G Model
SBMB 4783 No. of Pages 5
ARTICLE IN PRESS
Journal of Steroid Biochemistry & Molecular Biology xxx (2016) xxx–xxx
Contents lists available at ScienceDirect
Journal of Steroid Biochemistry & Molecular Biology
journal homepage: www.elsevier.com/locate/jsbmb

Review

Sunlight exposure: Do health benefits outweigh harm?

Mohammed S. Razzaque, MBBS, PhD[a,b,c,d,*]

[a] Department of Applied Oral Sciences, Forsyth Institute, Cambridge, MA, USA
[b] Department of Pathology, Saba University School of Medicine, Saba, Dutch Caribbean, Netherlands
[c] Department of Oral Health Policy & Epidemiology, Harvard School of Dental Medicine, Boston, MA, USA
[d] Department of Preventive & Community Dentistry, Rwanda University School of Dentistry, Kigali, Rwanda

ARTICLE INFO

Article history:
Received 25 July 2016
Received in revised form 31 August 2016
Accepted 10 September 2016
Available online xxx

Keywords:
Vitamin D
Sunlight
Supplements
Bone
Calcification
Toxicity

ABSTRACT

Vitamin D is a fat-soluble vitamin whose levels within the body are elevated following sunlight exposure. Numerous studies have shown that sunlight exposure can provide protection to a wide variety of diseases, ranging from different types of tumors to hypertension to type 1 diabetes to multiple sclerosis. Moreover, studies have shown that avoiding sunlight may influence the initiation and progression of some of these diseases. Avoidance of sunlight, coupled with the inclination towards consuming supplements, is becoming the primary choice to obtain vitamin D. The purpose of this article is to present evidences from published literature, to show that the expected benefits of vitamin D supplements are minimized by the potential risk of cardiovascular events and beyond. Since hypovitaminosis D status usually reflects reduced sunlight exposure, the obvious primary replacement should be safe sunlight exposure, and not exogenous supplements.

Contents

1. Vitamin D

Vitamin D, also known as the sunshine vitamin, plays an important role in calcium and phosphorous metabolism and skeletal mineralization [1–6]. Vitamin D synthesis is partly triggered when the skin is exposed to ultraviolet (UV) B rays from sunlight. The obtained Vitamin D from sunlight exposure then undergoes two hydroxylations – first in the liver and then in the kidney to produce the physiologically active form 1,25-dihydroxyvitamin D [1,25(OH)2D], which is also known as calcitriol (Fig. 1). It is believed that, in humans, around 10,000 units of vitamin D are generated within 30 min of full body exposure to the sun [7]. Exposure to sunlight is the main source of vitamin D. UVB radiation (wavelength of 290–320 nm) is able to penetrate exposed skin and can convert cutaneous 7-dehydrocholesterol to previtamin D3, which undergoes further hydroxylations in the liver and kidney to produce bioactive vitamin D3 [1]. Several factors influence UVB exposure and subsequent vitamin D synthesis such as the aging process, state of skin pigmentation, application of sunscreen, the time of sunlight exposure during the day, air pollution, and geographical locations (e.g., higher latitude) [8]. Of particular importance, UV energy is significantly reduced when the sun is completely covered by clouds, and the extent of cloud cover (light to very dark) and latitude can also influence the availability of UV energy. Also, shade by severe air pollution can reduce UV energy by 60% [9]. Moreover, indoor exposure of sunlight through a window does not induce dermal vitamin D

* Correspondence to: Department of Applied Oral Sciences, Forsyth Institute, 245 First Street, Cambridge, MA, 02142, USA.
E-mail addresses: mrazzaque@forsyth.org, mrazzaque@hms.harvard.edu (M.S. Razzaque).

http://dx.doi.org/10.1016/j.jsbmb.2016.09.004
0960-0760/

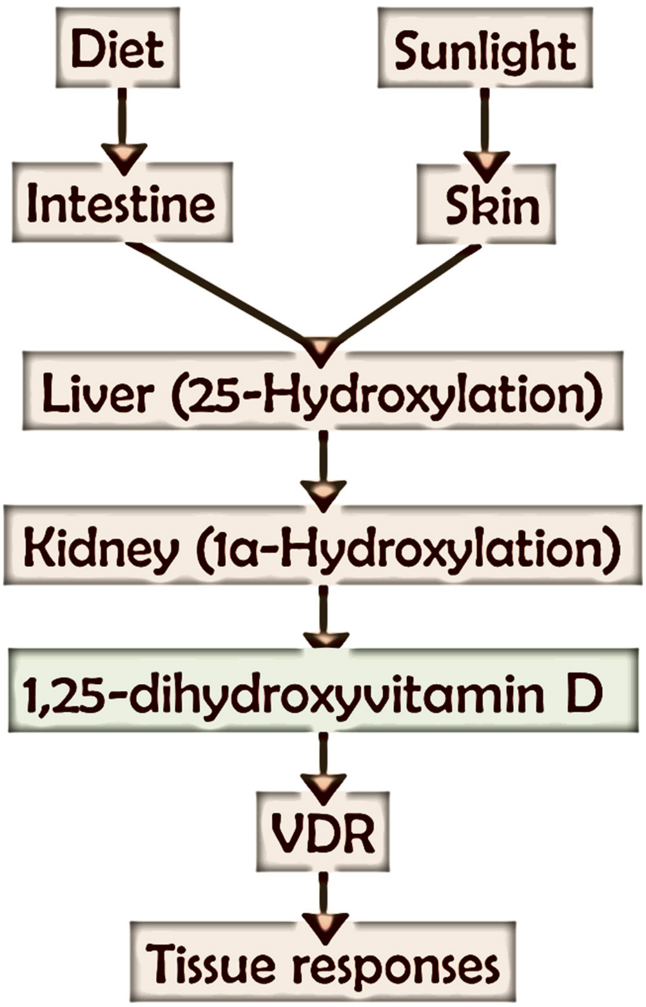

Fig. 1. Simplified diagram of the different stages of vitamin D synthesis, modified from earlier publications [1,69]. For simplicity, only essential steps of vitamin synthesis are included. **VDR**: vitamin D receptor.

synthesis, as UVB radiation is not able to penetrate through glass [10,11].

Though physiologic regulation of calcium and phosphate balance is an important function of vitamin D, the presence of vitamin D receptors (VDR) in the cellular components that are not actively involved in mineral ion metabolism raises the possibility of a wider biological role for vitamin D. In fact, studies have found a vital role for vitamin D in cell growth, immune regulation, and inflammatory modulation [12–17]. Serum level of precursor 25-hydroxyvitamin D [25(OH)D] is usually used to predict vitamin D status, with a circulating half-life of about 15 days [18]. However, serum 25(OH)D levels do not reflect the amount of vitamin D stored in various tissues, particularly in the adipose tissues. Experimental studies have shown that orally administered cholecalciferol rapidly accumulates in adipose tissue, and that it is very slowly released in periods of negative energy balance; the investigators concluded that adipose tissue is likely to act as a ‘buffer to functional vitamin D status’ by preventing unregulated production of 25(OH)D from dietary vitamin D up to a certain extent, and by slowly releasing vitamin D during fasting conditions [19]. Storage of the lipophilic vitamin D_3 molecule in the adipose tissue, therefore, can reduce the serum bioavailability [20,21]. Moreover, muscle tissue is also an important vitamin D reservoir, perhaps stored as 25(OH)D [22].

Table 1
Recommendations by Endocrine Society and Institute of Medicine (IOM) for vitamin D status by serum 25-hydroxyvitamin D [25(OH)D] levels [8].

	Endocrine Society	IOM
Deficient (ng/mL)	0–20	0–11
Insufficient (ng/mL)	21–29	12–20
Sufficient (ng/mL)	30–100	>20
Adverse effects (ng/mL)	>100	>50

While there is no debate on how inadequate vitamin D levels can induce certain bone diseases, including rickets (in children) and osteomalacia (in adults), there is, however, no general consensus on the optimal levels of vitamin D. According to Institute of Medicine (IOM), 25(OH)D levels of ≥20 ng/mL are considered sufficient, and when serum 25(OH)D levels are 12 ng/mL or less, persons are at risk of developing consequences related to vitamin D deficiency. According to IOM, serum levels >50 ng/mL could exert potential harmful effects as well (Table 1), and studies have shown that serum levels of 30–48 ng/mL can be linked to increase in all-cause mortality, higher risk of tumor formation and cardiovascular disorders, with more falls and fractures among the elderly individuals [8]. A large study conducted on 247,574 patients showed an increased risk for all-cause mortality (HR 1.42, 95%CI 1.31–1.52) above the range of 50–60 nmol/L of 25(OH)D. These authors concluded that 20–24 ng/mL is an optimal level [23], which supports the IOM findings and recommendations. Of relevance, the Vitamin D Council recommends serum 25(OH)D levels of 40–80 ng/mL as sufficient, while the Endocrine Society recommends 30–100 ng/mL as sufficient. It is important and perhaps alarming to note that the recommended upper limit from both expert groups falls into the harmful range of IOM recommended values (Tables 1 and 2).

2. Sunlight and vitamin D synthesis

It is an accepted fact that moderate sun exposure is sufficient to maintain adequate vitamin D levels to protect bones from diseases like rickets and/or osteomalasia [4,9]. Experts believe that approximately 5–30 min of sunlight exposure between 10 a.m. to 3 p.m. in most human populated latitudes, at least twice a week, to the face, arms, legs, or back without sunscreen can provide the required amount of vitamin D [7]. In addition to particular time of the day, seasons, likes winter can also influence production of vitamin D in skin; similarly, in some latitudes, vitamin D is not synthesized even between 10 a.m. to 3 p.m. The influence of time of the day, season, and solar zenith angle in the synthesis of vitamin D are summarized by Engelsen, and interested readers are recommended to that publication for more details [24]. Of relevance, National Health and Nutrition Examination Surveys (NHANES) found serum 25(OH)D levels were higher in blood samples

Table 2
Recommended daily intakes by Endocrine Society and Institute of Medicine (IOM) [8].

	Endocrine Society	IOM
Infants (IU/day)	400–1000	400
Children (IU/day)	600–1000	600
Adults (IU/day)	1500–2000	600 (seniors: 800)