Vitamin D In Cutaneous Biology and Dermatological Disorders: Photobiology, Immunomodulation, And Therapeutic Implications

Mrs. Supriya Sagar Patil[1], Utkarsha Ramdas Patil[2], Diksha Jalindar Koli[3], Vaishnavi Ashok Jadhav[4]
[1,2,3,4]*Womens College of Pharmacy, Pethvadgaon*

***Abstract*—A major global health concern, vitamin D insufficiency is mostly caused by insufficient sun exposure. There are two main types of vitamin D: cholecalciferol (vitamin D_3), which is produced in the skin by ultraviolet B (UVB) radiation, and ergocalciferol (vitamin D_2), which is taken from plants. UVB-induced skin synthesis provides around 80% of human vitamin D, with dietary sources contributing very little. Vitamin D deficiency is still common in tropical locations despite plenty of sunlight, indicating that the current recommendations for sun exposure need to be reviewed. Vitamin D is essential for immune system control, skin health, and calcium balance. By binding to the vitamin D receptor (VDR), its active form, 1,25-dihydroxyvitamin D, affects a number of cellular functions, including proliferation, differentiation, and death. Vitamin D has both therapeutic and preventative values in dermatitis. Through improved DNA repair and prevention of tumor cell proliferation, controlled UVB exposure increases vitamin D production, guarding against DNA damage and perhaps lowering the incidence of melanoma. Melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) are among the skin cancers that are still primarily caused by excessive UV exposure. In BCC and SCC, vitamin D and its analogs have been demonstrated to inhibit carcinogenic pathways like Hedgehog signaling, suggesting chemopreventive potential.**

Because of its immunomodulatory and anti-proliferative properties, vitamin D has positive benefits on inflammatory skin conditions. Both oral and topical vitamin D derivatives control keratinocyte differentiation and proliferation in psoriasis, providing efficient treatment options for mild to severe conditions. Similarly, vitamin D promotes melanocyte function and modulates immunological responses to aid in repigmentation in vitiligo. Low serum vitamin D levels are linked to the severity of acne vulgaris, and taking supplements may help by lowering bacterial growth, inflammation, and sebum production. All things considered; vitamin D is an essential mediator in preserving skin

homeostasis and averting a variety of dermatological conditions. For both systemic and cutaneous health, optimizing vitamin D status by balanced sun exposure, diet, or supplementation is crucial.

***Index Terms*—Vitamin D, UVB radiation, skin cancer, psoriasis, vitiligo, acne vulgaris, vitamin D receptor, photoprotection.**

I. INTRODUCTION

1.1. Vitamin D:

A worldwide health issue, vitamin D insufficiency is mostly brought on by inadequate sun exposure.[1] In general, vitamin D consists of two molecules: ergocalciferol (vitamin D2; derived from plant-based foods) and cholecalciferol (vitamin D3; derived from skin exposure to ultraviolet B radiation (UVB, typically sunlight) on its precursor, 7-dehydrocholesterol, in skin and primarily animal-based foods. About 80% of the vitamin D supply in humans is thought to come from UVB-induced vitamin D3 synthesis in the skin, with food intake typically playing a much smaller role. It was thought that countries with sunny temperatures closer to the equator would have enough endogenous synthesis of vitamin D3 to meet daily needs, but surprisingly, production in these areas is still insufficient.

Therefore, it is necessary to reevaluate how beneficial the current recommendations for sun exposure are across different populations. The World Health Organization (WHO) advises against being outside between 10 a.m. and 4 p.m. in order to prevent excessive exposure to UVB radiation, which can affect the skin, eyes, and immune system and raise the risk of skin cancer. [2]

Our skin produces the majority of our vitamin D through exposure to UV radiation from sunlight, with very modest quantities coming from food. Since we get the majority of our vitamin D from the sun, it has historically been referred to as the "sunshine vitamin," which is a particularly fitting

moniker for vitamin D. [3].

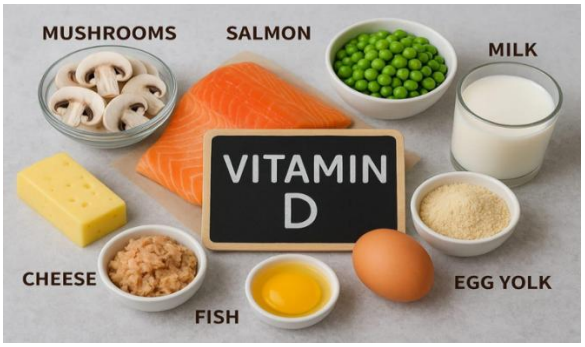

Fig 1. Sources of Vitamin D

Skin-resident 7-dehydrocholesterol is converted to vitamin D3 by solar UVB exposure. Vitamin D-25-hydroxylase in the liver subsequently transforms the resulting vitamin D3 and ingested vitamin D3 into 25-hydroxyvitamin D (25-D). The most prevalent circulating form of vitamin D, 25-D, is typically assessed when evaluating vitamin D status even though it is physiologically inactive. It doesn't activate the VDR in the cell nucleus until it has been converted to 1,25-dihydroxyvitamin D (1,25-D) by 25- hydroxyvitamin D-1α-hydroxylase in the kidney and other tissues. Deficiency in vitamin D is a very common illness. Despite the widespread use of supplements and foods fortified with vitamin D, an estimated 1 billion people do not have enough amounts of the vitamin.[4]

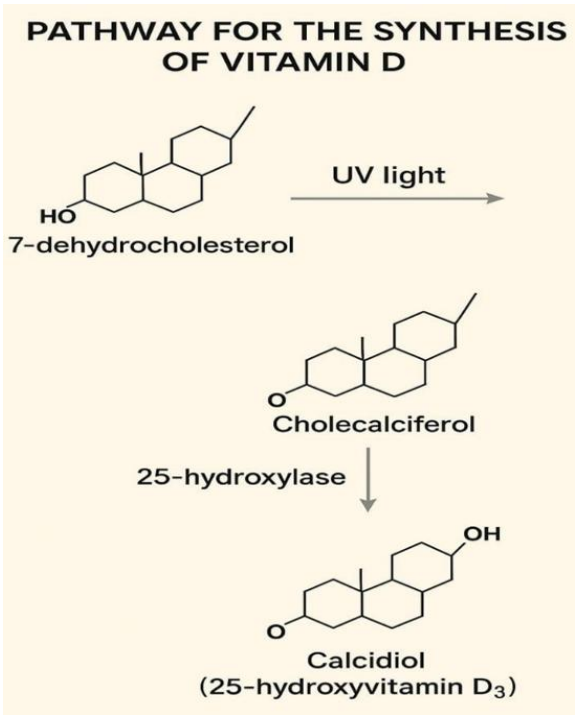

Fig 2. Pathway for the synthesis of Vitamin D

1.2. Vitamin D in skin pathology Skin cancer:

How much sunlight is enough to balance the benefits and drawbacks of solar UV exposure is a contentious topic in many scientific and public groups today.

Unquestionably, UV radiation damages skin cells' DNA and is a significant environmental risk factor for all forms of skin cancer. Geographically speaking, residing in regions of the world with higher average yearly bright light or erythemal UV increases the risk of developing skin malignancies, with squamous cell carcinoma having the highest risk, followed by basal cell carcinoma and melanoma. On the other hand, UV-B-mediated cutaneous photosynthesis of vitamin D is one of the ways that sunlight benefits human health.[5] Skin cancers come in three primary forms: cutaneous malignant melanoma (CMM), squamous cell carcinoma (SCC), and basal cell carcinoma (BCC), which is the most prevalent.[6]

1.3. Melanoma: -

There is clear proof that exposure to sunlight is the primary environmental factor that raises the risk of developing skin melanoma. Sunlight, however, is essential for the creation of vitamin D. Unquestionably, low vitamin D levels are linked to worse bone health, and a growing body of research indicates that low vitamin D levels raise the risk of numerous other illnesses, necessitating a balance between sun protection and exposure. We examine the data suggesting that exposure to sunlight may also prevent melanoma by promoting photoadaptation or increased levels of vitamin D. [7] The stratosphere's ozone layer absorbs the majority of the sun's UVB rays. The amount of solar UVB that reaches the earth's surface has progressively increased due to the stratosphere's ozone layer being destroyed. The proteins and DNA of cells frequently absorb energy from UV rays. Many kinds of mutagenic DNA damages are known to be induced by UV radiation. major photoproducts caused by UV lesions that cause cancer. Cyclobutane pyrimidine dimers (CPDs), pyrimidine-pyrimidone (6-4) photoproducts (6-4PPs), and their Dewar valence isomers are the main photoproducts caused by carcinogenic UV radiation. 5-methylcytosine-containing DNA regions have been found to be hotspots for UVB-induced mutations. It has been demonstrated more recently that UVB can also significantly degrade DNA, most likely through the p38 pathway by

generating oxidative stress and combining with the p53 process. [8]

The skin's synthesis of vitamin D shields the body from radiation and probably inhibits the development of melanoma. Vitamin D promotes DNA damage repair and lessens UV-induced DNA damage, including oxidative and genotoxic DNA damage. Both in vitro and in vivo, it prevents melanoma cells from proliferating and invading. Crucially, wearing sunscreen does not prevent the synthesis of vitamin D, but rigorous physical avoidance of sunlight raises the risk of vitamin D insufficiency. [9]

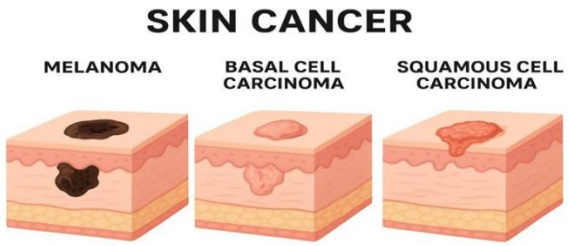

Fig 3. Melanoma skin cancer

1.4. Non- Melanoma: -

UV-B light (280–320 nm) from the sun and artificial sources can have both positive and negative impacts on human health. On the one hand, the most significant environmental risk factor for the development of NMSC, which is the most prevalent cancer in Caucasian people, is UV-B radiation. On the other hand, UV-B-induced cutaneous photosynthesis is primarily responsible for meeting the body's needs for vitamin D. This conundrum poses a significant issue for many people because it has been conclusively shown that vitamin D insufficiency is linked to a number of separate illnesses, including different forms of cancer.[10]

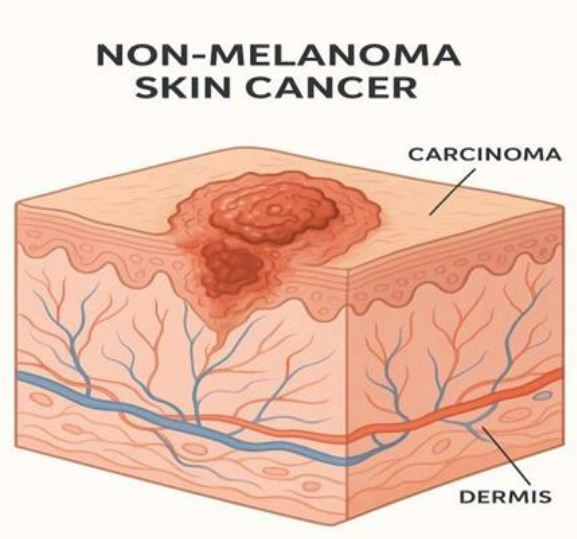

Fig 4. Non-melanoma skin cancer

Vitamin D's significance in basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) has been the subject of numerous investigations, much like in the case of melanomas. Similar to keratinocytes, BCC cells also express VDR; however, peripheral cells that develop BCC tumors exhibit considerably greater VDR expression than nearby, unaffected epidermal cells. Hedgehog signalling, a crucial tumor route in the development of BCCs, has been shown to be suppressed by vitamin D. After being exposed to a carcinogen, it was demonstrated that VDR-knockout mice were more likely than wild-type animals to acquire BCC skin tumors. In vitro and in vivo, topical vitamin D3 treatment suppresses the hedgehog signalling pathway and decreases BCC cell growth, according to additional mouse studies. Additionally, 1α,25(OH)2D3 suppresses SCC growth both in vitro and in vivo. Mice without VDR who are exposed to high and extended UVB doses are more likely to develop SCC tumors, according to similar research on animals. Furthermore, 1α,25(OH)2D3 administered topically inhibits the growth of chemically generated tumors in a dose-dependent manner, just like in BCCs. Furthermore, P450scc produces novel vitamin D3 analogues, 20(OH)D3, 20,22(OH)D3, and 20(OH)D3, which exhibit pro-differentiation, anti-proliferative, and anticancer qualities. Further human studies are required to evaluate the efficacy of topical or oral vitamin D3 supplementation in chemoprevention of non-melanoma skin cancer, even though in vitro and animal research indicated that vitamin D may inhibit the formation of BCCs and SCCs. [11]

1.5. Psoriasis: -

Psoriasis is a prevalent, inflammatory, chronic, and relapsing skin condition that affects between 1% to 4% of people worldwide. Vascular hyperplasia, inflammatory cell infiltration into the dermis and epidermis, and thicker, scaly cutaneous patches—all brought on by aberrant keratinocyte proliferation—are its defining features. Additionally, the quality of life is significantly reduced for psoriasis patients.[12]. In the skin and other tissues, vitamin D and its analogs have strong effects on the proliferation and differentiation of cells. These substances also have immunomodulatory and apoptosis-regulating properties. It has been demonstrated over the past few decades that vitamin D compounds are safe and effective when applied topically to psoriasis, and they are now considered a conventional treatment.[13]. Vitamin D derivative-containing topicals are frequently

utilized as a single or combination treatment for mild PsO, and occasionally they are also used in moderate to severe patients undergoing systemic anti-psoriatic treatments.[14] The use of topical vitamin D as a primary treatment for psoriasis has been widely accepted in recent decades. But there hasn't been much talk about oral vitamin D as a possible treatment or dietary supplement. According to recent research, oral vitamin D is a viable therapeutic option for psoriasis, and there may be a link between psoriasis patients' higher disease severity and low serum vitamin D levels.[15]

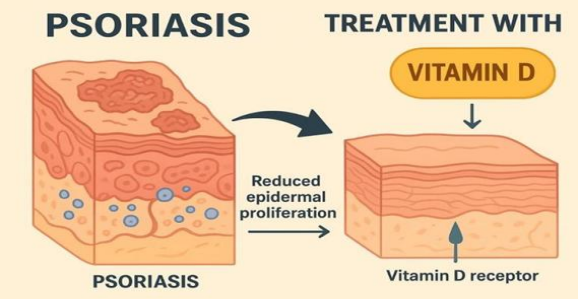

Fig 5. Vitamin D in treatment of Psoriasis

1.6. Vitiligo: -

A frequent pigmentary condition called vitiligo is brought on by the death of healthy melanocytes. Skin pigmentation is caused by the vital hormone vitamin D, which is produced in the skin. Patients with vitiligo and other autoimmune illnesses have been found to have low vitamin D levels.[16] Impact between 0.5% and 2% of the global population. Melanocytes are specifically destroyed in this disorder, resulting in non- scaly, chalky-white macules. The absence of epidermal pigmentation, or vitiligo, is a complex illness that can cause achromic macules and patches.[17]

Fig 6. Treatment of Vitiligo by Vitamin D

Medical, phototherapeutic, and surgical approaches are used to treat vitiligo.

Sometimes a mix of these approaches is the most effective. In order to achieve successful repigmentation, the goal is to stop the continuous loss of melanocytes and to supply mediators that can promote the growth and multiplication of already-existing melanocytes.[18]. Through a number of ways, vitamin D significantly affects the activity of melanocytes and keratinocytes. First of all, it encourages keratinocyte differentiation and maturation, which results in the formation of a well-organized epidermal barrier. This promotes the vitiligo repigmentation process and preserves the integrity of the skin. Furthermore, vitamin D suppresses excessive immunological responses that may lead to melanocyte loss in vitiligo through its immunomodulatory effects.[19] According to the majority of research, calcipotriene may hasten the repigmentation process and reduce the total amount of cumulative phototherapy exposure.[20]

1.7. Acne vulgaris: -

In 1938, there was an initial interest in the connection between vitamin D and acne. In 2016, PloS One published a comparison of 25(OH)D serum levels in teenagers with and without acne. Vitamin D levels were lower in acne sufferers than in healthy controls,

and there was an inverse correlation between vitamin D levels and the quantity and severity of inflammatory acne lesions.[21]

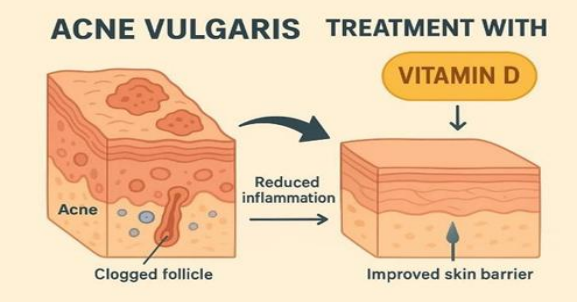

Fig 7. Vitamin D in the treatment of Acne vulgaris

Millions of individuals worldwide suffer with acne vulgaris, the most common skin condition and the ninth most frequent disease globally. Data from a few published in vitro investigations raise the possibility of a link between vitamin D and the pathogenesis of acne. [22] Changes in the sebaceous glands are the cause of acne, a skin illness. Acne vulgaris (or "common acne") is the most prevalent type of acne. The skin's reaction to the infection is inflammation, which causes the redness.[23] By inhibiting cell division, reducing sebum secretion, preventing pore blockage, and inhibiting the formation of Cutibacterium acnes, vitamin D has a pleiotropic action that prevents AV lesions. Vitamin D's positive effects on

AV sufferers' skin.[24]

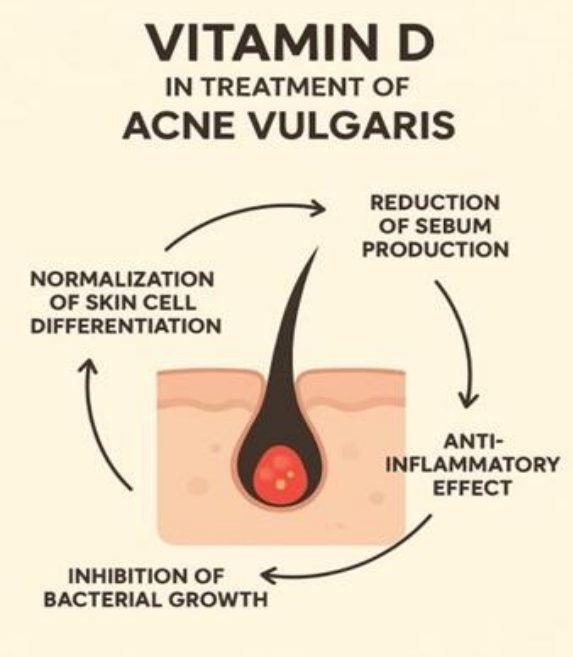

Fig 8. Vitamin D in treatment of Acne vulgaris

The primary pathogenic phases of acne vulgaris are influenced by vitamin D. The pathophysiology of acne vulgaris involves changes in sebum amount and quality, which occur in sebocytes themselves.[25]

II. CONCLUSION: -

Because vitamin D is involved in cellular proliferation, differentiation, immunomodulation, and DNA repair, it is essential for maintaining skin health. Even though there is enough sunlight in many parts of the world, vitamin D deficiency is still a major global health issue. This is mostly because of lifestyle choices, insufficient sun exposure, and public health advice meant to lessen UV-induced skin damage. This emphasizes the need for fair regulations that take into account sunlight's dual role as a major environmental carcinogen and a source of vitamin D.

Research continuously shows that a lack of vitamin D is linked to an increased risk and poorer results in a number of skin conditions. Vitamin D plays preventive roles in skin malignancies, such as melanoma, squamous cell carcinoma, and basal cell carcinoma, by promoting DNA repair, blocking carcinogenic pathways including hedgehog signaling, and reducing the growth of tumor cells. Similarly, vitamin D and its analogs promote better epidermal differentiation, less inflammation, and increased repigmentation in immune-mediated and inflammatory skin conditions like psoriasis and vitiligo. Additionally, new research indicates that low vitamin D levels are associated with more severe acne vulgaris, which may have therapeutic advantages.

All things considered; the body of research emphasizes how crucial it is to keep vitamin D levels at ideal levels for skin health. Although topical vitamin D formulations are well- established in the treatment of psoriasis and have potential for other dermatological disorders, oral vitamin D supplementation is a promising option that needs more extensive clinical testing. Future studies should concentrate on developing safe and practical methods to maximize vitamin D levels without raising the danger of UV-related skin damage. Finding this equilibrium is essential to maximizing vitamin D's therapeutic advantages and guaranteeing long-term skin protection.

REFERENCES

[1] Sahota, O., "Understanding vitamin D deficiency," *Age and Ageing*, vol. 43, no. 5, pp. 589–591, Jul. 2014.

[2] Benedik, E., "Sources of vitamin D for humans," *International Journal for Vitamin and Nutrition Research*, Oct. 2021.

[3] Borradale, D. and Kimlin, M., "Vitamin D in health and disease: An insight into traditional functions and new roles for the 'sunshine vitamin'," *Nutrition Research Reviews*, vol. 22, no. 2, pp. 118–136, Dec. 2009.

[4] Müller, D. N., Kleinewietfeld, M., and Kvakan, H., "Vitamin D review," *Journal of the Renin-Angiotensin-Aldosterone System*, vol. 12, no. 2, pp. 125–128, Jun. 2011.

[5] Mason, R. S. and Reichrath, J., "Sunlight vitamin D and skin cancer," *Anti-Cancer Agents in Medicinal Chemistry*, vol. 13, no. 1, pp. 83–97, Jan. 2013.

[6] Gandini, S., Raimondi, S., Gnagnarella, P., Doré, J. F., Maisonneuve, P., and Testori, A., "Vitamin D and skin cancer: A meta-analysis," *European Journal of Cancer*, vol. 45, no. 4, pp. 634–641, Mar. 2009.

[7] Field, S., Davies, J., Bishop, D. T., and Newton-Bishop, J. A., "Vitamin D and melanoma," *Dermato-Endocrinology*, vol. 5, no. 1, pp. 121–129, Jan. 2013.

[8] Maddodi, N. and Setaluri, V., "Role of UV in cutaneous melanoma," *Photochemistry and Photobiology*, vol. 84, no. 2, pp. 528–536, Mar. 2008.

[9] Sample, A. and He, Y. Y., "Mechanisms and prevention of UV-induced melanoma," *Photodermatology, Photoimmunology & Photomedicine*, vol. 34, no. 1, pp. 13–24, Jan. 2018.

[10] Reichrath, J. and Reichrath, S., "The relevance of the vitamin D endocrine system (VDES) for tumorigenesis, prevention, and treatment of non-melanoma skin cancer (NMSC): Present concepts and future perspectives," *Dermato-Endocrinology*, vol. 5, no. 1, pp. 38–50, Jan. 2013.

[11] Piotrowska, A., Wierzbicka, J., and Żmijewski, M., "Vitamin D in the skin physiology and pathology," *Acta Biochimica Polonica*, vol. 63, no. 1, pp. 17–29, Jan. 2016.

[12] Mattozzi, C., Paolino, G., Richetta, A. G., and Calvieri, S., "Psoriasis, vitamin D and the importance of the cutaneous barrier's integrity: An update," *The Journal of Dermatology*, vol. 43, no. 5, pp. 507–514, May 2016.

[13] Trémezaygues, L. and Reichrath, J., "Vitamin D analogs in the treatment of psoriasis: Where are we standing and where will we be going?" *Dermato-Endocrinology*, vol. 3, no. 3, pp. 180–186, Jul. 2011.

[14] Moosazadeh, M., Damiani, G., Khademloo, M., Kheradmand, M., Nabinezhad-Male, F., and Hessami, A., "Comparing vitamin D level between patients with psoriasis and healthy individuals: A systematic review and meta-analysis," *Journal of Evidence-Based Integrative Medicine*, vol. 28, 2023.

[15] Wilchowski, S. M. and Lareau, T., "Psoriasis: Are your patients D-pleted? A brief literature review on vitamin D deficiency and its role in psoriasis," *The Journal of Clinical and Aesthetic Dermatology*, vol. 15, no. 3 Suppl 1, p. S30, Mar. 2022.

[16] AlGhamdi, K., Kumar, A., and Moussa, N., "The role of vitamin D in melanogenesis with an emphasis on vitiligo," *Indian Journal of Dermatology, Venereology and Leprology*, vol. 79, p. 750, Nov. 2013.

[17] Joge, R. R., Kathane, P. U., and Joshi, S. H., "Vitiligo: A narrative review," *Cureus*, vol. 14, no. 9, Sep. 2022.

[18] Bishnoi, A. and Parsad, D., "Clinical and molecular aspects of vitiligo treatments," *International Journal of Molecular Sciences*, vol. 19, no. 5, p. 1509, May 2018.

[19] Al-Smadi, K., Ali, M., Alavi, S. E., Jin, X., Imran, M., Leite-Silva, V. R., and Mohammed, Y., "Using a topical formulation of vitamin D for the treatment of vitiligo: A systematic review," *Cells*, vol. 12, no. 19, p. 2387, Sep. 2023.

[20] Bouceiro Mendes, R., Alpalhão, M., and Filipe, P., "UVB phototherapy in the treatment of vitiligo: State of the art and clinical perspectives," *Photodermatology, Photoimmunology & Photomedicine*, vol. 38, no. 3, pp. 215–223, May 2022.

[21] Navarro-Triviño, F. J., Arias-Santiago, S., and Gilaberte-Calzada, Y., "Vitamin D and the skin: A review for dermatologists," *Actas Dermo-Sifiliográficas*, vol. 110, no. 4, pp. 262–272, May 2019.

[22] Rasti, S. D., Dewinta, N. R., Kamal, R. H., Adissadah, A. F., Madanny, A. E., and Dewanti, L., "Correlation between serum 25-hydroxy vitamin D levels and the severity of acne vulgaris: A systematic review," *Indian Journal of Dermatology*, vol. 67, no. 1, pp. 31–36, Jan. 2022.

[23] Kameswararao, K., Sujani, C., Koteswararao, N. V., Rajarao, A., and Satyanarayanamma, P. N., "A brief review on acne vulgaris," *Research Journal of Pharmacology and Pharmacodynamics*, vol. 11, no. 3, pp. 109–119, Jul. 2019.

[24] Podgorska, A., Puścion-Jakubik, A., Markiewicz-Żukowska, R., Gromkowska-Kępka, K. J., and Socha, K., "Acne vulgaris and intake of selected dietary nutrients—a summary of information," *Healthcare*, vol. 9, no. 6, p. 668, Jun. 2021.

[25] Bukvić Mokos, Z., Tomić Krsnik, L., Harak, K., Marojević Tomić, D., Tešanović Perković, D., and Vukojević, M., "Vitamin D in the prevention and treatment of inflammatory skin diseases," *International Journal of Molecular Sciences*, vol. 26, no. 11, p. 5005, May 2025.