Topical Vitamins in Dermatology

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Abstract

There’s an increasing interest in the use of natural products in topical skin care regimens. Vitamins are natural products with many beneficial effects on the skin. They maybe used as prescription drugs in the treatment of skin diseases and are also incorporated into cosmeceuticals, which are products with active substances that cannot be considered cosmetics or drugs.

The most important vitamins in topical formulations are vitamin A, B_3, B_5, B_{12}, C, D, E and K.

The effect of topical vitamins used individually as well as in combinations in the treatment of various skin conditions and in cosmetic dermatology will be highlighted.

Key words: Topical Vitamins, acne, photoaging, psoriasis, melasma

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List of Abbreviations

(AD) Atopic dermatitis

(AGA) Androgenetic alopecia

(AK) Actinic keratosis

(AP-1) Activating protein

(APS) Sodium L-ascorbyl-2-phosphate

(BCC) Basal cell carcinoma

(CTCL) Cutaneous T-cell lymphomas

(DCLE) Dark circles of the lower eyelid

(DZR) Dermal Repair Zone

(HQ) Hydroquinone

(IF) Intrinsic factor

(INFγ) Interferon γ

(iNOS) Inducible nitric oxide synthase

(MAP) Magnesium ascorbyl phosphate

(MMP-1) Matrix metalloproteinase-1

(MMPs) Matrix metalloprotinases

(mRNA) Messenger ribonucleic acid

(MNA+) 1-Methylnicotinamide

(MED) Minimal erythema dose

(MF) Mycosis Fungoides

(NAD) Niacinamide adenine dinucleotide

(NADH) Niacinamide adenine dinucleotide hydrogen

(NADP) Niacinamide adenine dinucleotide phosphate

(NF-κβ) nuclear factor kappa beta

(NO) Nitric oxide

(OTC) Over the Counter

(PABA) Para-amino-benzoic acid

(PIH) Postinflammatory hyperpigmentation

(pKa) acid dissociation constant

(PPAR) peroxisome proliferator-activated receptors

(ppm) Part per million

(PUVA) Psoralen + UVA

(RA) Retinoic acid

(RAR) Retinoic acid receptors

(RARE) Retinoid hormone response elements

(ROS) Reactive oxygen species

(RXR) Retinoid X receptors

(SAP) Sodium ascorbyl phosphate

(SPF) Sun protection factor

(TCA) Trichloroacetic acid

(TEWL) Transepidermal water loss

(TPA) 12-O-tetradecanoylphorbol-13-acetate

(TNF-α) Tumor necrosis factor alpha

(UV) Ultraviolet

(UVA) Ultraviolet A

(UVB) Ultraviolet light B

(VC-IP) Tetra-isopalmitoyl ascorbic acid

(VCP-Na) Sodium L-ascorbic acid 2-phosphate

(VCP-IS-2Na) Disodium isostearyl 2-O-L-ascorbyl phosphate

(VVG) Verhoeff-Van Gieson

(VDR) Vitamin D receptor

Introduction

There is a growing public awareness and concern among individuals regarding the condition of their skin, with a concomitant desire to use natural products to treat skin conditions. There is evidence that there may be reduced side effects when using natural products or their derivatives **[*Wu, 2008*].**

Vitamins are a natural constituent of human skin. They are essential compounds for many functions of the human skin and are part of a system of antioxidants that protect the skin from oxidative stress **[*Burgess 2008; Manela-Azulay and Bagatin, 2009*].**

Because of an increased interest in the use of natural compounds, the number of topical products that contain vitamins has increased in recent years **[*Burgess, 2008*].** These days, new vitamin-rich creams and serums seem to pop up on the market all the time. Given the number of products available, it can be difficult for consumers--and even dermatologists--to distinguish those products that genuinely produce benefits from those that do not **[*Wu, 2008*].**

The most important vitamins, particularly in topical formulations, are A, B, C, D, E, and K **[*Manela-Azulay and Bagatin, 2009*].**

The increased interest in these products has spurred scientific and clinical studies evaluating the composition and clinical usefulness of topical vitamins in the treatment of skin dermatoses **[*Wu, 2008*].**

There is evidence that these products are particularly useful for photoprotection, treatment of photodamage, inflammatory dermatoses and hyperpigmentation disorders **[*Burgess, 2008*].**

In addition to their specific functions as precription drugs, scientific evidence shows that, certain vitamins are useful for cosmeceutical products. These are products with an active ingredient that cannot be considered as a drug or as a cosmetic product **[*Manela-Azulay and Bagatin, 2009*].**

However, not all cosmeceutical products containing vitamins are effective. The efficacy of topical vitamin formulations is dependent on the ability to formulate a product that contains stable active ingredients that can be delivered into the skin in sufficient quantities to reach therapeutic levels **[*Burgess, 2008*].**

It is important to understand the science behind the use of topical vitamins as they are increasingly being incorporated into the skin by daily use of skin care products **[*Manela-Azulay & Bagatin, 2009*]**.

AIM OF THE WORK

The aim of this work is to review the commonly used topical vitamins including vitamins A, B, C, D, E and K. The effect of topical vitamins used individually as well as in combinations in the treatment of various skin conditions and in cosmetic dermatology will be highlighted.

VITAMIN A

Vitamin A (retinol) and its naturally occurring and synthetic derivatives (with either structural or functional analogy) are collectively referred to as retinoids. They exert a wide variety of profound effects in regulation of inflammation, growth, and differentiation of normal and neoplastic cells in vertebrates **[*Becherel et al., 1994*].**

The importance of vitamin A in dermatology dates back to ***Wolbach and Howe in (1925)***, who identified epidermal changes as abnormal keratinization in vitamin A deficient animals **[*Wolbach and Howe, 1925*].** These observations were followed by numerous studies, which focused on the metabolism and pharmacological action of retinoids in the skin leading to the establishment of its effect in treatment of various skin diseases **[*Roos et al., 1998*].**

Vitamin A and its derivatives, both natural and synthetic, have been popular additives in topicals for years. Topical retinoids have proved to be effective in various skin diseases, including acne, psoriasis, photoaging, genodermatoses and to a lesser extent neoplasms **[*Weindl et al., 2006*].**

Historically, ***Stüttgen, 1959*** was the first to use topical retinoids in the treatment of skin diseases [***Stüttgen, 1986*].** Later, ***Kligman et al., 1969*** reported the efficacy of tretinoin in the treatment of acne vulgaris, intensifying the interest in the diverse possibilities for the therapeutic use of retinoids in topical formulations.

Chemistry

Vitamin A is a fat soluble vitamin that cannot be synthesized in vivo by the human body. It is an essential nutrient that must be acquired through diet **[*Drummond, 1920*].** Retinyl esters and ß-carotene are the two major precursors of retinol that are present in our diet. About 50% of the intake of vitamin A is derived from animal products such as egg yolk and liver, whereas the remaining 50% is provided by plant carotenoids found in carrots, tomatoes, and other yellow vegetables **[*Davidovici et al., 2007*].**

Approximately 50 to 80% of the total body vitamin A in humans is stored in the liver in the form of retinyl esters, especially retinol palmitate **[Roos et al., 1998].** In the skin, vitamin A is present mainly in the form of retinol and retinyl esters which account for more than 99% (approximately 1 nmol/g) of total cutaneous retinoids, whereas retinaldehyde and retinoic acid (RA) are under the limit of detection **[*Vahlquist et al., 1982*].**

Retinol (the natural form) is oxidized to retinaldehyde, then to all-trans-retinoic acid (the biologically active form). This conversion can occur in the skin **[*Kuenzli and Saurat, 2003*].**

Natural retinoids include retinol (vitamin A alcohol), retinyl-palmitate (vitamin A ester), retinyl-acetate (vitamin A ester), retinaldehyde (vitamin A aldehyde), tretinoin (all-trans-retinoic acid), isotretinoin (13-cis-retinoic acid) and alitretinoin (9-cis-retinoic acid) **[*Kuenzli and Saurat, 2003*].**

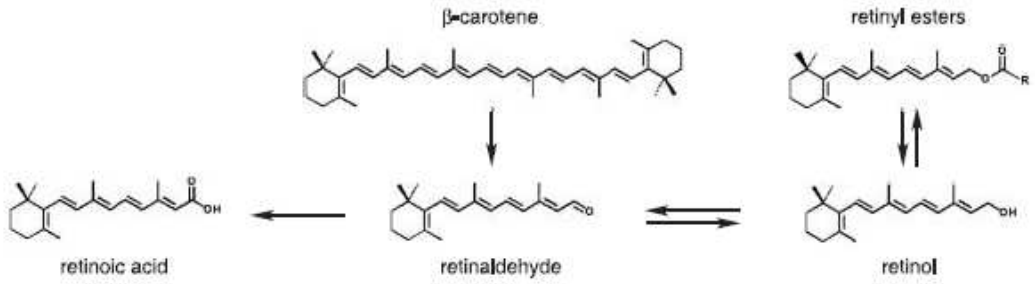

Figure (1): Structure of natural retinoids. The arrows show the enzyme-catalyzed conversions [*Sorg et al., 2006*].

Synthetic retinoids have been developed to achieve maximum therapeutic efficacy of viramin A with minimal side effects **[*Kuenzli and Saurat, 2003*].**

The first generation of retinoids, synthesized by manipulation of the polar end group and the polyene side chain of vitamin A (non-aromatic) includes:

- Tretinoin (all-trans retinoic acid),
- Isotretinoin (13-cis-retinoic acid),
- Alitretinoin (9-cis retinoic acid).

The second-generation retinoids (monoaromatic) are synthesized by replacing the cyclic end group of vitamin A with various substituted and non-substituted ring systems. They include:

- Etretinate
- Acitretin

The third-generation retinoids (polyaromatic or arotinoids) were developed by cyclizing the polyene chain. They bear little structural