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Dietary Sources of Vitamin D, Vitamin D Supplementation, and Its Bio-Viability

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The focus of this paper is to review the data on the dietary sources of vitamin D, vitamin D supplementation and its bio-viability. Vitamin D is a fat-soluble vitamin that plays an important role in human health. Low vitamin D levels (<75 nmol/l) have been reported worldwide in all age groups in recent years. Vitamin D deficiency is rising, mainly due to modern lifestyle and malabsorption disorders. There are two main sources of vitamin D; dietary source which includes food of animal and plant origin as well as dietary supplements and endogenous synthesis under the UVB radiation in the skin. Dietary sources rich in vitamin D are mainly fish oil, sea fish, eggs, and margarines fortified with vitamin D. As the adequate intake of vitamin D is hard to achieve through the diet alone, dietary supplements of vitamin D are recommended. However, there are different factors influencing the bioavailability of vitamin D and are explained within this review article. There is no universal consent on the amount and the frequency of vitamin D supplementation. Furthermore, there is still missing information for better understanding the vitamin D absorption, bioavailability, and metabolism in human. **Conclusion** – A brief mini review article on vitamin D summarizes the current knowledge about dietary sources of vitamin D, vitamin D supplements, and its bio-viability. The best source of vitamin D is *in vivo* synthesis in the skin under the UVB radiation. The main dietary sources of vitamin D includes food of animal and plant origin. Adequate intake of vitamin D through the diet alone is hard to achieve, therefore vitamin D supplementation is recommended.

Introduction

Vitamin D, traditionally known as an essential nutrient, is a precursor of a potent steroid hormone that regulates a broad spectrum of physiological processes. It has many functions in our body; it optimizes bone health, muscle function, cardiovascular system, immune system, inhibits cancerogenesis, positively alters the gut microbiota, and many other (1–5).

The term "vitamin D" encompasses two molecules: cholecalciferol (vitamin D_3; sourced from the skin exposure to ultraviolet B radiation (UVB, usually sunlight) and food of animal origin) (6) and ergocalciferol (vitamin D_2; source: food of plant origin) (7). It is believed that the cutaneous *in vivo* synthesis of vitamin D due to sun exposure is sufficient to meet daily vitamin D requirements (6). However, geographical reasons (latitude above/below 40° during from October till April), socio-cultural reasons (clothing, strong sunscreen protection factor, inadequate nutrition such as vegan diet), religious reasons (veiled clothing), and physiological reasons (skin pigmentation, age, obesity, chronic diseases, genetic abnormalities), may have a strong negative impact on synthesis of vitamin D in the skin (6–9).

Despite all the beneficial effects from vitamin D, the World Health Organization recommends avoiding outdoor activities at midday, especially between 10 a.m. and 4 p.m. (10). Nevertheless, the current policy of sun avoidance is creating probable harm for the general population, therefore different experts engage the World Health Organization, and other health entities in an immediate effort to define and quantify comprehensively the benefits and harms of sun exposure. Concrete recommendations for exposure at an individual level that are both safe and beneficial should be created (11).

Vitamin D metabolism may begin in the stomach where foods are subjected to acidic conditions and gastric enzymes. In the duodenum, digestive enzymes, e.g. proteases, amylases and lipases, continue to release vitamin D from the food matrix. Vitamin D is assumed to follow the fate of lipids in the human upper gastrointestinal tract. It is also assumed that it is secreted in the chylomicrons and then transported to the liver (12). The absorption of vitamin D is facilitated by protein-mediated diffusion transport, depending upon its concentration and the affinity of these transporters which may vary regarding the molecular forms of vitamin D (6). Partly also cholesterol transporter mechanisms might be involved in vitamin D absorption (13). Recently it was hypothesised that gut microbiota may also have an important role in vitamin D metabolism (14). Specific enzymes in the liver convert vitamin D into 25-hydroxyvitamin D3 (25(OH)D3), followed by the hydroxylation of 25(OH) D3 into the 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) which is the highly bio-active form of vitamin D. Excess concentration of vitamin D in the blood stream is stored in adipose tissue and skeletal muscles (15). The level of 25(OH)D3 in the blood is an indicator of vitamin D status of the patient. Its blood concentration depends on dietary intake (food and/or dietary supplements) and exposure to ultraviolet B radiation (UVB, usually sunlight) (15, 16). It would be hard to reach acceptable blood levels of vitamin D through the diet alone, so supplementation is advised for all age groups, especially during winter time above/below 40° latitude (October to April) when the production of vitamin D in the skin through the sun exposure is insufficient (16–18).

However, there is a lack of standardised methods used to measure 25(OH)D3 status, with different tests producing very different results (19). Some laboratories use conventional units (ng/ml), whereas other laboratories use international system (SI) units (nmol/l) for reporting 25(OH)D3 concentration (conversion: 1 ng/ml = 2.496 nmol/l). Endocrine Society established ranges of serum 25(OH)D3 concentration indicating vitamin D deficiency (<20 ng/ml (<50 nmol/l)), suboptimal status (20 – 30 ng/ml (50–75 nmol/l)) and target concentration for optimal vitamin D effects (30–50 ng/ml (75–125 nmol/l)) (20, 21). Generally the concentration above the 125 nmol/l is not recommended as the long-term safety of such level is still unknown (22). However, in clinical practice the phrase international unit (IU) for vitamin D intake is often used (conversion: 1µg of vitamin D_2 or D_3 = 40 IU).

When vitamin D is supplemented, caution should be taken into account, because of possible toxicity of excessive oral vitamin D intake (6). However, the increasing use of vitamin D supplements has also seen a substantial increase in the number of reports of vitamin D intoxication (23). The features of vitamin D toxicity are mediated through hypercalcaemia, and symptoms range from mild, such as thirst and polyuria, to severe, including seizures, coma and death (24). It is found there is no risk for vitamin D toxicity from prolonged exposure of UVB to the skin (25).

To avoid the overdosing, European Food Safety Authority (EFSA) has set the Tolerable Upper Intake Levels (UL) for vitamin D intake. UL for adults (including pregnant and lactating women and adolescents aged 11-17 years) is set at 100 μg/day (4,000 IU/day), for children aged 1-10 years at 50 μg/day (2,000 IU/day), for infants aged 6-12 months at 35 μg/day (1,400 IU/day), and for infants aged up to 6 months at 25 μg/day (1,000 IU/day) (26, 27).

This paper presents data from the scientific literature, and discusses the role of dietary sources of vitamin D, vitamin D supplementation, and its bio-viability.

Dietary Sources of Vitamin D

Dietary sources of vitamin D (vitamin D_3 and D_2) generally account a very small amount of total vitamin D in the body (28). It was thought that bioavailability of vitamin D_3 and D_2 are not the same (29), but similar absorption efficiency was recently proven (6). Apart from vitamin D_2 and vitamin D_3, hydroxylated vitamin D (25(OH)D3) also contributes significantly in dietary vitamin D, if food derives from animal origin. The difference in their polarity (polar-hydroxylated form and nonpolar-nonhydroxylated form) may contribute to their biological equivalence inconsistency. It was found that bioavailability of hydroxylated form (25(OH) D3) is 10 times greater than that of the non hydroxylated forms (vitamin D_2 and vitamin D_3) vitamin D (6). Dietary sources rich in vitamin D are mainly fish oil, sea fish, eggs, and margarines fortified with vitamin D. A

Table 1. Selected dietary sources of vitamin D (μg and IU/100 g) (30)

Food items	μg/100 g	IU/100 g
Fish oil		
Cod liver oil	250	10000
Fishes		
Smoked herring	32	1280
Salted mackerel	25	1000
Carp	25	1000
Eel	20	800
Salmon	16	640
Trout	15	600
Sole	15	600
Marinated herring	13	520
White fish	12	480
Canned salmon	12	480
Caviar	12	480
Sardines	11	440
Oysters	8	320
Tuna	5	200
Meat and meat products		
Chicken liver, beef frankfurter	1.2	48
Turkey frankfurter	0.6	24
Veal, liver	0.3	12
Eggs		
Yolk	5.6	224
Egg powder	5.0	200
Hens eggs, fresh or boiled	2.9	116
Milk and milk products		
Butter	1.2	48
Cheese (45.0% milk fat)	1.0	40
Yoghurt (3.5% milk fat)	0.1	4
Pasteurized milk (3.5% milk fat)	<0.1	<4
Sterilized milk (1.6% milk fat)	<0.1	<4
Human milk	<0.1	<4
Margarines		
Becel pro-activ, maja	7.5	300
Rama klasik, back, creme	2.5	100
Plant based sources and vegetable drinks		
Soy drink	1.4	56
Enriched rice drink	1.1	44
Mushrooms	<0.1	<4

compilation of vitamin D content of various food groups based on food composition data base (30) is provided in Table 1. Individuals who avoid consuming food of animal origin, such as vegetarians and vegans, might have lower 25(OH)D3 concentration in comparison with meat and fish eaters and therefore supplementation with vitamin D is advised (31, 32). Due to the lack of representative survey data, it is hard to estimate vitamin D daily intake accurately as food consumption patterns vary with social economic status. Besides, the food database is often incomplete or lacking compositional data regarding vitamin D concentration in a certain food/dish, which may result in lower dietary intake of vitamin D (33). However, the web-based application's assessment of dietary vitamin D intake, as well as other macro- and micronutrients of the patient, is very useful (34).

Vitamin D Supplementation

As adequate intake of vitamin D is hard to achieve through diet alone, even when fortified, the dietary supplements with vitamin D are recommended (35). However, there is data speculating the daily intake of vitamin D via food alone and in combination with dietary supplements. In most European countries, there seems to be a shortfall in achieving current vitamin D recommendations (7, 18, 36–41). Vitamin D insufficiency, as well as deficiency, are well-documented, not only in Europe, but also in the general population around the world (16). It has been estimated that 80% of young people in Europe do not have adequate vitamin D intake (42). An exception is Finland, where dietary survey data indicates that recent national policies that include fortification and supplementation, coupled with a high habitual intake of oil-rich fish, have resulted in an increase in vitamin D intake, but this may not be a suitable strategy for all European population (36).

Calcitriol (1,25-hydroxyvitamin D), calcidiol (25-dihydroxyvitamin D), cholecalciferol (previtamin D_3), ergocalciferol (previtamin D_2) and 7-dehydrocholecalciferol (provitamin D) are the major forms of vitamin D available on the market (6). Calcitriol is considered as the most active form of vitamin D, while calcidiol is an inactive form of vitamin D which helps in the storage of vitamin D in tissues. Further, vitamin D_2 and vitamin D_3 are precursors of the active vitamin D (6).

The bioavailability of vitamin D in oil vehicles is greater than that of powder-based vehicles such as starch and cellulose. In contrast to this, the bioavailability of vitamin D in lactose capsule is higher than that of oily drop formulation. These supplements are made by changing physical properties (encapsulation of vitamin D) as well as chemical alteration of vitamin (vitamin D ester and salt) (6).

Currently, there is no universally accepted dose and frequency for the vitamin D supplementation among neonates, children, adolescents, pregnant and lactating women, adults and elderly – every country has their own recommendation regarding vitamin D supplementation (43). Interestingly, sufficient vitamin D supplementation (4,000 IU/day) of the lactating mother (38) is resulting in sufficient amount of vitamin D in human milk (400 IU/day) which is named as "shifting the vitamin D paradigm" (44). However, further research on this field is needed before making such a strong recommendation for nursing mothers.

Benedik et al., 2013 summarized different recommended vitamin D allowances for different age groups across the world; the recommended values varies from 200 IU/day in Australia and New Zealand for general population (children to adults) and up to 2,000 IU/day for pregnant and lactating mothers in Canada (43). This supports lactating mothers who take great pride in providing complete nutritional support to their breastfed infants.

However, maternal supplementation supports the health of mother and infant at once, nevertheless, current infant supplementation can leave the nursing mother with severe vitamin D deficiency (45). Recent evidence supports the fact that low maternal vitamin D status is also associated with an increased risk of adverse pregnancy outcomes (46).

However, EFSA set the adequate intake (AI) for vitamin D for infants aged 7–11 months to be 10 µg/day (400 IU/day), for children aged 1–17 years and adults, including pregnant and lactating women, set at 15 µg/day (600 IU/day) (26), similar recommendations have also other international institutions which are summarized elsewhere (47). For example in Austria, Germany and Switzerland they have the following recommendations: 10 µg/day (400 IU/day) for 0-12 month infants and 20 µg/day (800 IU/day) for all others (children, teenagers, adults, pregnant and lactating women and elderly persons) (17).

Particular population subsets, such as pregnant women, neonates, elderly persons (not adequately exposed to sun radiation), and patients (affected by fat metabolism and genetic variations in protein associated to vitamin D uptake in intestine) are obligated to get vitamin D from supplements (48).

Bioavailability of Vitamin D from Food and Dietary Supplements

Bioavailability is defined as the proportion of ingested amount (total vitamin in food) which ultimately ends up in the systemic circulation (6).

The acidic pH of gastric juice might affect the bioavailability of vitamin D as well as protein-digesting enzymes (pepsin and trypsin) might be also involved in vitamin D absorption as they cleave vitamin D-binding proteins present in food and thus facilitate its release (6). Further, in duodenum digestive enzymes (amylases, lipase and protease) continue the release of vitamin D from food matrix (6). Before absorption, vitamin D needs to be released from its matrix and get accessible to enterocytes. Recently it was thought that the bioavailability of vitamin D is affected by amount of ingested food and its complexity, but it was found that this does not impose any variation of bioavailability of vitamin D and it was found as effective as vitamin D_3 supplements (48, 49).

The absorption of vitamin D supplements (vitamin D_2 and vitamin D_3) may be increased up to 50%, if taken with a large meal (usually lunch). Increased absorption might be caused by high secretion of digestive enzymes (after a heavy meal) or due to some specific food components in the meal (fat) (35). When vitamin D was supplied through meat, its bioavailability was estimated to be 60% as compared to vitamin D supplement. The vitamin D_2 from UV radiated mushroom was also tested, but their bioavailability was not compared with any other food matrix (50, 51). However, it was demonstrated that the mushrooms containing vitamin D_2 have similar biological equivalence as supplemental vitamin D_2 and vitamin D_3 (53).

Vitamin D absorption might be affected by the species of fatty acids of different chain length and degree of saturation. It is proposed that monounsaturated fatty acids increase the absorption of vitamin D more than polyunsaturated fatty acids (6, 53). Besides, the amount of fat ingested does not affect vitamin D absorption (12). Dietary fiber may also affect the bioavailability of vitamin D from food matrix, but more dedicated studies are required to understand the effect of dietary fibers on vitamin D bioavailability (6). Nutrient status of the host might also have an important role on vitamin D absorption. Nutrients such as vitamin A, E and K, as well as different phytosterols, follow common pathway used in vitamin D uptake, which imposes competitions for vitamin D absorption in intestine. Vitamin A reduces absorption for 30%, vitamin E for 15-17% and phytosterols for 16-36% (6, 54). Person suffering from obesity consumes several antiobesity drugs and fat substitutes to reduce the fat quantity in their diet, which impairs vitamin D absorption. Absorption of vitamin D is also low when using inhibitors of gastric and pancreatic lipases. In addition, different cholesterol derivatives from plant origin that are used for cholesterol absorption reduction may also affect the bioavailability of vitamin D (6).

Conclusion

This review shows the main dietary sources of vitamin D, which includes food of animal and plant origin, as well as dietary supplements. Adequate intake of vitamin D through the diet alone is hard to achieve, therefore vitamin D supplementation is recommended. However, the best source of vitamin D is *in vivo* synthesis in the skin under the UVB radiation. There are different factors influencing the bioavailability of vitamin D from food as well as from dietary supplements, but still, the fundamental mechanisms involved in vitamin D absorption are far from fully understood. Clinical studies with labelled vitamin D (deuterated or 13 C) are needed to be done to assess the effects of different factors on vitamin D bioavailability.

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