

The Skin Melanin: An Inhibitor of Vitamin-D3 Biosynthesis: With Special Emphasis with Structure of Skin. A Mini Review

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Abstract

Skin is the largest organ of the human body. It performs many functions like protection, acts as a physical, chemical and biological barrier, and also helps in the synthesis of vitamin D when exposed to UVB radiations. The color of the skin is usually determined by a pigment "The Melanin" which is present in the skin and is synthesized by melanocytes. The objective of the current review is to evaluate the effect of Melanin of Vitamin D synthesis.

Different search databases like Google Scholar, Pubmed, Mendeley, and Scopus were being utilized to find the relation between the production of vitamin D in the skin and its level of pigmentation. If the level of melanin increases, the skin becomes darker in color and vice versa. Melanin secretion is increased when skin is exposed to UV radiations. Melanin has photoprotective action and protects the skin from harmful effects of ultraviolet radiations. High melanin level inhibits the production of vitamin D in the skin. Vitamin D is a prohormone that helps in the absorption of calcium from the gut. Deficiency of vitamin D leads to many threats.

Keywords: Skin; Melanin; UV radiation; Vitamin-D3

Introduction

Vitamin D is a prohormone that facilitates the absorption of calcium from the gut. The insufficiency of vitamin D results in rickets in children while in adult its deficiency shows the way to osteomalacia [1]. A human receives vitamin D from many sources like from their diet, sun exposure, and other food supplements [2]. Daily recommended a dose of vitamin D for adult, children (between 6 months to 3 years) and infants in the United Kingdom (UK) is 400 IU (10 µg), 280 IU (7 µg) and 340 IU (8.5 µg) respectively [3].

Nearly 80% of the world population's skin is pigmented [4]. The four major types of pigments present in the skin are melanin, hemoglobin, carotene, and bilirubin, amongst this hemoglobin and melanin, are the skin color contributors [5]. Melanocyte cells in the basal layer of the epidermis are the ancestors of melanin production. The sun exposure, hyperpigmentation, and melasma are the initiator factors for melanin from melanocytes. Tyrosinase catalyzes melanin in melanocytes. This enzyme catalyzes two types of reactions; hydroxylation of tyrosine and oxidation of dopa. Oxidation of dopa produces highly reactive metabolites that form melanin by free radical coupling pathway. So production of melanin can be controlled; by protecting the skin from UV radiation and by inhibition of tyrosinase enzyme [6].

Anatomy of Human Skin

Skin is the largest organ and main physical barrier of the human body [7-11]. Its surface area is 2 m². An individual with 70 kg weight, his skin covers 5 kg of that total weight i.e. it is approx. 8% of total body mass. Its thickness is 1.5-4.0 mm in the range [8,12]. It has acidic pH, normally ranging from 4-6.8 [13,14]. Skin also have the ability to

retain moisture contents, that protect the skin from the fissure and cracking [15]. There is a balance of water content in skin, if this balance disrupts, then skin becomes dry and cause several infections like allergy and eczemas [16]. Hydration level of skin is important not only for barrier functions of skin but also it affects the enzymatic activity of stratum corneum [17]. Normally skin is divided into three layers; Epidermis, Dermis, and Hypodermis [18-22]. The epidermis is the outer most layer of skin generally composed of stratified squamous epithelia (Figure 1). It has variable thickness i.e. 50 µm on the eyelid, while on palm and sole it is about 1.5 µm thick [18]. It is divided into following layers; Stratum basale or stratum germinativum, Stratum spinosum or prickle cell layer, Stratum granulosum or granular layer, Stratum lucidum and Stratum corneum or top layer [23]. Dermis present below epidermis while above the hypodermis. It contains blood vessels to provide nourishment to epidermal cells [24]. It is the thickest layer of skin ranging from 0.3 mm-3.0 mm in diameter, usually thicker on the back while thinner on forearm [15,25]. It is usually composed of approximately 65% water and 20%-25% cells, ground substances, elastin and collagen protein [26]. The hypodermis is a lower layer of skin located under the dermis and chiefly consists of the adipocyte. These adipocytes are arranged in lobules forms that are separated from each other by connective tissue. About 80% of the total body fats store in subcutaneous adipose tissue [27].

Epidermal Cells

There are four different types of cells present in different layers of epidermis; Keratinocyte, Merkel cells, Langerhans cells, and Melanocytes cells [9]. Keratinocyte constitutes 80% total epidermal cells [28]. These cells contain a specific protein called keratin that plays important skin functions [9]. Merkel cell was first discovered by Freidrich Sigmund Merkel in 1875, mostly present in the basal epidermal layer of human skin [29-31]. These are clear, an oval-shaped cell with 10-15 µm diameter on the long axis and have spin like

projections on their surface with 2.5 μm in length [21]. These cells function as neuroendocrine sensory receptors as well as slowly adapting mechanoreceptors [32]. These cells were first time reported by Paul Langerhans in 1868, mostly present in lower epidermis and constitute of 3%-8% total epidermal cells [33-36]. These are clear branch shaped dendritic cells, produced in the bone marrow to participate in body immune system [37,38].

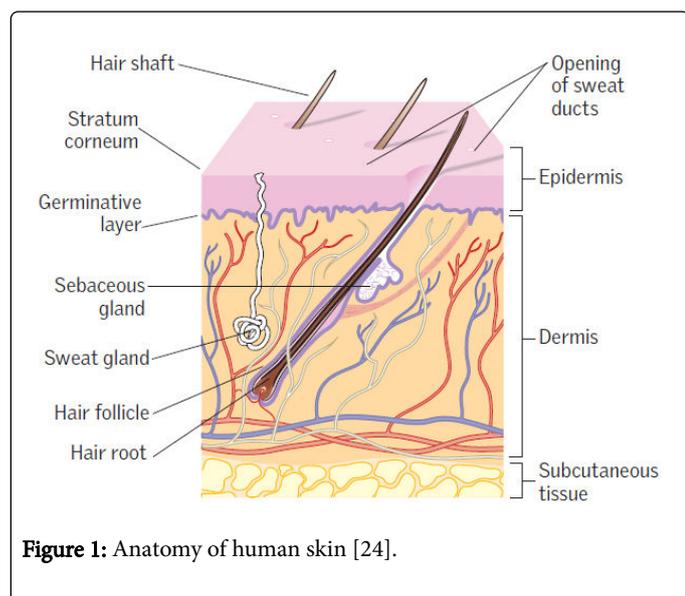


Figure 1: Anatomy of human skin [24].

Melanocytes

The melanocyte is the melanin manufacturing cells, habitually present on the inferior epidermal layer and matrix of hair bulbs [39,40]. These are exocrine in nature and about 1 mm^2 area of skin surrounded nearly about 1000-2000 melanocytes cells [41,42]. However, above the age of 30, there is diminishing the definite amount of melanocytes by 8%-20% per decade [43]. Melanocyte synthesizes melanosomes, which are gigantic in size in black skin peoples than white skin peoples and form a single unit rather than groups, yet it was found that if the size of melanosomes is smaller than $0.8 \times 0.3 \mu\text{m}$ they are physically aggregate to a single membrane unit called as phagosome, whereas the melanosomes greater than $0.8 \times 0.3 \mu\text{m}$ in size, do not group together in a single unit [41,44,45]. These melanosomes contain enzyme tyrosinase that is responsible for the production of melanin [46]. Melanocytic Golgi apparatus is the progenitor of this enzyme, whereas they manufactured and fetch to melanosomes during 1st stage of melanosomal development [41]. Melanosomal development accomplishes in four stages. The 1st stage is also called 'premelanosomes' with globe-shaped granules pack with unformed matrix; the stage 2 melanosomal granules are egg-shaped with febrile matrix; melanin toppling in the melanosomal matrix is more conspicuous during stage 3 and at the end of stage 4, melanosomal granules thoroughly charge with melanin [47].

Melanin is a biopolymer complex mixture of quinone/indole-quinone derivatives, it has two types; brown or black eumelanin and red or yellow pheomelanin [48]. Eumelanin is produced and stored in elliptical melanosomes, while rounded melanosomes usually produce pheomelanin [49]. Mature melanocytes form a branch-like structure that makes contact with neighboring keratinocytes, through these branching structure each melanocyte cell make contact with 30-40

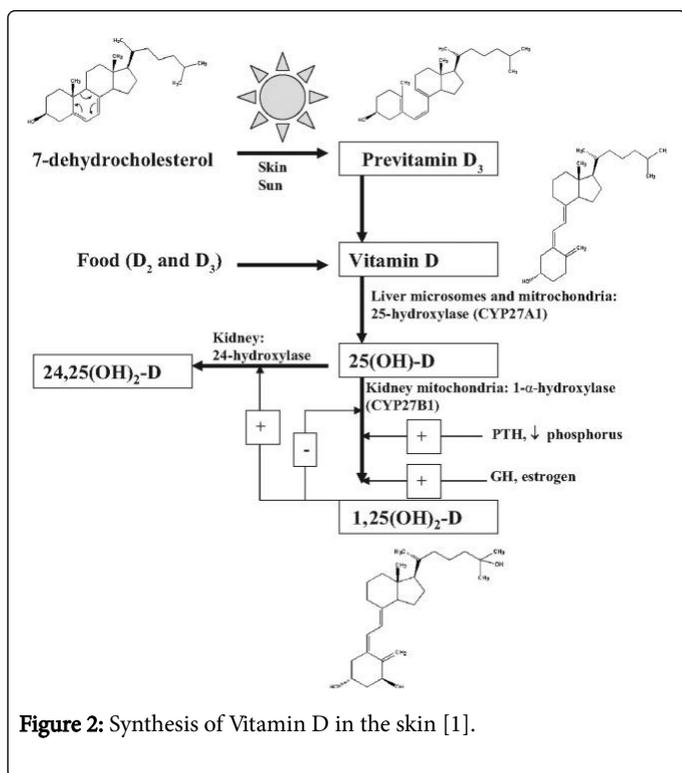
keratinocyte cells and this is known as epidermal melanin units. Through these units, melanocytes transfer melanin to keratinocytes [45]. Melanin level plays an important role in the determination of skin color and also have a protective role in sun-induced skin cancer i.e. chance of occurrence of skin cancer are more in the people with low melanin level and vice versa [24]. Eumelanin also plays an important role in the scavenging of free radicals. Melanin has photoprotective action and helps in the prevention of photoaging caused by ultraviolet radiation [40]. The degree of photoprotection is directly allied to the level of skin pigmentation. A white skin person can tolerate 1 SED before burning while black skin persons can tolerate 20 times as much [43].

Skin and Synthesis of Vitamin D3

Vitamin D3 is also known as calcitriol [3]. It is a fat-soluble vitamin, mostly found in fish, eggs, liver, butter, and margarine. It is also a synthesis in our body naturally when skin exposed to adequate sun exposure [50]. Skin epidermis plays an important role in the synthesis of vitamin D (Figure 2). When skin exposed to ultraviolet radiation (UVB wavelength 290-315nm), in epidermal cells it converts 7-dehydrocholesterol to pre-vitamin D3 [51]. The isomerization of pre-vitamin D3 produce vitamin D2, and then the process of hydroxylation in the liver converts this vitamin D3 into 25-hydroxyvitamin-D3. However, when this hydroxylated molecule arrives at kidneys, it transfers into 1- α , 25-dihydroxy-vitamin-D3 (calcitriol), which is an active form of vitamin D3 and help in calcium and bone metabolism [49,52,53]. It has been reported that if Vitamin D3 does not enter in the bloodstream before the exposure of next day, it rapidly degrades into suprasterol1, suprasternal and 5,6 trans vitamin D3, which are biologically inactive [54].

Melanin and Synthesis of Vitamin D3

Dark skin peoples have high melanin level in their skin than light skin peoples. Melanin has photoprotective action that protects the skin from the harmful effect of Ultra Violet radiation [40]. When melanin level increase in the skin, along with their photoprotective action it also reduce the production of vitamin D3 that's why darker skin peoples of high latitude are usually deficient with vitamin D3 than light-skinned peoples [54,55]. Natural sunlight consists of UVA and UVB, UVA is not much biological active than UVB. Only UVB help in the synthesis of vitamin D in the skin. But the question arises that how many doses of sun exposure or UVB exposure is required to maintain an optimum level of 25-OH-D. Because excessive Ultraviolet radiation exposure causes skin cancer [51]. However it has been reported that, for light skin peoples an exposure time from 20-30 min, two three times in a week is enough to produce around 20,000 IU of vitamin D3, while for dark skin peoples with high melanin level this exposure time increase 2-10 fold to get the same level of vitamin D3 [3,56]. Dark skin or pigmented skin protects the dermis from the harmful effect of Ultraviolet radiation. Light skin woman synthesis more vitamin D3 necessary for lactation and pregnancy [57]. Most of the African and Americans have dark skin and that's why they have usually with vitamin D3 deficiency [56]. Vitamin D deficiency and insufficiency is most common in the UK. Food Supplementations like infant's formula milk (1-2.5 μg (40-100 IU) per 100 kCa) and margarine (8 μg (320 IU) per 100 g) are required for infants and preschool children in UK, for those who have dark skin and hype pigmented [3].



Conclusion

Dark skin peoples have high melanin level in their skin. When melanin level increases it protects the skin from ultraviolet radiation and inhibit the synthesis of vitamin D in the skin. On the other hand, white skin or fair skin peoples have low melanin level in their skin. It has been noted that most African and Americans have dark skin and they have usually deficient with vitamin D. For this reason to overcome this problem in the UK, many food supplements contain vitamin D used as dietary products.

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