg bodyweight [36]. That is, UV irradiation was more effective. Based on the data obtained, it was concluded that changing the conditions for raising pigs when animals are allowed to be in the sun provides an effective natural increase in the vitamin D content of pork products.

Similar data were obtained for other animal species. Insolation improves the vitamin D supply in cattle. Thus, in late summer and autumn, the blood concentration of 25OHD in calf was significantly higher than in early June (55.2-63.8 vs. 26.3 ng/ml) [37]. Exposure to UV B increased the amount of vitamin D in the muscular tissue of chickens 4 times more effectively than feeding them with a diet with maximum permissible vitamin D_3 level. UV exposure increased the amount of vitamin D in chicken meat from 0.16 to 0.96 μg/100 g, even under 3,000 MU of vitamin D_3/kg feed [38].

Mushrooms. Many mushroom species contain high concentrations of ergosterol, which is transformed into vitamin D_2 under the UV radiation. Vitamin D_2 formation is influenced by temperature, humidity, UV spectrum (B or C), duration and dose of exposure [39-41]. The table shows the vitamin D_2 content of UV-irradiated freshly picked and freeze-dried mushrooms.

Vitamin D_2 content (μg/g of dry weight) **after UV irradiation of fresh and freeze-dried mushrooms** (*M*±SEM) [42-44]

Mushrooms	Fresh	Freeze-dried and crushed
Shiitake (*Lentinus edodes*)	29.46±2.21	60
Champignon (*Agaricus bisporus*)	3.55±0.11	119
Oyster mushroom (*Pleurotus ostreatus*)	58.96±1.15	34.6

The amount of vitamin D_2 under optimal conditions of UV irradiation of shiitake mushrooms (*Lentinula edodes*) was 29.87±1.38 μg/g dry weight [45]. Drying Shiitake mushrooms in the sun increased their vitamin D_2 content 16 times, from 100 to 1,600 MU per 100 g [15]. The original method of obtaining a functional food component was to obtain a shiitake mushroom extract with an ergosterol content of 15%, and then convert it to vitamin D_2 under the influence of UV radiation at $\lambda = 254$ nm [6]. Freeze-dried shiitake extract after UV irradiation contained about 37 μg/g of vitamin D_2, which was more than 6 times its original amount. The extract can be used as a dietary supplement to food, 0.4 g of which fully meets the daily requirement for vitamin D [46]. The vitamin D_2 content in the fruitbody of six fungal genera (*Agaricus*, *Agrocybe*, *Auricularia*, *Hypsizygus*, *Lentinula* and *Pholiota*) and five species of *Pleurotus* irradiated with ultraviolet light for 2 hours increased significantly from 0-3.93 to 15.06-208.65 μg/g [47]. The maximum content (204.7 μg/g) was in oyster mushrooms. Drying of pre-cut mushrooms significantly increased the amount of vitamin D_2 produced during subsequent UV treatment, i.e. up to 406 vs. 45 μg/g of whole mushrooms [48]. Irradiation of dry white mushroom powder at room temperature for about 10 minutes resulted in an increase in the vitamin D_2 content to 741.50 ± 23.75 μg/g [41].

Fresh mushrooms are currently exposed to UV radiation in the United States, Ireland, the Netherlands, and Australia, which leads to an increase in the vitamin D_2 content of up to 10 μg/100 g of raw weight [43, 49]. As a result, a portion of mushrooms (100 g) provides 50-100% of the recommended vitamin norm. The vitamin D content of the mushrooms treated in this way is similar to that of fatty fish [50]. This is essential for vegetarians typically lacking in vitamin D due to refusal of animal food [51-53]. The vitamin D_2 content in mushrooms with different methods of preparation is 62-88% of the original ($p \le 0.05$) [54].

In rats with experimental vitamin D deficiency it was shown that vitamin D_2 from UV irradiated fungi is digested by these animals: the blood amounts of 25OHD and calcium increased and the mineral density of bone tissue was significantly higher ($p < 0.01$) than in the control rats receiving conventional mushrooms [55].

As per estimates of the vitamin D bioavailability from mushrooms, its absorption is sufficiently high. It was shown that consumption of mushrooms after their UV irradiation led to an increase in the blood concentration of $25OHD_2$ in human up to 24.2 nmol/l, especially in case of initial lack of this vitamin. However, there was a 12.6 nmol/l decrease in $25OHD_3$ [44]. Vitamin D_2 is well absorbed from UV irradiated shredded chanterelles and porcini mushrooms, helps to increase the $25OHD_2$ concentration and reduce the amount of $25OHD_3$ in blood [56]. It has been found that 2,000 MU of vitamin D_2 contained in mushrooms is as effective in increasing and maintaining the required amount of 25OHD in human blood as 2,000 MU of vitamin D_2 or D_3 [57].

A 30-day feeding calves with vitamin D2-enriched mushrooms prior to slaughter resulted in an increase in the vitamin D content of the meat, although less pronounced than that of the diet with vitamin D_3 [58].

Bakery yeast. The UV irradiation on *Saccharomyces cerevisiae* bakery yeast has induced the conversion of the ergosterol they contain into vitamin D_2 (see Fig.). The amount of vitamin D_2 was almost 30-50 times higher than its original concentration (less than 20 MU/100 g) and averaged 3,065 thousand MU/100 g (fluctuations within the range of 2,560-3,750 thousand MU/100 g), or 770 μg/g (640-940 μg/g) [59]. In 2012, the European Food Safety Authority (EFSA, Italy) approved UV-treated yeast enriched with vitamin D_2 as a new food ingredient in the production of yeast bread, rolls, flour confectionery products, the maximum dose is 5 μg/100 g. Such yeast is also permitted as a component of dietary supplements.

Consumption of bread made with D_2-rich yeast had a comparable effect with pure vitamin D_2 on the 25OHD concentration in women blood plasma [59]. The vitamin D_2 from UV-irradiated yeast used in bread baking was shown to be digestible and improve bone health in rats with an initial vitamin D deficiency [60]. According to the effect on the content of 25OHD in experiments on growing rats, the effectiveness of the used form of vitamin D decreased in the series vitamin D_3 > vitamin D_2 > UV-treated yeast cells or their individual fractions [61].

In Canada, vitamin D_2 containing yeast are allowed as an ingredient of bread products in quantities up to 90 MU (2.25 μg) per 100 g, which is 23% of the D_2 recommended consumption rate [62]. In the United States, legislation was amended in 2012 to ensure the safe use of vitamin D_2 from baking yeast in baking products: it is permissible to add no more than 400 MU of vitamin D_2 per 100 g of finished products, or 50% of the recommended intake [63]. Food yeast remains a potential source of biologically active substances [64].

Vegetable oils. Vegetable oils can also be a potential source of vitamin D. They contain significant amounts of not only ergosterol but also 7-dehydrocholesterol (7-DHC) [65]. The ergosterol concentration is 22.1-34.2 μg/g in wheat germ oil, 4.2-23.4 μg/g in avocado oil, 7.9-17.4 μg/g in sunflower oil, 4.1-9.5 μg/g in rapeseed, soybean, flax oil, and < 4.5 μg/g in olive oil. UV-exposure resulted in the partial conversion of ergosterol and 7-DHC to vitamins D_2 and D_3 in these oils [65]. After 1-minute UV irradiation of 1.6 mm layer of wheat germ oil, the concentration of vitamins D_2 and D_3 was 1035 and 37 ng/g, respectively [65]. At the same time, such influence practically did not reduce the content of tocopherols and did not intensify peroxidation [65]. Assessment of the bioavailability of vitamin D showed that mice with an initial deficit of vitamin D improved, which was confirmed by an increase in the blood 25OHD concentration and accumulation in the liver compared to mice that received conventional wheat germ oil. However, the plasma content of 25OHD in mice fed UV-treated oil did not reach the values observed in the group that consumed oil with pure vitamin D added [65].

Chicken egg. Enrichment of eggs with vitamin D instead of adding it to the feed of chickens can be achieved by artificially irradiating birds with ultraviolet (bio-addition), or through free-range poultry.

In eggs from laying hens irradiated with ultraviolet for 3 hours daily for 4 weeks vs. those fed diet with the adequate vitamin D_3 content (3,000 MU/kg feed), the amount of vitamin D (cholecalciferol and 25OHD) usually reaches 2.5 μg. It is almost 5 times higher than in eggs of hens on the same diet but not UV irradiated [38]. Curiously, the endogenous formation of the vitamin occurs mainly in the legs of chickens, where the plumage is the smallest. The dependence of the increase in the vitamin D content in the egg yolk on the time of daily UV radiation is non-linear. With daily exposure to UV light for 300 minutes, the vitamin D_3 content increased to 28.6 μg/100 g of egg yolk dry weight, but did not reach the plateau, while the amount of 25OHD was already maximum with exposure for 60 min [66].

A similar increase in the vitamin D content is due to natural insolation. The amount of vitamin D_3 in the egg yolk in birds exposed to sunlight (free and closed/free keeping) was 3-4 times higher ($p < 0.001$) than its accumulation in the egg yolk of chickens in closed range [67]. The concentration of vitamin D_3 in the egg yolk of birds in free range was 14.3 μg/100 g vs. 3.8 μg/100 g of dry weight. The vitamin D content in the egg yolk of chicken eggs under the mixed keeping mode is in an intermediate position. The amount of $25OHD_3$ in the egg yolk also depended on sunlight, although it was lower than the concentration of vitamin D_3 ($p < 0.05$).

It should be noted that in recent years there has been a kind of rehabilitation of the chicken egg. Consumption of 6 to 12 eggs per week in balanced diets has no negative effect on major risk factors for cardiovascular disease and type 2 diabetes [68]. A nutritional analysis of 7,216 participants aged 55-80 found that moderate egg intake was not associated with increased risk of cardiovascular disease in both diabetic and non-diabetic patients [69]. In addition, the simultaneous consumption of whole eggs cooked with fresh vegetable salad is an effective way to increase the absorption of α-tocopherol and γ-tocopherol, as well as carotenoids from plant foods [70, 71].

An adequate supply of vitamin D_3 is essential to maintain public health. In recent years, many countries have applied technological fortification of food products (yoghurt, bread, etc.) [27, 72, 73]. As to the role of biofortification, it should be noted that there is no production of vitamin substances in Russia. Food, medical and agricultural requirements for vitamin substances are met only through imports [72].

Thus, the use of alternative ways of enriching food products with vitamin D is vital, to some extent contributing to the solution of the problem of import substitution. Biofortification of chicken, pork, eggs and dairy products with vitamin D by UV irradiation of animals is perspective. So far, plant sources of vitamin D have not been given due importance, but the possibility of increasing the vitamin D content of mushrooms and plant oils through UV irradiation, makes it advisable to obtain these products that are important for vegetarians.

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