REVIEW ARTICLE

Vitamin A as a Dermal Sentinel: From Traditional Diagnostic Biomarker to a Futuristic Anti-Aging and Oncodermal Frontier

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ABSTRACT

Vitamin A is a vital micronutrient having multifaceted roles in skin health, immune regulation, and cellular differentiation. Among the signs of Vitamin A deficiency, the most important is phrynoderma, which is more closely associated with general malnutrition than with isolated vitamin deficiencies (e.g., vitamins A, B complex, C, or E). In resource-poor countries and regions with fewer health care facilities, detecting phrynoderma is crucial to identify individuals with fat malabsorption, inflammatory bowel disease, coeliac disease, short bowel syndrome, or recent bariatric surgery. Some other cases that can be detected early by recognizing phrynoderma are anorexia nervosa, individuals with fad diets, and older or disadvantaged people who live alone. Beyond classical deficiency syndromes, retinoids (Vitamin A derivatives) in developed countries offer therapeutic benefits for anti-aging, photoprotection, and adjunctive oncology by enhancing collagen synthesis, epidermal turnover, and immune surveillance. Oral carotenoids help protect the skin from UV radiation, and oral Vitamin A supplements are recommended to protect the skin from UV-induced oxidative damage. The antioxidant and collagen-boosting effects of this vitamin have led to its use as an anti-aging, anti-wrinkle, and longevity drug. Vitamin A has also been studied for its ability to modulate the tumor microenvironment, and this effect has been used in the chemoprevention of various cancers. This review has been compiled after an exhaustive study of online resources on Vitamin A, its related compounds, and their uses for health in general and dermatology in particular. It integrates the biochemical mechanisms underlying its role in health and immunity, clinical clues helpful for early diagnosis of its deficiency, and therapeutic applications that reaffirm Vitamin A's central role in traditional and modern dermatologic practice.

Keywords: *Anti-Aging, Dermatology, Immunomodulation, Nutritional Deficiency, Phrynoderma, Retinoids, Skin Barrier, Vitamin A, Xerosis.*

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Introduction

Vitamin A is a biologically potent fat-soluble micronutrient that is primarily stored by the body in the liver. It is considered indispensable for systemic health and for cutaneous homeostasis due to its varied roles in vision, maintaining epithelial integrity, immune regulation, reproduction, and cellular differentiation.[1] Deficiency of Vitamin A affects multiple organ systems, among which, skin and mucosal signs serve as early indicators, especially phrynoderma, xerosis, mucosal keratinization, and night blindness.[2] These cutaneous signs offer valuable diagnostic clues, whether the cause is either primary deficiency of Vitamin A or secondary to undiagnosed systemic disease leading to malabsorption of vitamins.

Besides classical roles of Vitamin A, it has gained more importance due to its emerging antioxidant, anti-aging, and anti-tumor potential. It is the very first antioxidant which has been approved by the FDA for anti-wrinkle and anti-aging use.[3] Retinoids are Vitamin A derivatives and have the potential to

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stimulate collagen synthesis, suppress matrix-degrading enzymes (matrix metalloproteinases), and enhance epidermal turnover.[4] In addition, the ability of retinoids to modulate the tumor micro-environment and enhance immune surveillance points towards their futuristic, promising use as an adjunctive treatment in oncologic care.[5] This review of Vitamin A will flow from mentioning the classic clinical signs of deficiency towards the modern-day therapeutic implications in anti-aging and evolving relevance in cancer prevention in modern dermatologic practice.

Methods

This review article aims to accumulate past and current knowledge available on Vitamin A and its role in both traditional and modern dermatological practices. The scope of this paper includes sources and daily requirements of Vitamin A, its biochemical mechanisms, deficiency manifestations, and its evolving applications, from classical antioxidant functions to modern day uses in photoprotection, anti-aging, and cancer prevention with a touch on current global spending on research related to Vitamin A. Original and review articles including systematic reviews and meta-analysis published between 2021-2026 will be eligible for inclusion in the study. Studies mentioning Vitamin A, Retinoids, or Carotenoids and their role in dermatology, as mentioned above in the scope of study, will be included. Only full-text articles published in English will be included. Articles published before 2021, in any other language, and those on Vitamin A and not relevant to dermatology will be excluded. Articles lacking clear methodology, results, duplicate records, repetitive reviews, not relevant to our scope, and without any additional insight will also be excluded. The study's search and selection protocol was adopted from PRISMA guidelines to ensure transparency and reproducibility. The quality of selected articles was assessed by critical appraisal based on study design, sample size, and consistency of findings. Since this is a narrative review article, formal risk-of-bias assessment tools were not applicable. Relevant data from eligible studies were selected, analyzed, interpreted, and cross-referenced with multiple other online sources to ensure accuracy and consistency. Irrelevant information, including datasets, figures, and tables, was excluded. The final collection was organized into a narrative framework to highlight both established and emerging dermatological roles of Vitamin A.

Results

A structured literature search was conducted across PubMed, ScienceDirect, ResearchGate, and Google Scholar, supplemented by a targeted Google search. The study selection process was conducted in accordance with the adapted PRISMA guidelines to ensure transparency and reproducibility. Search

Table 1: Search strategy table with database, search terms, filters, and estimated number of records

Database	Search Terms / Keywords	Filters Applied	Records Retrieved
PubMed	(Vitamin A OR retinoids OR retinol OR retinoic acid OR carotenoid) AND (xerophthalmia OR "Vitamin A deficiency" OR Bitot OR phrynoderma OR night blindness) AND (biomarker OR "anti-aging" OR antioxidant OR "anti-cancer")	English; 5 Years, Full-text articles	127
ScienceDirect	Same concept	English; 2021–2026, open access, review articles, medicine and dentistry	5635 (estimate)
Google Scholar	Same concept	English; 2021–2026, review articles	5410 (estimate)
ResearchGate	Same concept + full texts	English; 2021–2026	100 (estimate)
Manual / Targeted Search	Reference lists and supplementary searches	–	70

This table summarizes the search protocol

terms, as mentioned in Table 1, were used. Both original research articles and review papers, including systematic reviews and meta-analyses, published between 2021 and 2026 were searched using the above-mentioned search databases. Initial database search yielded approximately 11342 records (Table 1).

Searched articles' titles, abstracts, and conclusions were then screened for relevance to our scope of sources and daily requirements of Vitamin A, biochemical processes related to epidermal proliferation and differentiation, clinical signs of Vitamin A deficiency, role of Vitamin A and its derivatives as antioxidants, and applications in anti-aging, photoprotection, and cancer prevention. After extensive scrutiny and removal of duplicates and irrelevant studies, 113 articles meeting the inclusion criteria were selected for full-text review (Figure 1).

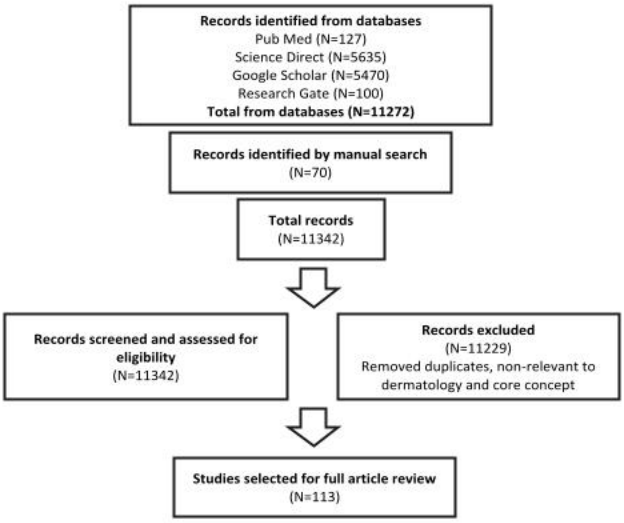

Fig.1: PRISMA style flowchart

Note: This figure shows a flowchart based on the PRISMA method of review study progression from identification of key articles, followed by screening using inclusion and exclusion criteria, and final eligibility selection protocol for enrolment into the study

Our research yields that vitamin A is a fat-soluble vitamin, considered essential for growth, immunity and normal cell turnover of skin and mucosa. It is obtained in the diet from a variety of sources, notable among which are milk, dairy products, and vegetables. The average daily requirement of vitamin A is 700-900 µg/day. Age-wise daily recommended amount of vitamin A is given below (Table 2).

The most important visual clues to diagnosing a deficiency of vitamin A are observed in the skin and eyes. Skin signs are xerosis and phrynoderma, while the most indicative eye clues are xeropthalmia, night blindness (nyctalopia), conjunctival xerosis, Bitot's spots (conjunctival keratinization), corneal xerosis, keratomalacia, corneal scars, and xerophthalmic fundus. (Table 3). Growth and immunity are some other functions affected by the deficiency, but they are less helpful in clinical diagnosis of vitamin A deficiency.

We also observed in our research that traditionally, vitamin A was taken only as a nutrient considered essential for development and immunity, with supplements used at all ages to boost vision. But modern-day dermatology has expanded utilization of vitamin A and its derivatives (carotenoids and retinoids) as sun protective agents, anti-oxidants, anti-aging, and anti-cancer therapy. A summary of various uses of Vitamin A to date is given in Table 4.

This narrative review establishes that Vitamin A is an essential nutrient for the normal turnover of skin and mucosa. It plays a vital role in vision, especially in dim light. Carotenoids have established roles as antioxidants and sun-protective agents, while retinoids are recognized as anti-aging and chemoprotective agents.

Table 2: Title: Age wise recommended daily intake of Vitamin A

Age group	RDI (µg retinol equivalents/day)	Upper safe limit (µg/day)
Infants (0–6 months)	400	600
Children (1–3 years)	300	600
Adolescents (9–13 years)	600	1,700
Adults (Males/Females)	900/700	3,000
Pregnant/Lactating Women	770–1,300	2,800–3,000

Note: Adapted from WHO Guideline: Vitamin A Supplementation in Infants and Children 6–59 months of age. Updated 2020

Table 3: Clinical signs of vitamin A deficiency

System/Organ	Clinical Sign	Description	Pathophysiology
Skin	Xerosis	Dry, rough, scaly skin	Impaired keratinization and reduced sebaceous activity
	Phrynoderma ("toad skin")	Follicular hyperkeratotic papules are commonly found on extensor surfaces	Follicular plugging due to abnormal epithelial differentiation
	Hyperkeratosis	Thickened stratum corneum	Defective epidermal turnover and differentiation
Eyes (Ocular)	Night blindness (Nyctalopia)	Difficulty seeing in dim light	Reduced rhodopsin synthesis in the retina
	Xerophthalmia	Dryness of the conjunctiva and cornea	Loss of goblet cells and mucin production
	Bitot spots	Foamy, keratinized plaques on the conjunctiva	Keratin debris accumulation due to epithelial metaplasia
	Keratomalacia	Corneal softening and ulceration	Severe epithelial breakdown and necrosis
Immune System	Increased infections	Recurrent respiratory or gastrointestinal infections	Impaired mucosal barrier and immune dysfunction
Growth & Development	Growth retardation	Delayed physical development in children	Altered cell differentiation and protein synthesis
Mucosal Surfaces	Epithelial metaplasia	Replacement of normal mucosa with keratinized epithelium	Loss of mucin-secreting cells

Note: This table summarizes different clinical manifestations of Vitamin A deficiency

Table 4: Summary of traditional vs modern applications of vitamin A in dermatology

Aspect	Traditional Applications	Modern Applications
Primary focus	Correction of deficiency states	Therapeutic and preventive dermatology
Key conditions treated	Xerosis, xerophthalmia, phrynoderma, night blindness	Acne, photoaging, psoriasis, skin cancers
Forms used	Dietary Vitamin A (retinol, carotenoids)	Topical, systemic retinoids (tretinoin, adapalene, isotretinoin) and oral carotenoids
Mechanism of action	Restoration of epithelial integrity and keratinization	Regulation of gene expression via retinoic acid receptors (RAR/RXR), modulation of cell proliferation and differentiation
Role in skin biology	Maintains normal epidermal differentiation	Enhances collagen synthesis, reduces matrix degradation, and promotes epidermal turnover
Antioxidant role	Limited, indirect	Significant role in reducing oxidative stress and neutralizing free radicals
Photoprotection	Not a primary indication	Reduces UV-induced damage and photoaging changes
Anti-aging effects	Minimal	Improves fine wrinkles, pigmentation, and skin texture
Anti-cancer role	Prevents deficiency-related epithelial dysplasia	Chemopreventive role in non-melanoma skin cancers and premalignant lesions
Mode of administration	Oral dietary intake	Topical formulations and systemic pharmacotherapy
Evidence base	Clinical observations and nutritional studies	Molecular studies, randomized trials, and dermatological research
Global perspective	Focus on malnutrition and public health	Expanding cosmeceutical and pharmaceutical market

Note: This table summarizes the traditional supplement role of Vitamin A and the modern antioxidant, anti-aging, and chemopreventive uses of Vitamin A in a tabulated form

Discussion

Vitamin A (retinol form) has a chemical structure with a cyclohexane ring, a conjugated polyene chain and a hydroxyl group. It has a chemical formula $C_{20}H_{30}O$ and a molar mass of 286.46 g/mol.

Vitamin A is present in the human diet in one of two forms. One is in the form of preformed retinoids, examples are retinol, retinal, and retinoic acid, and are primarily sourced from animal products such as liver, egg yolk, dairy, and fish oils. The other form is provitamin A, or carotenoids, of which an example is β-carotene, which are abundant in colorful fruits and vegetables, such as carrots, spinach, and mangoes.[6] These carotenoids undergo enzymatic cleavage within the intestinal mucosa and generate retinol via the action of enzyme β-carotene 15,15′-monooxygenase. This conversion process occurs inside enterocytes after carotenoids are absorbed in the presence of dietary fat and bile salts. Following ingestion and conversion, Vitamin A participates in micelle formation in the duodenum, facilitated by bile salts. Once retinol and carotenoids are inside enterocytes, and carotenoids are converted to retinol intracellularly by enterocytes using the enzyme, this retinol is then esterified to retinyl esters and is incorporated into chylomicrons, which are then transported via the lymphatic system to the liver for storage. Within hepatic stellate cells, retinol is stored and subsequently mobilized into circulation bound to retinol-binding protein (RBP) and transthyretin. Whenever required, retinol is oxidized to retinal by alcohol dehydrogenases (predominantly expressed in the liver and intestinal epithelium), and retinal is further oxidized to retinoic acid by aldehyde dehydrogenases for subsequent function.[7]

Retinol obtained from different dietary sources is absorbed around 70–90%, and this absorption is fat-dependent, whereas carotenoid absorption ranges from 20–50% and is bile salt-dependent. Excretion of Vitamin A metabolites occurs primarily in bile and feces, with minimal urinary loss. The biological half-life of retinol is around 12–24 hours, while retinoic acid is rapidly cleared, with a half-life of around 1 hour.[8]

The average daily requirement of Vitamin A is 700–900 µg of retinol equivalents. Animal sources of Vitamin A and their equivalent retinol contents are: one cup of whole milk gives around 150 µg of Vitamin A, one large egg gives around 75 µg of Vitamin A, 100 g cooked chicken liver can give 3,300 µg of Vitamin A and one serving of cheddar cheese gives 300 µg of Vitamin A. Vegetable sources of Vitamin A and their equivalent retinol contents are: one medium carrot gives around 500 µg of Vitamin A, one cup cooked spinach around 950 µg of Vitamin A, one cup sweet potato around 1,100 µg of Vitamin A and one mango nearly 1,000 µg of Vitamin A. In summary, a balanced daily intake of 1–2 servings of dairy plus 1–2 servings of dark green or orange vegetables typically suffices for most adults.

The active metabolite of Vitamin A is retinoic acid, which can cross cell membranes and nuclear membranes to reach its nuclear receptors. Retinoic acid receptors have four different types: retinoic acid receptors (RAR-α, β, γ), retinoic X receptors (RXR-α, β, γ), retinoic acid receptor-related orphan receptor (ROR-α, β, γ), and peroxisome proliferative-activated receptors (PPARs). The binding of retinoic acid with its receptors forms heterodimers (RAR/RXR), which further bind to specified regions on DNA called retinoic acid response elements (RAREs). After this binding, the complex functions as a genetic switch, turning certain genes on or off. The final outcome of this genetic switching in the skin and immune system is the promotion of keratinocyte growth & differentiation, the reduction of enzyme activity (such as MMP-1 and MMP-3) that break down connective tissue, and the simultaneous stimulation of collagen production. Through similar biochemical pathways, it also influences melanin pigment formation and strengthens immune defenses by regulating cytokine release and guiding dendritic cell maturation. In short, Vitamin A can fine-tune the structure of skin by keeping skin cells renewing at a healthy pace, maintaining structural integrity, balancing pigmentation, and supporting immune functions.[9] Retinoid acid receptors (RAR) are abundant in epidermis and hair follicles, while retinoid X receptors (RXR) are found in sebaceous glands and dermal fibroblasts.[10] Ligand binding causes conformational changes in these receptors, followed by the recruitment of coactivators or corepressors, resulting in modulation of gene transcription. By doing so, this cascade modulates epidermal cell turnover, reinforces barrier function, and promotes antimicrobial peptide expression.

Vitamin A regulates a number of cellular pathways at the molecular and genetic levels to maintain epidermal integrity, and it is vital in this role. Retinoids accelerate basal keratinocyte proliferation and promote upward migration of keratinocytes, ensuring their timely desquamation and renewal of the stratum corneum.[11] Retinoic acid also regulates the expression of different key proteins like filaggrin, involucrin, and loricrin, which are essential regulators in the terminal differentiation of keratinocytes and cornified envelope formation.[12] It also upregulates tight junction proteins (claudins, occludins) and desmosomal cadherin proteins, in turn improving intercellular adhesions, cohesion, and barrier resilience.[13] Synthesis of natural fats like ceramides, cholesterol, and free fatty acids in keratinocytes during their maturation process is also controlled by Vitamin A at the nuclear level. These fats function like mortar, which holds skin cells together. These lipids keep the stratum corneum (the outer layers of the skin) well hydrated and strong, while the same lipid barrier prevents excessive water loss from the skin, a process called transepidermal water loss (TEWL). Deficiency of Vitamin A results in reduced production of protective fats and reduced adhesion between epidermal cells, thus weakening the barrier and impairing recovery in case of damage. Clinical findings include dry, rough skin (xerosis), cracks or fissures, and increased sensitivity to irritants.[14]

Vitamin A has mechanisms that modulate innate and adaptive immunity. Retinoic acid increases the production of β-defensins and cathelicidins, thereby enhancing innate cutaneous defense against microbes, including bacteria, fungi, and viruses.[15] Further support to innate immunity occurs by increased tolerogenic dendritic cell phenotypes and enhanced antigen presentation. It also upregulates gut-homing receptors (α4β7 integrin, CCR9) on T cells, hence favoring regulatory T-cell (Treg) differentiation over Th17 lineage by activating the FOXP3 gene.[16] Adaptive responses are enhanced by Vitamin A because it promotes IgA class switching and secretion at mucosal surfaces of respiratory and GI epithelium, which is crucial for mucosal defenses at these sites. A deficiency of this essential micronutrient leads to impaired immunity and heightened mucosal vulnerability, resulting in higher infection rates and poor vaccine response.[17]

Vitamin A deficiency (VAD) can occur for a number of reasons; the most notable are dietary nutritional deficiency, repeated diarrhea & infections, and sometimes increased physiological demands, depending on age group and geographic region. On a Global scale, approximately 190 million children under the age of five years have been observed with VAD, and the highest burden is recorded in South Asia and Sub-Saharan Africa.[18] Prevalence of VAD in children under age five is 44% in South Asia and 48% in Sub-Saharan Africa, as presented in UNICEF's 2023 Nutrition Report. Therefore, VAD is considered one of the leading preventable causes of childhood morbidity and mortality. Some important causes of VAD in infants and young children are insufficient dietary intake, low retinol content in maternal breast milk, early start of weaning and lack of complementary feeding practices. Frequent episodes of infection, e.g., measles, diarrhea, and pneumonia, can further deplete hepatic retinol stores, thereby exacerbating the nutritional deficit.[19] Low retinol levels have been observed in patients hospitalized due to measles in a study by Mason.[20] Additionally, maternal deficiency during pregnancy and lactation predisposes neonates to low hepatic stores and early-onset xerophthalmia.[21]Predominant contributors of VAD among school-age children and adolescents include dietary monotony and low intake of animal-sourced foods and carotenoid-rich vegetables.[22] In rural and underserved communities, a high incidence of parasitic infections such as giardiasis and helminthiasis also impairs intestinal absorption of Vitamin A.[23] In food-insecure populations, rapid growth during puberty also increases micronutrient requirements, which remain unfulfilled due to non-availability.[24] Different surveys from developing nations like Ethiopia indicate subclinical VAD in adolescents, with much higher rates in girls due to gender-based dietary disparities.[25,26]

In adults and elderly individuals, chronic gastrointestinal disorders, e.g., celiac disease, Crohn's disease, and chronic pancreatitis, lead to fat malabsorption and result in secondary VAD. Alcoholism and liver disease also impair hepatic storage and mobilization of retinol, with a prevalence of 10% to 15% in affected populations.

Institutionalized elderly individuals are the most vulnerable due to low dietary diversity and socioeconomic limitations.[27] Global analysis of micronutrient deficiency in 2025 by Liang et al has shown that Vitamin A deficiency remains a global issue in older adults, particularly in regions with lower socioeconomic status.[28]

Pregnant and lactating females represent one of the high-risk groups, owing to their increased physiologically demand. As per WHO estimates, 15–20% of pregnant women in South Asia and Africa are vitamin A-deficient. Night blindness during pregnancy is considered a significant clinical marker of VAD and is associated with increased maternal mortality and adverse neonatal outcomes. A study from Pakistan has shown the prevalence of VAD around 27% (serum retinol levels below 0.70 µmol/L) and night blindness of 12.7% in Pakistani pregnant women.[29]

Vitamin A deficiency presents with a variety of clinical signs, and most are considered not only pathognomonic but also useful as clinical diagnostic tools, especially in peripheral resource-poor settings where laboratory biochemical testing is usually unavailable. The most important visual clues to VAD in skin are xerosis and phrynoderma, and in the mucosa, xeropthalmia. Clinical signs under the umbrella of xeropthalmia are night blindness (nyctalopia), conjunctival xerosis, Bitot's spots (conjunctival keratinization), corneal xerosis, keratomalacia, corneal scars, and xerophthalmic fundus. It is essential for frontline clinicians to recognize these classic signs, especially in endemic regions like Pakistan, South Asia, and Central Africa, where subclinical Vitamin A deficiency is widespread.[30] Such signs reflect underlying biochemical disruptions in epithelial integrity, immune competence, and retinoid signaling. The prevalence of these signs in vulnerable populations underscores the need for a vigilant clinical approach and emphasizes the role of dermatologic and ophthalmologic examinations in nutritional screening programs.

Dry skin (xerosis) clinically presents as roughness, flaking, and cracks. This occurs in VAD due to improper lipid production in epidermal cells, resulting in outer skin layers that are malformed, poorly desquamated, and fail to protect. Since Vitamin A plays a crucial role in regulated lipid production, its deficiency leads to reduced lipid production, poor barrier formation, increased transepidermal water loss, and reduced desquamation.[10] Cutaneous xerosis has also been reported alongside phrynoderma in micronutrient deficiencies in countries such as South Asia (Pakistan, India, Bangladesh) and Central Africa.[2] Phrynoderma (toad skin) appears when an individual suffers from a moderate to severe deficiency of Vitamin A and clinically presents as small, bumpy spots clustered around hair follicles, mainly on the outer parts of limbs like arms, legs, and back, giving a coarse texture and rough feeling due to blocked pores and thickened outer layers. Histopathology of these lesions may show plugged hair follicles due to excessive keratin buildup. In rural areas of Pakistan, it has been observed in nearly every second child of school-going age due to a lack of variety in meals or repeated episodes of infections at this age.[31] The literature now relates phrynoderma to general malnutrition with multiple micronutrient deficiencies, rather than being specific to Vitamin A or essential fatty acids alone.[32]

Bitot's spots appear as pale, yellow, thick, wedge-shaped plaques on the temporal side of the bulbar conjunctiva in VAD individuals. They are formed as a result of abnormal keratinization of surface cells and are often associated with dryness in the conjunctiva. If not recognized and treated in time, it can progress to involve the cornea, resulting in corneal ulcers, sclerosis, and keratomalacia. According to community-based and regional surveys, the prevalence of Bitot's spots varies across regions of the world, at 4% in India, 20% in Pakistan, and 2.2% in Ethiopia.[33-35] WHO has classified Bitot's spots as a clinical indicator of moderate to severe VAD.

Nyctalopia or night blindness is one of the earliest manifestations of VAD and occurs when the eye fails to regenerate rhodopsin in the absence of sufficient quantities of Vitamin A in rod cells of the retina. Rhodopsin is a substance vital for rod cells to detect low light. Without enough of it, vision dims when daylight fades. Children suffering from night blindness find it difficult to move in dim, at dusk, and are unable to perform activities in shadowed spaces after sunset. Evening tasks become harder without clear sight. Such symptoms during pregnancy signal

deeper nutritional gaps that affect both the mother and the child later in life. Research published in 2025 by Springer Public Health found that one in eight expectant mothers in Pakistan is affected by night blindness. Rural and tribal regions saw more cases than urban centers.[29] According to the World Health Organization (WHO) report, night blindness during pregnancy is a public health problem if more than 5% of women in a population are affected.

In addition to pathognomonic cutaneous and ocular signs, VAD presents with classic mucosal changes that predominantly affect the respiratory, gastrointestinal, and genitourinary tracts. There is squamous metaplasia of epithelial cells in these organs, presenting with keratinization. This, together with reduced immunoglobulin secretion in mucosal surfaces due to VAD, results in repeated episodes of respiratory infections and diarrheal illnesses. This fact has been reported in several studies.[36] According to UNICEF's data on VAD, updated in August 2025, high-dose Vitamin A supplementation reduces all-cause mortality from 12 to 24% in children aged 6–59 months.

In peripheral settings lacking laboratory facilities, recognizing these visual signs of VAD is invaluable for timely diagnosis and intervention. Analysis of these clinical signs in the context of age, dietary history, and infection burden is enormously helpful in devising appropriate public health intervention strategies, such as mass supplementation, fortified community diets, and targeted community education. Specificity and easy recognition of these signs make them a powerful tool in the early detection of VAD, which is helpful in preventing irreversible complications such as night blindness, severe infections, and growth retardation. WHO has suggested, depending on these observable signs and questionnaires focusing on night blindness in pregnant women or young, as a rapid screening tool in resource-poor settings. During Pakistan's 2018 National Nutrition Survey, UNICEF applied these forms and uncovered VAD levels exceeding 10% in certain regions. Although laboratory diagnostics are very precise and highly accurate, the use of standardized questionnaires offers a cheaper and more practical substitute where resources remain tight.

Vitamin A and its derivatives are widely implicated in skin treatments due to their diverse effects on cells at the molecular and genetic levels. This allows for application of retinoids in a multitude of disorders, including acne, psoriasis, aging from sunlight exposure, precancerous conditions, and even some forms of skin cancer. Over time, researchers have uncovered more about this micronutrient's abilities as a sun-protective, antioxidant, anti-aging, and anti-tumor agent. As evidence grows, so does its status in clinical dermatology as well as the aesthetic industry.[9,11] Vitamin A and retinoids are available on the market as creams, ointments, tablets, and supplements, each addressing distinct skin concerns based on individual needs. A survey has found that demand for Vitamin A and related compounds is expected to rise to USD 1.1 billion in 2035, up from USD 0.6 billion a decade earlier.[37] This rise in demand is due to the use of Vitamin A in skincare and cosmetics due to its ability to counter aging and oxidative stress. Meanwhile, medical professionals are further exploring the use of Vitamin A on new fronts and are pushing its frontiers.

Vitamin A stands out among other micronutrients and supplements due to its ability to effectively counter oxidative damage. Its plant-based form, carotenoids like beta-carotene, lycopene, and retinol scavenge radical oxygen species (ROS), preventing lipid peroxidation and DNA damage from occurring from UV radiations, environmental pollutants, toxins, and intrinsic aging factors.[38] Vitamin A and retinoids also stabilize mitochondrial membranes from oxidative damage and lead to reduced levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) in body fluids, which is a biomarker of oxidative DNA damage.[39] Building of ROS in sun-exposed skin can damage it, accelerate the aging process, and even raise cancer risk. Research across multiple countries supports the use of Vitamin A and carotenoids in neutralizing these harmful molecules. A study by Boswan et al. reports that oral mixed carotenoids increase carotenoid content in human skin and provide protection against UVB-induced erythema and UVA-induced pigmentation.[40] A study by Putthong et al. has demonstrated that the use of oral chewable tablets containing natural β-carotene, omega-6, and omega-3 fatty acids enhances UV resistance and skin density in healthy male individuals.[41] All this evidence from multiple trials

highlights Vitamin A's function as a key agent in fighting oxidative harm caused by UV rays and reactive molecules in skin care. These micronutrient supplements are marketed in different formulations, e.g., creams, lotions, oral pills, and fortified food supplements. In developed countries, these are promoted for wellness and appearance, whereas in developing nations like South Asia and Pakistan adopt β-carotene capsules as a skin shield from sunlight and airborne contaminants. Evidence from research supports the use of β-carotene, along with phytochemical antioxidants, in reducing tissue injury triggered by solar exposure and molecular instability, reinforcing their use in medical treatments and skincare formulations.[42,43] North America and Asia-Pacific are among the leading regional contributors to market revenue for antioxidant-based skincare products, which is expected to rise by7% by 2035.

One of the most studied nutraceutical supplements of today with excellent age-reversing effects is Vitamin A and related compounds. These effects are achieved at the cellular level through binding to RAR and RXR nuclear receptors, which in turn modulate the activity of various transcription factors controlling epidermal turnover and dermal remodeling. Such gene regulation results in increased collagen types I and III synthesis, suppression of matrix metalloproteinase enzymes (MMP-1 and MMP-3), and activation of glycosaminoglycan synthesis, thereby manifesting clinically as improved skin elasticity, reduced wrinkle depth, and increased dermal density.[44] A number of reports published worldwide support these molecular and clinical claims of Vitamin A and related compounds when either used topically or taken orally. A study by Halai et al has concluded that topical all-trans retinoic acid (ATRA) and retinol significantly enhance epidermal and dermal remodeling in photoaged skin as compared to the untreated controls.[45] A meta-analysis of 8 randomized controlled clinical trials by Huang et al has demonstrated a significant improvement in fine and coarse wrinkles with the use of topical tretinoin compared with vehicle controls.[46] Another study by Sadick et al has demonstrated the efficacy of tazarotene in photoageing.[47] A report has shown that the anti-aging skincare market is expected to reach USD 112 billion by 2035, and Vitamin A derivatives are one of the major contributors to this expansion. All these age-reversing benefits are the main reason for widespread use of retinoids and related compounds in prescription and over-the-counter products.

Besides cosmetic uses of Vitamin A, one of the recent claimed benefits is its anti-tumor potential. Retinoids can alter the tumor microenvironment in several ways. One important alteration is to inhibit angiogenesis and limit neovascularization of rapidly growing dysplastic tissue by downregulating vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF).[48] Other relevant anti-tumor mechanisms are inhibition of cell growth and migration, dendritic cell maturation, and cytotoxic T-cell recruitment resulting in better immune surveillance against neoplastic cells, and apoptosis of precancerous keratinocytes via caspase activation and mitochondrial destabilization.[49] A number of studies have supported the role of retinoids as adjunctive therapy in cutaneous T-cell lymphoma and NMSC.[50] Retinoid-based chemoprevention is thus a cost-effective approach alongside other surgical and topical treatments. Interest of researchers in retinoid-based oncologic therapies is steadily increasing, especially their role in chemoprevention of dermatologic cancers and precancerous conditions, since topical retinoids have proven their worth in field cancerization by reducing the burden of subclinical dysplastic lesions in chronically sun-damaged skin.

Some important limitations in this study must be taken into account before interpreting its findings. It's a narrative review and lacks the methodological rigor of a systematic review and meta-analysis, and can result in selection bias. No validated risk-of-bias assessment tool has been applied, which may limit objectivity. Although three major databases were used for the search, there is still a chance of missing relevant articles due to database limitations, indexing variability, and search term constraints. The restriction to English language publications can result in language bias and inclusion of heterogeneous study designs. There is a profound possibility of publication bias, as mostly studies with positive findings of Vitamin A as antioxidant, anti-aging, and anti-cancer are more likely to be selected. Despite these limitations, this is a comprehensive,

clinically relevant, and up-to-date review of the comprehensive roles of Vitamin A in dermatology.

Conclusion

Vitamin A plays a central role in maintaining healthy skin and mucosa, vision, and a well-functioning immune system. Vitamin A deficiency can be diagnosed promptly by recognizing pathognomonic skin, mucosal, and ocular signs. In resource-poor settings and remote areas where lab testing facilities are not readily available, recognizing signs of VAD, such as phrynoderma, dry skin (xerosis), Bitot's spots, and night blindness, becomes especially important for timely diagnosis. In many underserved locations, skin and eye signs are often the first visible clues of nutritional deficiency. Training frontline doctors, nurses, and community health workers to recognize these signs can be very helpful in detecting deficiencies early, reducing preventable complications, and, over time, providing guidance on proper supplementation.

Beyond its traditional role as a micronutrient, in modern dermatological practice, Vitamin A has proved its role as an effective sun protector, antioxidant, and anti-wrinkle agent. Oral carotenoids are recognized as an antioxidant form of Vitamin A and help to protect the skin from ROS produced as a result of pollutants, toxins, and UVR. Vitamin A and Retinoids are the gold standard in anti-aging due to their role in epidermal and dermal remodeling at the cellular and genetic level. In the field of cancer dermatology, topical and systemic retinoids have proved their worth by modulating abnormal cell growth, reducing new blood vessel formation in growing tumors, and supporting immune defenses. They are now increasingly being considered as a cost-effective and supportive treatment for certain skin cancers.

As research continues, the role of Vitamin A is expanding from cosmetic skin regenerative to an immune-modulating cancer therapy. The diverse functions and utility of Vitamin A and its derivatives have enabled clinicians to harness its therapeutic potential not only to improve skin health but also for chemoprevention, thereby providing effective, evidence-based care across different populations.

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REFERENCES

1. Joshi M, Hiremath P, John J, Ranadive N, Nandakumar K, Mudgal J. Modulatory role of vitamins A, B3, C, D, and E on skin health, immunity, microbiome, and diseases. Pharmacology Reports. 2023; 75: 1096-1114. doi: 10.1007/s43440-023-00520-1
2. Park SE, Williams M, Crew AB, Hsiao JL. Cutaneous signs of nutritional deficiencies. Current Geriatrics Reports. 2024; 13: 189-99. doi: 10.1007/s13670-024-00425-8
3. Adamantidi T, Lafara MP, Venetikidou M, Likartsi E, Toganidou I, Tsoupras A. Utilization and bio-efficacy of carotenoids, vitamin A and its vitaminoids in nutricosmetics, cosmeceuticals, and cosmetics' applications with skin-health promoting properties. Applied Sciences. 2025; 15: 1657. doi: 10.3390/app15031657
4. Wang K, Yang Z, Ma Y, Liu W, Li G, Xu X, et al. Retinoids in scarless skin regeneration: from molecular mechanisms to therapeutic strategies. Frontiers in Cell and Developmental Biology. 2025; 13: 1683851. doi: 10.3389/fcell.2025.1683851
5. Bi G, Liang J, Bian Y, Shan G, Besskaya V, Wang Q, et al. The immunomodulatory role of all-trans retinoic acid in tumor microenvironment. Clinical and Experimental Medicine. 2023; 23: 591-606. doi: 10.1007/s10238-022-00860-x
6. Ahmed E, Jahan I, Md Irfan N, Khan IN, Mashreky SR, Ferdous T, et al. Dietary vitamin A intake and its major food sources among rural pregnant women of South-West Bangladesh. Heliyon. 2023; 9: e12863. doi: 10.1016/j.heliyon.2023.e12863
7. Bandara S, Saadane A, Ravichandran P. Structural bias in vitamin A metabolism: Why α-retinoids miss the eye. Journal of Biological Chemistry. 2025; 301: 110713. doi: 10.1016/j.jbc.2025.110713
8. Martin N, Leung M, Radhakrishnan R, Lobo GP. Vitamin A transporters in visual function: a mini review on membrane receptors for dietary Vitamin A uptake, storage, and transport to the eye. Nutrients. 2021; 13: 3987. doi: 10.3390/nu13113987
9. Balado-Simó P, Morgado-Carrasco D, Gómez-Armayones S, López-Ferrer A, Barco D, Ferrándiz-Pulido C, et al. An Updated Review of Topical Tretinoin in Dermatology: From Acne and Photoaging to Skin Cancer. Journal of Clinical Medicine. 2025; 14: 7958. doi: 10.3390/jcm14227958
10. Carazo A, Macakova K, Matousova K, Krcmova LK, Protti M, Mladenka P. Vitamin A Update: Forms, Sources, Kinetics, Detection, Function, Deficiency, Therapeutic Use and Toxicity. Nutrients. 2021; 13: 1703. doi: 10.3390/nu13051703
11. Łuczak JW, Palusińska M, Maślińska-Gromadka K, Pietrzak D, Szopiński T, Lewicki S, et al. The next generation of skin care: transforming retinoid therapeutics. Cells. 2025; 14: 1650. doi: 10.3390/cells14211650
12. Lee DD, Stojadinovic O, Krzyzanowska A, Vouthounis C, Blumenberg M, Tomic-Canic M. Retinoid-responsive transcriptional changes in epidermal keratinocytes. Journal of Cell Physiology. 2009; 220: 427-39. doi: 10.1002/jcp.21784

13. Li J, Li Q, Geng S. All-trans retinoic acid alters the expression of the tight junction proteins Claudin-1 and -4 and epidermal barrier function-associated genes in the epidermis. International Journal of Molecular Medicine. 2019; 43: 1789-1805. doi: 10.3892/ijmm.2019.4098
14. Schild J, Kalvodova A, Zbytovska J, Farwick M, Pyko C. The role of ceramides in skin barrier function and the importance of their correct formulation for skincare applications. International Journal of Cosmetic Sciences. 2024; 46: 526-43. doi: 10.1111/ics.12972
15. Roche FC, Harris-Tryon TA. Illuminating the role of vitamin A in skin innate immunity and the skin microbiome: A narrative review. Nutrients. 2021; 13: 302. doi: 10.3390/nu13020302
16. Amimo JO, Michael H, Chepngeno J, Raev SA, Saif LJ, Vlasova AN. Immune impairment associated with vitamin A deficiency: insights from clinical studies and animal model research. Nutrients. 2022; 14: 5038. doi: 10.3390/nu14235038
17. Bos A, van Egmond M, Mebius R. The role of retinoic acid in the production of immunoglobulin A. Mucosal Immunology. 2022; 15: 562-72. doi: 10.1038/s41385-022-00509-8
18. Imdad A, Mayo-Wilson E, Haykal MR, Regan A, Sidhu J, Smith A, et al. Vitamin A supplementation for preventing morbidity and mortality in children from six months to five years of age. Cochrane Database of Systematic Reviews. 2022; 3: CD008524. doi: 10.1002/14651858.CD008524
19. Hu Q, Lyu J, Li J, Lin X, Li S, Bu Y, et al. A comprehensive analysis of vitamin a deficiency burden and trends: insights from the global burden of disease study 2021 and future predictions to 2050. Frontiers in Nutrition. 2025; 12: 1673576. doi: 10.3389/fnut.2025.1673576
20. Mawson AR. Pathogenesis of measles and the mechanism of vitamin A treatment. Journal of Translational Medicine. 2025; 23: 587. doi: 10.1186/s12967-025-06545-9
21. Ishaq MU, Kunwar D, Qadeer A, Komel A, Safi A, Malik A, et al. Effect of vitamin A on maternal, fetal, and neonatal outcomes: An overview of deficiency, excessive intake, and intake recommendations. Nutrition in Clinical Practice. 2024; 39: 373-84. doi: 10.1002/ncp.11096
22. Rima FS, Kundu S, Tarannum S, Jannatul T, Sharif AB. Spatial variations and determinants of vitamin A and iron rich food consumption among Bangladeshi children aged 6–23 months. Scientific Reports. 2025; 15: 17881. doi: 10.1038/s41598-025-92068-8
23. Lin K, Yanfei Qi, Jing Sun. Trend and Burden of Vitamin A Deficiency in 1990–2021 and Projection to 2050: A Systematic Analysis for the Global Burden of Disease Study 2021. Nutrients. 2025; 17: 572. doi: 10.3390/nu17030572
24. Ara G, Little DC, Mamun AA, de Roos B, Grieve E, Khanam M, et al. Factors affecting the micronutrient status of adolescent girls living in complex agro-aquatic ecological zones of Bangladesh. Science Reports. 2023; 13: 6631. doi: 10.1038/s41598-023-33636-8
25. Melesse Y, Abebe Z. Minimum diet diversity-women score and predictors of school adolescent girl stunting and thinness in Northwest Ethiopia. BMC Public Health. 2025; 25: 637. doi: 10.1186/s12889-025-21913-2
26. Abera M, Workicho A, Berhane M, Hiko D, Ali R, Zinab B, et al. A systematic review and meta-analysis of adolescent nutrition in Ethiopia: Transforming adolescent lives through nutrition (TALENT) initiative. PLoS One. 2023; 18: e0280784. doi: 10.1371/journal.pone.0280784
27. Choudhry HS, Zhu A, Choudhry HS, Pyrsopoulos N, Dastjerdi MH. Vitamin A Deficiency Screening in Patients with Chronic Alcohol-Associated Liver Disease: Implications for Liver Transplant Candidates. American College of Gastroenterology Case Reports Journal. 2023; 10: e01099. doi: 10.14309/crj.0000000000001099
28. Liang S, Xi SZ, Liu JY, Tang GC, Zhang WG, Guo XR. et al. Global burden and cross-country inequalities of nutritional deficiencies in adults aged 65 years and older, 1990–2021: population-based study using the GBD 2021. BMC Geriatrics. 2025; 25: 74. doi: 10.1186/s12877-025-05728-9
29. Haseeb M, Latif J, Lund MS, Abbasi HI, Iqbal J. Prevalence and consequences of vitamin A deficiency in pregnant women in Pakistan and the role of strategic nutritional policies. Discover Public Health. 2025; 22: 379. doi: 10.1186/s12982-025-00775-4
30. Almehamad KA, Alkhaleefah KS, Juwaid YA, Alzahrani MA, Alhazzaa AS, Alharbi MM, et al. Vitamin A Deficiency: Diagnosis, Management, and Nutritional Therapy. Saudi Journal of Medicine and Public Health. 2024; 1: 1154-69. doi: 10.64483/202412322
31. Gonzalez FD, Cousens S, Rizvi A, Chauhadry I, Soofi SB, Bhutta ZA. Infections and nutrient deficiencies during infancy predict impaired growth at 5 years: Findings from the MAL-ED study in Pakistan. Frontiers in Nutrition. 2023; 10: 1104654. doi: 10.3389/fnut.2023.1104654
32. Verheyden MJ, Howard V, Gupta M. Phrynoderma: an under-recognised condition reflecting nutritional deficiency. The Medical Journal of Australia. 2024; 221: 86-7. doi: 10.5694/mja2.52362
33. Giramkar SV. Prevalence of vitamin a deficiency, scleral melanocytosis, tooth decay and skin infection among rural preschool children in mulshi tehsil, m/s, india. Asian Journal of Advances in Research. 2020; 4: 1-5.
34. Khan MA, Khan MD. Classification of 154 clinical cases of vitamin A deficiency in children (0-15 years) in a tertiary hospital in North West Frontier Province Pakistan. Journal of Pakistan Medical Association. 2005; 55: 77-8
35. Bantihun A, Gonete KA, Getie AA, Atnafu A. Child Night Blindness and Bitot's Spots Are Public Health Problems in Lay Armachiho District, Central Gondar Zone, Northwest Ethiopia, 2019: A Community-Based Cross-Sectional Study. International Journal of Pediatrics. 2020; 2020: 5095620. doi: 10.1155/2020/5095620
36. Zhang X, Dai X, Li X, Xie X, Chen Y, Chen Y, et al. Recurrent respiratory tract infections in children might be associated with vitamin A status: a case-control study. Frontiers in Pediatrics. 2024; 11: 1165037. doi: 10.3389/fped.2023.1165037
37. Future market insights. Vitamin A Market Size and Share Forecast Outlook 2025 to 2035. 2025. Available from: https://www.futuremarketinsights.com/reports/vitamin-a-market

38. Vaskova J, Stupak M, Vidova Ugurbas M, Zidzik J, Mickova H. Therapeutic Uses of Retinol and Retinoid-Related Antioxidants. Molecules. 2025; 30: 2191. doi: 10.3390/molecules30102191
39. Kotodziejczyk AM, Karwowski B. Anti-DNA Damage Mechanisms and the Role of Carotenoids, Vitamin A, and Its Derivatives. Nutrients 2025; 17: 2721. doi: 10.3390/nu17172721
40. Baswan SM, Marini A, Klosner AE, Jaenicke T, Leverett J, Murray M, et al. Orally administered mixed carotenoids protect human skin against ultraviolet A-induced skin pigmentation: A double-blind, placebo-controlled, randomized clinical trial. Photodermatology Photoimmunology & Photomedicine. 2020; 36: 219-25. doi: 10.1111/phpp.12541
41. Putthong C, Panmanee T, Charoensit P, Ross S, Tongpoolsomjit K, Viyoch J. Efficacy of Natural β-Carotene Chewable Tablets Derived from Banana (Musa AA) Pulp in Reducing UV-Induced Skin Erythema. Nutrients. 2025; 17: 65. doi: 10.3390/nu17010065
42. Maji K, Mallick S, Basak A, Ghosh S. Carotenoids as a nutraceutical for human health and disease prevention. Dietary Supplements and Nutraceuticals. 2025: 473-94. doi: 10.1007/978-981-96-8622-3_14
43. Shanaida M, Mykhailenko O, Lysiuk R, Hudz N, Balwierz R, Shulhai A, et al. Carotenoids for Antiaging: Nutraceutical, Pharmaceutical, and Cosmeceutical Applications. Pharmaceuticals. 2025; 18: 403. doi: 10.3390/ph18030403
44. Ye S, Lee S, Kang S, Jun SH, Kang NG. Improvement of skin condition through RXR alpha-activating materials. Biomolecules. 2025; 15: 296. doi: 10.3390/biom15020296
45. Halai P, Kiss O, Wang R, Chien AL, Kang S, O'Connor C, et al. Retinoids in the treatment of photoageing: A histological study of topical retinoid efficacy in black skin. Journal of European Academy of Dermatology and Venereology. 2024; 38: 1618-27. doi: 10.1111/jdv.20043
46. Huang HY, Lee LT. Tretinoin for Photodamaged Facial Skin: Systematic Review and Meta-Analysis of Randomized Controlled Trials. Dermatology Practical & Conceptual. 2025; 15: e20255172. doi: 10.5826/dpc.1504a5172
47. Sadick N, Pannu S, Abidi Z, Arruda S. Topical Treatments for Photoaged Skin. Journal of Drugs in Dermatology. 2023; 22: 867-73. doi: 10.36849/JDD.7753
48. Yang Z, Chen L, Chen H, Li L, Zhang R, Tang S, et al. Retinoic acid inhibits the angiogenesis of human embryonic stem cell-derived endothelial cells by activating FBP1-mediated gluconeogenesis. Stem Cell Research and Therapy. 2022; 13: 239. doi: 10.1186/s13287-022-02908-x
49. Jin Y, Teh SS, Lau HLN, Xiao J, Mah SH. Retinoids as anticancer agents and their mechanisms of action. American Journal of Cancer Research. 2022; 12: 938-60.
50. Ayuthu S, Chauhan YD, Mirza AA, Saad MZ, Bittla P, Paidimarri SP, et al. Role of Retinoids and their analogs in the Treatment of Cutaneous T-cell Lymphoma: A Systematic Review. Cureus. 2024; 16: e69318. doi: 10.7759/cureus.69318

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SB: Manuscript writing for methodology design, investigation, and approval for final submission

UR is the nominated guarantor and takes full responsibility for the overall content and integrity of the work