Vitamin D and the skin: A complicated relationship

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ABSTRACT

We have known for centuries that vitamin D is a key player in keeping our bones strong. It has only been known for a few decades that it is also crucial in the functioning of many other tissues, including the skin. However, the skin is not just a place of vitamin D synthesis, but also an organ that needs vitamin D for undisturbed physiological processes. Studies have shown vitamin D deficiency to be involved in inflammation-related skin diseases, such as acne, atopic dermatitis, psoriasis, systemic lupus erythematosus, vitiligo, skin cancer and hair loss.

Keywords: cosmetics, skin, sun, vitamin D

Article category: Professional article
Presern A. Vitamin D and the skin: A complicated relationship. Cos ACTIVE J. 2021;1:22–26

BRIEF INTRODUCTION

In relation to the COVID-19 pandemic, vitamin D has been gaining growing attention lately, and you have probably heard that much of the world's population is vitamin D deficient. What is it and why is it so important (also for the skin)?

FIRST THERE WERE HEALTHY BONES

Vitamin D is a lipid-soluble vitamin that has been primarily recognised for its significance in bone formation, but it has so much more to offer. It is involved in the serum **homeostasis of calcium** where it increases the absorption of calcium and phosphate in the intestines. This consequently stimulates bone calcium mobilisation, but in case of vitamin D deficiency, calcium is pulled from the bones in order to increase its serum levels (1, 2).

Other effects of vitamin D at the cellular level include cell proliferation and the inhibition of angiogenesis, cell differentiation and the promotion of apoptosis, as well as the regulation of more than 200 genes. It plays a role in the functioning of almost every tissue and organ, including the **heart, immune system, muscles, pancreas, brain, skin** and others in addition to the **bones**. Vitamin D deficiency has been linked to many health disorders, including autoimmune, cardiovascular and neurological diseases, psychological issues and cancers (1, 2).

NAVIGATING BETWEEN NEEDS AND SUPPLY

There are three sources of vitamin D for the human body: synthesis in the skin following sun exposure, diet and vitamin D supplements. It exists in two forms: as **vitamin D2** (ergocalciferol) and **vitamin D3** (cholecalciferol). In the skin, only vitamin D3 is formed after exposure to the UVB spectrum of light (maximum of around 295 nm), but with food and supplements, we can get both. The main food sources of vitamin D3 are certain fishes (salmon, mackerel, sardine and tuna) and egg yolks, while vitamin D2 is found, in much smaller amounts, in fungi. Since it is almost impossible to achieve sufficient vitamin D levels from food sources alone, there are some fortified foods (mostly milk and dairy products), food supplements and medicines available on the market. They mostly contain vitamin D2, but both forms are believed to act equally (1–3).

Regardless of the vitamin D source and form, once it is in the blood circulation, it must be converted first by a hepatic enzyme and later also in the kidneys to reach its final active form, named 1,25-dihydroxyvitamin D or calcitriol. Since it is a lipid molecule, it can be stored in body fat tissue, which extends the half-life of vitamin D up to a few weeks (1).

There are many possible reasons for **vitamin D deficiency**: limited sunlight exposure, dietary intake and absorption inadequacy, insufficient conversion in the liver or kidneys, elevated requirements and also increased excretion. Some clinical conditions that predispose patients to vitamin D deficiency are osteoporosis, chronic kidney disease, liver failure, celiac and inflammatory bowel disease, as well as endocrine disorders. Individuals on medications such as corticosteroids, anticonvulsants, antiretrovirals and hormonal treatments prescribed for cancer are also at greater risk for vitamin D deficiency. Pregnancy can also cause lower vitamin D levels (3).

VITAMIN D AND THE SKIN

In this article, we will focus on the relationship between vitamin D and the skin. It is a fundamental vitamin in skin physiology, not just because it can be synthesised in the skin, but also because of its multiple roles in many skin processes and diseases.

A good estimate seems to be that around 5–30 minutes of **sun exposure in spring and summer**, especially between 10 am and 4 pm, to the face, arms, hands and legs without a sunscreen usually leads to the sufficient synthesis of vitamin D. If an adult in a bathing suit is exposed to sun radiation strong enough to cause minimal erythema (slight pink colour of the skin 24 hours after exposure), one is able to synthesise more than 10,000 IU of vitamin D. For comparison, up to 1000 IU in food supplements is recommended per day (3, 4).

However, vitamin D production in our skin depends on many different factors. Among environmental factors are geographic latitude (the zenith angle of the sun), altitude, weather conditions and the level of air pollution where we live, as well as the season and time of the day. Keep in mind that in the winter months, when living above or below approximately 30° latitude, sun exposure can account for very little or no vitamin D production in the skin at all (5).

Important variables regarding vitamin D synthesis are mostly age, weight and skin type. The lighter the skin tone, the more efficient is vitamin D synthesis in the skin. People with darker skin absorb more radiation by melanin and consequently need more sun exposure to synthesise the same amount of vitamin D. Thinner skin in elderly people makes them less able to produce vitamin D. In addition, obesity has been linked to lower vitamin D levels, since the vitamin can get 'trapped' in body fat. Our habits also affect the production of vitamin D, such as the amount of time spent outdoors (yes, sitting by an office window won't help, since glass blocks most UVB radiation), how we dress during the time we spend outdoors and whether we are keen on using sun protection or not.

Using a sunscreen with a SPF of 30 already inhibits the synthesis of vitamin D by more than 95%. Controversially, the use of sunbeds increases vitamin D synthesis (but don't forget that they increase the risk of skin cancer) (3).

DEEPER IN THE SKIN

Vitamin D is known to regulate the skin differentiation process, stimulating the formation of the cornified envelope in keratinocytes and inhibiting proliferation, both as the result of increased intracellular calcium levels. It also regulates processes involved in the formation of a so-called skin barrier and the initiation of the innate immune response in the skin. Vitamin D is therefore crucial for skin defence and antimicrobial functions. Since vitamin D receptors are also present in the cells of the adaptive immune system (B and T cells), it plays an important role here, too. It suppresses their proliferation and modulates the production of cytokines. Vitamin D also promotes wound healing and tissue repair, and is important in the progression of the hair cycle and in the growth regulation of sebaceous glands (1).

Probably the most challenging aspect is how to achieve a healthy combination of the good and bad effects of sun radiation. It is well-known that UV light can be harmful, as it causes inflammation, skin aging, DNA damage, skin cell apoptosis and skin cancer. On the other hand, UV light is, as explained, the driving force behind vitamin D synthesis in the skin, and some studies have even confirmed the photoprotective effects of vitamin D: decreased erythema and DNA damage, reduced apoptosis and the increased survival of skin cells (1).

A STEP IN THE AREA OF DERMATOLOGY

Vitamin D deficiency can be involved in (sometimes an extremely complex set of) causes that lead to skin diseases. Those are, for example, acne, atopic dermatitis, autoimmune skin disorders such as psoriasis, systemic lupus erythematosus and vitiligo, skin cancer and hair loss (1). However, vitamin D deficiency is more likely to be related to the co-occurring inflammation processes than be the primary cause of a disease.

Acne

There is a significant role of inflammation in this very common skin disorder, resulting from increased colonisation by Propionibacterium acnes. Studies have shown an inverse relationship between the number and severity of acne lesions and serum levels of vitamin D.

Atopic dermatitis

Vitamin D is believed to improve atopic dermatitis, mainly through immunomodulation, as the disease is crucially connected to the impairment of the dermal immune system. Studies have shown that vitamin D alleviates symptoms of atopic dermatitis and thus decreases the severity of the disease.

Psoriasis

The pathogenesis of this chronic inflammatory skin disease includes the deregulation of the skin's immune cells, inflammation and angiogenesis. Vitamin D was shown to be effective in the treatment and/or mitigation of the disease due to its antiproliferative, anti-inflammatory and antiangiogenic activity. Alone or in combination, it is one of the most frequently prescribed topical medications for psoriasis.

Systemic lupus erythematosus

Vitamin D is believed to be effective in these patients due to its protective effects on the cardiovascular system, immunomodulation and the stimulation of cognitive development.

Vitiligo

Controlling the activation, proliferation and migration of melanocytes and pigmentation pathways are only some of the ways vitamin D protects the epidermal melanin units and restores melanocytes' integrity. It also acts as an antioxidant, reduces the apoptotic activity caused by UVB light and decreases the autoimmune response.

Skin cancer

Many studies have shown the tumour-protective effect of vitamin D, reducing risk for many different cancers, including those of the skin, and decreasing cancer-associated mortality. The main role of vitamin D seems to be its involvement in the regulation of many signalling pathways, the inhibition of proliferation, the promotion of apoptosis, the inhibition of angiogenesis and the altering of cellular adhesion.

Hair loss

Studies have shown that vitamin D stimulates the differentiation of hair follicles and thus regulates their growth cycle. Topical calcitriol was also found to protect against chemotherapy-induced alopecia.

LET'S NOT FORGET

We can conclude that vitamin D is really a 'skin vitamin': not only does it come from it, it is also vitally intertwined in so many of the skin's physiological processes. It is thus not surprising that many studies have linked vitamin D deficiency to various skin diseases, clearly demonstrating that our skin relies on our responsible lifestyle to provide enough vitamin D for the undisturbed activity of vitamin D-dependant functions.

However, vitamin D is categorised as an **active ingredient in medicines**. The European Union prohibits the use of both vitamin D3 and D2 in cosmetic products (listed as no. 335 in Annex II of Regulation (EC) No 1223/2009). Nevertheless, the vitamin D precursor **7-dehydrocholesterol** is described in the CosIng database as an emulsion stabilising, skin conditioning and viscosity controlling ingredient. Vitamin D provitamins are also permitted for use in cosmetic products in the US (4, 6, 7).

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