

## REVIEW ARTICLE

# VITAMIN C, TOPICAL RETINIDS, AND SUNSCREEN IN CLINICAL PRACTICE: ESSENTIALS FOR FAMILY PHYSICIANS

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## KEYWORDS

Dermatology

Sunscreen

Oncology

## ABSTRACT

The field of skincare has been rapidly evolving, making it harder to navigate the plethora of products and trends. Vitamin C, topical retinoids, and sunscreen effectively prevent and combat the effects of photoaging with sunscreen being the most crucial product for daily use. Daily application of a broad-spectrum mineral sunscreen 15 minutes prior to sun exposure demonstrates the greatest protection from ultraviolet (UV)-induced skin damage. Vitamin C and retinol prevent the breakdown of collagen and stimulate its growth, which prevents and repairs photodamaged skin. Application of vitamin C prior to sunscreen in the morning is most advantageous, whereas retinol use at night is preferred to avoid photosensitivity. The most effective vitamin C formulations contain 15% L-ascorbic acid, 1% vitamin E, and 0.5% ferulic acid, while strengths ranging from 5% to 20% are safe. Tretinoin, only available via prescription, is the gold-standard retinol for photoaging with a strength of 0.05% being most utilized. Overall, these three products are safe to use together and when used correctly can effectively prevent and treat signs of photoaging with sunscreen providing the additional benefit of protection from skin cancer. The purpose of this paper is to review popular skincare products currently circulating on the internet, focusing on vitamin C, retinol, and sunscreen, by examining their ingredients, benefits, and different formulations based on the available literature on these products. This will better equip family physicians in navigating the ever-evolving landscape of skincare while enabling them to make informed recommendations to their patients.

## INTRODUCTION

Attaining flawless skin has been a rising desire for many patients; however, due to the variety of opinions and vast range of cosmeceutical products available, many remain uncertain on how to attain unblemished skin safely and effectively. "Cosmeceuticals," a term coined in 1984 by Dr. Kligman, refers to widely available products in retail stores across the United States and are defined as hybrid products that have active ingredients providing therapeutic effects that supersede simple cosmetic enhancement but do not qualify as a pharmaceutical drug. This article will concentrate on three commonly used products in daily skincare routines: vitamin C, retinol, and sunscreen. The review will provide a comprehensive overview explaining the benefits, ingredients, and different formulations of the products, allowing family physicians to make appropriate and safe recommendations to their patients.

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The authors declare no conflict of interest.

## VITAMIN C

Vitamin C, also known as ascorbic acid, has been widely used in the cosmetology industry for its photoprotective, antipigmentary, and antiaging properties.<sup>1,2</sup> The reduced form of vitamin C, L-ascorbic acid, is the biologically active form, which acts as a cofactor for various enzymes, aids in the synthesis of collagen, and helps maintain the integrity of the skin.<sup>2</sup> Due to the inherent functions of this hydrophilic vitamin, it has been widely used in the skincare industry as a product that protects against sun-induced skin damage, lessens hyperpigmentation, and reverses signs of aging.<sup>3</sup>

One of the most important environmental factors that cause cancer and photoaging is exposure to ultraviolet (UV) radiation.<sup>4</sup> UV radiation damages the skin by creating reactive oxygen species (ROS), which upregulate certain factors, such as activator protein 1 (AP-1) and nuclear factor-B.<sup>4</sup> Collectively, the factors increase the production of metalloproteinases (MMPs), which break down collagen and inhibit the production of new fibers, resulting in skin manifestations such as photoaging, pigmentation and wrinkles.<sup>4</sup> Vitamin C neutralizes free radicals with its antioxidant characteristics and has been shown to inhibit the UV-induced upregulation of AP-1, leading to an overall decrease in the production of matrix MMP and subsequent collagen breakdown.<sup>2</sup>

Vitamin C is involved in various stages in the synthesis of collagen and the molecule stimulates the transcription of procollagen

I and procollagen III genes, which provides antiaging properties.<sup>5</sup> Collagen is essential for the preservation of skin firmness and elasticity while also smoothing out wrinkles.<sup>6</sup> Additionally, the molecule acts as a cofactor for the proline and lysine hydroxylases, which play a vital role in stabilizing the tertiary structure of collagen.<sup>3</sup>

Additionally, hyperpigmentation is associated with certain areas of the skin appearing darker in color, which may be a result of increased melanin deposition in keratinocytes.<sup>5</sup> L-ascorbic acid inhibits the enzyme tyrosinase, which is the rate-limiting step in melanogenesis, making the compound potentially useful in treating certain causes of hyperpigmentation.<sup>3,5</sup>

### Vitamin C Formulations

A barrier to the topical application of L-ascorbic acid is its high reactivity and lipophobicity; therefore, even if the molecule resists oxidation before application, it may not be able to penetrate the skin due to the lipophilic stratum corneum.<sup>3</sup> The absorption and stability of vitamin C can be increased by applying a derivative of L-ascorbic acid instead of the pure compound or by generating an environment with a pH that is less than 3.5.<sup>2</sup>

The most stable derivative of vitamin C is magnesium ascorbyl phosphate (MAP), a hydrophilic compound that is stable at a neutral pH.<sup>2</sup> The phosphate group adds protection against oxidation, which is also seen in another derivative: sodium L-ascorbyl-2-phosphate (SAP).

Formulations of SAP contain various strengths, ranging from 0.3% to 5%.<sup>7</sup> Effects of skin brightening are observed in SAP concentrations of 3% or above, while antiaging properties are noticed in formulations containing 5% SAP.<sup>8</sup> Additionally, application of topical formulations with 5% SAP has been shown to reduce inflammatory and noninflammatory lesions induced by acne vulgaris, due to its antimicrobial activity against *Propionibacterium acnes*, the major bacterium responsible for the development of acne vulgaris.<sup>8</sup> Compared to other vitamin C derivatives, SAP has shown superior penetration into human skin as well as a higher rate of bioconversion into the biologically active form of the vitamin.<sup>8</sup> This vitamin C derivative has shown minimal irritation, making it a popular option for patients with acne-prone skin or those who experience irritation from conventional acne treatments.<sup>9</sup> In patients with acne vulgaris, formulations containing SAP may be especially beneficial; however, patients using benzoyl peroxide should be educated to use vitamin C products on alternate days or at different times of the day since benzoyl peroxide oxidizes and, therefore, inactivates vitamin C.<sup>10</sup>

A more novel derivative of vitamin C is 3-O-ethyl ascorbic acid (EAA), which is a water-soluble molecule that displays minimal skin irritation while aiding in skin brightening and reversing signs of aging.<sup>10,11</sup> Moreover, a combination of 30% EAA with 1% lactic acid has been shown to lessen manifestations of hyperpigmentation by reducing melanin content.<sup>11</sup> These effects allow EAA to be recommended for patients with hyperpigmented or sensitive skin.

The stability of L-ascorbic acid in product formulations can be increased by adding ferulic acid, a ubiquitous plant antioxidant. Ferulic acid acts as an antioxidant by scavenging free radicals,

inhibiting reactions that form ROS, and providing stability to other antioxidants' damage.<sup>12</sup> Additionally, ferulic acid has demonstrated prevention of photoaging by protecting against UV-induced skin damage.<sup>12</sup> The addition of a ferulic acid formulation with a pH of less than 3.5 reduces the reactivity of vitamin C and adds synergistic photoprotection.<sup>2,13</sup> The acidity of ferulic acid-containing formulations may cause skin irritation and, therefore, should not be recommended to patients with sensitive skin. In patients with normal resilient skin, formulations containing pure L-ascorbic acid may be used, while patients with sensitive skin or acne may experience better results with a vitamin C derivative, such as SAP or EAA, since they are stable at a higher pH and, therefore, have a decreased risk of skin irritation.<sup>10</sup>

Vitamin E—another vitamin that functions as an antioxidant—has been shown to protect the skin's lipid structure via its oxidative properties.<sup>13</sup> When used in combination with vitamin E, the actions of vitamin C are potentiated fourfold.<sup>13</sup> Moreover, studies have shown that adding 0.5% ferulic acid to a combination of 1% vitamin E and 15% vitamin C increases the efficacy of vitamin C eightfold.<sup>13</sup>

Overall, further investigation is required to determine the efficacy of topical vitamin C derivatives; however, usage of these products is safe and has not been associated with adverse effects. Vitamin C may be used with other topical antiaging products, such as sunscreen and tretinoin, without causing adverse effects.<sup>13</sup>

### Recommendations

Vitamin C products are easily accessible since they are sold over the counter at most stores and may be purchased online. A formulation containing pure vitamin C in the form of L-ascorbic acid may be purchased from SkinCeuticals. The formulation sold by SkinCeuticals is a patented formula containing 15% L-ascorbic acid, 1% vitamin E, and 0.5% ferulic acid. Despite extensive research on the efficacy of this product, its price of \$182 for 30 mL may not make it a viable recommendation for all patients. Alternatively, other companies, such as CeraVe, Olay, and VERSED, may be more budget-friendly recommendations, with the cost of vitamin C products starting around \$20. Even though the optimal concentration of vitamin C depends on the formulation, a safe recommendation in order to attain the biologic benefits provided by vitamin C is a strength of 5% to 20%.<sup>2</sup> Formulations containing 20% or more vitamin C have not demonstrated increased efficacy and may cause skin irritation.<sup>2</sup>

Patients with a history of sensitive skin should be advised to begin with a formulation that contains a lower concentration of vitamin C to prevent unwanted skin irritation.<sup>10</sup> Patients complaining of signs of skin irritation, such as erythema or stinging, should be informed that applying moisturizer to the affected area should resolve the irritation. Studies have shown that the appearance of wrinkles on the face improved when using a vitamin C formulation for at least 3 months; therefore, patients should be educated that the benefits are not immediate and that application of the product once or twice per day is required to attain optimal saturation levels of the vitamin and experience its subsequent benefits.<sup>3,13</sup>

TABLE 1:  
Products containing different vitamin C formulations<sup>14</sup>

PRODUCTS CONTAINING L-ASCORBIC ACID			
Product	Ingredients	Approximate Price*	Properties
SkinCeuticals - C E Ferulic	L-ascorbic acid (15%), ferulic acid (0.5%, alpha tocopherol (1%)	~\$182/30 mL	<b>Antioxidant:</b> L-ascorbic acid (15%), alpha tocopherol (1%), ferulic acid (0.5%) <b>Skin brightening:</b> L-ascorbic acid (15%)
La Roche-Posay - Pure Vitamin C Face Serum	L-ascorbic acid (10%), tocopherol, salicylic acid, glycerin	~\$44.99/30 mL	<b>Antiacne:</b> salicylic acid <b>Antioxidant:</b> L-ascorbic acid, tocopherol <b>Skin brightening:</b> L-ascorbic acid
CeraVe - Skin Renewing Vitamin C Serum	L-ascorbic acid (10%), glycerin, tocopheryl acetate, ceramides, phytosphingosine	~\$29.99/30 mL	<b>Antiacne:</b> phytosphingosine <b>Antioxidant:</b> L-ascorbic acid (10%), tocopheryl acetate <b>Skin brightening:</b> L-ascorbic acid (10%)
Olay - Age Defying Anti-Wrinkle Night Cream	L-ascorbic acid, niacinamide, glycerin, tocopheryl acetate, retinyl propionate, benzyl alcohol	~\$16.49/60 mL	<b>Antiacne:</b> niacinamide <b>Antioxidant:</b> ascorbic acid, tocopheryl acetate <b>Skin brightening:</b> L-ascorbic acid, niacinamide
PRODUCTS CONTAINING SODIUM ASCORBYL PHOSPHATE (SAP)			
Product	Ingredients	Approximate Price*	Properties
Olay Regenerist – Brightening Vitamin C Serum	SAP, niacinamide, glycerin, panthenol	~\$29.99/~40 mL	<b>Antiacne:</b> SAP, niacinamide <b>Antioxidant:</b> SAP <b>Skin brightening:</b> niacinamide
Paula’s Choice – Resist Anti-Aging Clear Skin Hydrator	SAP, glycerin, niacinamide, dimethicone, adenosine	~\$39.00/50 mL	<b>Antiacne:</b> SAP, niacinamide <b>Antioxidant:</b> SAP, adenosine <b>Skin brightening:</b> niacinamide
BLISS – Bright & Radiant Whipped Mask	SAP, zinc pca, L-ascorbic acid, glycerin, tocopheryl acetate, ascorbyl glucoside	~\$15.00/50 mL	<b>Antiacne:</b> SAP, zinc pca <b>Antioxidant:</b> SAP, tocopheryl acetate, ascorbyl glucoside, L-ascorbic acid <b>Skin-brightening:</b> L-ascorbic acid, ascorbyl glucoside
PRODUCTS CONTAINING MAGNESIUM ASCORBYL PHOSPHATE (MAP)			
Product	Ingredients	Approximate Price*	Properties
Paula’s Choice – Skin Recovery Replenishing Moisturizer	MAP, tocopherol acetate, glycerin, ceramides, squalene, ethylhexyl stearate, seed oil	~\$35.00/60 mL	<b>Antioxidant:</b> MAP, tocopherol acetate, SAP <b>Antiacne:</b> SAP <b>Skin brightening:</b> MAP
The Ordinary – Magnesium Ascorbyl Phosphate 10%	MAP (10%), tocopherol, glycerin	~\$11.70/30 mL	<b>Antioxidant:</b> MAP, tocopherol acetate <b>Skin brightening:</b> magnesium ascorbyl phosphate
PRODUCTS CONTAINING ETHYL ASCORBIC ACID (EAA)			
Product	Ingredients	Approximate Price*	Properties
The Ordinary – Ethylated Ascorbic Acid 15% Solution	EAA 15%	~\$20.00/30 mL	<b>Antioxidant:</b> EAA <b>Skin brightening:</b> EAA
Paula’s Choice – 5% Vitamin C Sheer Moisturizer SPF 50w	EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate, tocopherol, glycerin, ethylhexyl methoxycinnamate, butyl methoxycinnamate, titanium oxide	~\$45.00/60 mL	<b>Antioxidant:</b> EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate, tocopherol <b>Skin brightening:</b> EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate <b>Sunscreen:</b> glycerin, ethylhexyl methoxycinnamate, butyl methoxycinnamate, titanium oxide

\*These price averages can differ based on where purchased.

The instability of vitamin C may cause the formula to undergo oxidative changes, resulting in yellow discoloration of the skin.<sup>13</sup> Patients should be educated that even though this side effect is harmless, it indicates that the antioxidant properties were lost and subsequently will not produce the desired benefits. Vitamin C products should be stored in cool and dark environments to minimize compound oxidation and subsequent skin discoloration.

Vitamin C serums can be applied in the morning or at night, following use of a thorough cleanser. For added protection against UV-induced damage, sunscreen may be applied after the vitamin C serum has completely dried. Additionally, due to their ability to improve vitamin C stability and absorption, formulations containing L-ascorbic acid, vitamin E, and ferulic acid can be recommended, keeping individual skin sensitivity in mind.

Table 1 provides a summary of various vitamin C formulations from different companies to give physicians an overview of the ingredients in different products. While this list includes commonly used commercial products, it is not exhaustive. The ingredients and their properties are detailed for each product. It is important to be cautious when recommending these products since cosmeceutical products in the United States do not require FDA approval before being sold since the FDA does not formally recognize cosmeceutical products.<sup>1</sup> As seen in Table 1, some brands list the concentration of vitamin C within their product, whereas others do not. The only product with specific research on its patented formulation is SkinCeuticals. The other listed products contain ingredients backed by research supporting their efficacy. Physicians should exercise caution when advising patients to use a specific brand. To avoid a severe reaction upon first-time use to any product, physicians may advise their patients to consider testing on a small area of the skin prior to using on the entirety of the face.

## RETINOIDS

Topical retinoids are utilized to treat acne and signs of photoaging (fine lines, wrinkles, hyperpigmentation).<sup>15</sup> In the epidermis, aging is attributed to the loss of proliferation and turnover of its most abundant cell—the keratinocyte, which provides support to the outermost layer of skin—its loss resulting in thin, fragile skin.<sup>16</sup> Meanwhile, in the dermis, collagen fibrils are tightly woven to provide strength and durability; the breakdown of these collagen fibers by MMPs is attributed to aging.<sup>15</sup> Retinoids treat photoaging through keratinocyte proliferation, epidermal and dermal thickening, fibroblast growth, formation of new blood vessels within the dermis, and TGF- $\beta$ /CTGF (transforming growth factor beta/connective tissue growth factor) pathway activation (resulting in mature collagen growth).<sup>15,17</sup> Additionally, the use of topical retinoids has been shown to decrease the production of MMPs, resulting in an additional collagen-enhancing effect.<sup>15,17,18</sup>

Retinoids are comprised of vitamin A (retinol) and its natural derivatives, retinoic acid, retinaldehyde, and retinyl esters, in addition to other synthetic derivatives.<sup>15</sup> Topical retinoids are FDA approved to treat photoaging, acne vulgaris, psoriasis, cutaneous T-cell lymphoma, and Kaposi sarcoma.<sup>17</sup> This article will focus on topical retinoids indicated specifically for photoaging.

There are four generations (Table 2) of retinoids that exist in both oral and topical formulations. The FDA-approved topical retinoids to treat photoaging are tretinoin and tazarotene, and adapalene is used off label (Table 3). Within the first generation, there are retinol, retinaldehyde, and retinyl esters (precursors to retinoic acid) that are not FDA approved but are available over the counter (OTC) in cosmeceutical products marketed to combat photoaging (Table 3).

The potency of topical retinoids plays a large role in the product's efficacy. The difference between FDA-approved products available via prescription vs OTC is that OTC products are less potent.<sup>15</sup> Retinoic acid, also known as tretinoin, is the biologically active component and therefore more potent and effective. Retinyl esters (least potent) are converted to retinoic acid through these steps:

*Retinyl esters → Retinol → Retinaldehyde → Retinoic Acid*<sup>20</sup>

The forms that take the least number of steps to convert to retinoic acid such as retinaldehyde (only requiring one conversion) will be more potent and effective.<sup>19</sup> Keeping this in mind can help discern which forms of topical retinoids are best for patients for improving skin texture, fine lines, and dyspigmentation. It is important to be aware that since tretinoin is the most potent, its use topically has an increased risk of side effects such as retinoid dermatitis.<sup>19</sup>

Topical tretinoin is the gold-standard treatment for photoaging and the most studied retinoid to date. Its 0.05% emollient is most commonly prescribed due to strong research backing its efficacy, although 0.025% is considered therapeutically beneficial and generally safe.<sup>20</sup> A 2-year long placebo controlled clinical trial with 204 subjects concluded that 0.05% tretinoin emollient used once a day was safe and effective.<sup>20</sup> Alternatively, a study revealed that tazarotene has comparable effectiveness to tretinoin, however, the product is less budget friendly.<sup>19,20</sup>

Adapalene has been shown to be less irritating and maintain similar efficacy to tretinoin; therefore, it may be recommended to patients with sensitive skin, although further research is warranted.<sup>17,20,26</sup> Additionally, in comparison to tretinoin and tazarotene, which are photolabile, adapalene is more stable and therefore, will not undergo molecular photodegradation, which allows daytime use.<sup>26</sup>

Moreover, retinol, retinaldehyde, and retinyl palmitate, none of which are FDA approved, are the most common agents in cosmeceuticals.<sup>20</sup> While these are widely used in cosmetic products, their concentrations and stability vary since they are not regulated.<sup>20</sup> Meanwhile, multiple studies have compared different concentrations of these retinoids and shown successful treatment of photodamage in addition to decreased adverse effects.<sup>19,20</sup> Retinaldehyde has been deemed the most effective, although retinol is the most studied with substantiated improvements to photodamage through epidermal thickening and collagen synthesis.<sup>19,20</sup> Additionally, retinol is less irritating than tretinoin but is

TABLE 2:

Retinoid generations<sup>15,17,19</sup>

Generation	Generic Names	Available Topically?	Formulation Type and % Available
1st Generation <i>(naturally occurring retinoids)</i>	Tretinoin (all-trans-retinoic acid)	Yes	Gel, cream 0.1%, 0.08%, 0.06%, 0.05%, 0.04%, 0.025%, 0.02%, 0.01%
	Isotretinoin (13-cis retinoic acid)		Gel 0.05%
	Alitretinoin (9-cis retinoic acid)		Gel 0.1%
	Retinol (all-trans-retinol, vitamin A)		Cosmeceutical products 0.15%-0.3%
	Retinal (retinaldehyde)		Cosmeceutical products 0.05%-0.1%
	Retinyl esters (retinyl palmitate, retinyl propionate, retinyl acetate, retinyl retinoate, and retinyl N-formyl aspartame (retinyl aspartate))		Cosmeceutical products Various/unknown %
2nd Generation	Acitretin	No	--
	Etretinate		--
3rd Generation	Adapalene	Yes	Gel, cream, lotion 0.1%, 0.3% *0.1% available OTC
	Tazarotene		Gel, cream, lotion, foam 0.045%, 0.05%, 0.1%
	Bexarotene		Gel 1%
4th Generation	Trifarotene	Yes	Gel, cream, lotion 0.1%, 0.3% *0.1% available OTC
	Seletinoid G	No	--
	Tamibarotene		--

TABLE 3:

Topical retinoids to treat photoaging<sup>15,17,19-25</sup>

	Generic	Brand Name/Formulations	Notes/Extra
FDA-approved topical retinoids for photoaging	Tretinoin	Retin-A (cream, 0.02%, 0.05%)	• Apply once topically at bedtime • 0.05% is the most studied strength • 0.025% is considered therapeutically beneficial and generally safe
	Tazarotene	Avage (cream, 0.1%)	Apply pea-sized amount topically at bedtime
	Adapalene (off label)	Differin (gel, 0.3% or OTC gel, 0.1%)	• Most studied • 0.3% is recommended for best efficacy and outcomes • 10 times less potent than tretinoin but more tolerable
OTC cosmeceutical products used to treat photoaging (not FDA approved)	Retinol	--	• Most studied • 0.3% is recommended for best efficacy and outcomes • 10 times less potent than tretinoin but more tolerable
	Retinaldehyde	--	Most effective for photoaging
	Retinyl esters (retinyl palmitate, retinal acetate, retinol propionate, retinyl aspartate)	--	• Further research is needed



tenfold less potent.<sup>20</sup> Although the latter is better tolerated than tretinoin, the potency and efficacy of these products cannot be validated due to the lack of regulation.<sup>20</sup> For example, there are brands available in retail stores that advertise their product as retinol based but include additional ingredients (hyaluronic acid, ceramides, etc) and may not include the percentage of retinol within the product. These products may combat fine lines and wrinkles, but it is difficult to isolate which ingredients are responsible for any antiaging benefits.

Ultimately, one should exercise caution when recommending OTC cosmetic products due to the lack of regulations over those containing retinol, retinaldehyde, or retinyl esters.

## RECOMMENDATIONS

Educating patients on the side effects and expectations regarding the outcomes of topical retinoid use is important. The major side effect of topical retinoids is retinoid dermatitis, which manifests as erythema, peeling, scaling, dryness, burning, pruritus, and photosensitivity.<sup>17</sup> Other uncommon side effects that can occur are hypo- or hyperpigmentation, allergic contact dermatitis, or sticky skin.<sup>17</sup>

Recommendations regarding topical retinoid application include the application of a pea-sized amount to clean dry skin at bedtime (30 minutes after face washing). This decreases absorption through the dermis, which may decrease skin irritation.<sup>19</sup> Moreover, to combat dryness, use of a moisturizer should be applied to create a hydration barrier.<sup>19</sup> To allow for proper retinol penetration, moisturizers should be applied 30 minutes after retinol application.<sup>19</sup> Individuals with sensitive skin and those prone to acne and/or hyperpigmentation should use moisturizers that do not contain pore-clogging ingredients (cocoa butter, coconut oil, mineral oil etc).<sup>27</sup> Patients can look for moisturizers labeled “noncomedogenic,” indicating that the product does not block pores. Cetaphil Moisturizing Cream, La Roche-Posay Double Repair Facial Moisturizer with SPF, and Vanicream Daily Facial Moisturizer are available to the public and are known for their noncomedogenic properties. Retinol application to the eyelids and perioral areas should be limited or avoided due to increased sensitivity and peeling.<sup>17,26</sup> As retinoids are lipophilic, it is advised that patients use non-oil-based or noncomedogenic makeup, sunscreens, and other skin care products in addition to nonalkaline synthetic detergent cleansing products (gentle cleansers).<sup>26</sup>

When first using a topical retinoid, patients should start at a low concentration (0.025% for tretinoin specifically) and slowly incorporate this product into their skincare regimen.<sup>19</sup> Patients can begin using the product three times a week and gradually increase the frequency of use based on tolerance.<sup>19</sup> Moreover, short-contact application (washing the medicine off after an hour) may prevent adverse effects.<sup>17</sup> The irritative effects of topical retinoid use may cause hyperpigmentation in patients with darker skin colors; therefore, starting at a low concentration and providing counseling on preventative measures are important.<sup>27</sup>

To improve adherence to medication regimens, patients should be advised that the benefits of using retinol are more noticeable over time. When used for the treatment of photoaging, results can take from 3 to 6 months of daily application to become apparent.<sup>17,19</sup> Despite the lack of conclusive research, patients should understand that the proven teratogenic effects of oral retinoids discourage topical retinoids during pregnancy.<sup>20</sup> Lastly, topical use of retinoids is considered a long-term treatment since its benefits cease with discontinuation.<sup>20</sup>

## SUNSCREEN

Sunscreen is recommended for everyone by the American Academy of Dermatology (AAD) for baseline skin protection.<sup>28</sup> Its use is encouraged over exposed skin regardless of if the sun is visible or not. Prolonged exposure to the sun can lead to loss of skin elasticity, cancers, and other discoloration issues. One in five Americans will develop skin cancer regardless of age, gender, and skin type.<sup>28</sup> The AAD currently recommends the use of sunscreen with an SPF of at least 30, broad spectrum protection against UVA and UVB rays, and water-resistant properties.<sup>29</sup> SPF is defined as the sun protective factor, or the measure of how much UV radiation is necessary to produce sunburn on protected skin vs on unprotected skin.<sup>30</sup> The higher the SPF, the more protection against UV radiation.<sup>30</sup> The most important outcomes of sunscreen include antiphotaging and cancer protection.<sup>31</sup>

The sun emits UVA, UVB, and UVC rays.<sup>32</sup> Ultraviolet radiation can directly damage DNA, and the accumulation of this DNA damage leads to cancer development.<sup>33</sup> The combined effects of UV damage can potentially lead to photoaging and the development of melanoma and nonmelanoma skin cancers.<sup>28</sup>

Sunscreen products are categorized as mineral or chemical compounds that include inorganic and organic ingredients respectively.<sup>32</sup> Chemical sunscreens absorb UVA and UVB rays and then deactivate them, whereas physical or mineral sunscreens use inorganic ingredients to act as a barrier and shield the skin by reflecting and scattering the UV rays.<sup>32</sup> Mineral sunscreens are recommended over chemical sunscreens for those with sensitive skin due to their nonirritant and noncomedogenic properties.<sup>29</sup> The white chalky cast that appears when using mineral sunscreens can be an undesirable cosmetic result for people, however, this can be minimized with different formulations.<sup>34</sup>

The two main inorganic ingredients in mineral sunscreens are zinc oxide (ZnO) and titanium dioxide (TiO<sub>2</sub>).<sup>33</sup> These ingredients are integrated as nanoparticles and are used in nearly every sunscreen because of their effectiveness in protecting against UVA and UVB rays.<sup>30</sup> Together they create a broad-spectrum filter that blocks UV rays, with zinc oxide primarily blocking UVA rays and titanium dioxide reflecting UVB rays.<sup>30</sup> ZnO and TiO<sub>2</sub> are the only two ingredients that are FDA approved as generally recognized and safe and effective for people over 6 months of age or those with sensitive skin.<sup>35-37</sup> For cosmetic reasons, the addition of inorganic substances is more favorable when creating

a desirable sunscreen formulation as they do not cause skin irritation, comedogenic acne, or discoloration.<sup>32</sup>

There are several organic, soluble filters that make up chemical sunscreens such as avobenzone, octinoxate, homosalate, octisalate, and octocrylene.<sup>36</sup> Avobenzone is an oil soluble ingredient in sunscreen that filters UVA rays while octinoxate, homosalate, octisalate, and octocrylene cater to UVB rays, and oxybenzone does both (Table 4).<sup>31</sup> Organic sunscreens function by absorbing the harmful UV rays and deactivating them through a reaction that releases them as heat.<sup>36</sup> This reaction has been linked to worsening preexisting skin conditions such as melasma or rosacea.<sup>38</sup> According to the National Eczema Association, organic ingredients such as oxybenzone, avobenzone, and benzophenone-4, along with high alcohol concentrations, can exacerbate eczema as well.<sup>39</sup> Organic ingredients tend to be comedogenic, compared to mineral sunscreens.<sup>40</sup> However, a chemical (organic) sunscreen that has comedogenic properties can still help prevent skin cancer, hyperpigmentation, and erythema.<sup>39</sup> Patients can discuss their personal considerations with their physician when deciding between mineral or chemical sunscreen utilization.

Mineral sunscreens are generally preferred due to their noncomedogenic and hypoallergenic properties; however, because the sunscreen is not absorbed into the skin and has reflective properties, more frequent reapplication is needed. It is beneficial to recommend purchasing mineral sunscreens labeled “water resistant” or “waterproof” to maximize their efficiency. Chemical sunscreens are indicated when the skin is exposed to water or sweat. Chemical sunscreens are absorbed into the skin, allowing for a longer-lasting sun protective factor that can be beneficial with prolonged water/sweat exposure with UVA/B rays.<sup>42</sup>

UV radiation can also be physically blocked by wearing hats, sunglasses, and tightly woven clothes. The ultraviolet protective factor (UPF) measures the amount of UV radiation that can penetrate clothing and reach the underlying skin.<sup>42</sup> Clothing with polyester or cotton blends typically have a UPF value of 50 (Table 5).<sup>42</sup>

Avoiding the sun between the hours of 10 am and 4 pm and using an SPF of 30 or higher that has a broad spectrum will also provide significant protection.<sup>32,42</sup> To ensure optimal protection, adults should apply 1 to 2 ounces of sunscreen to all exposed areas 15 minutes before sun exposure. Reapplication of sunscreen every 2 hours, if exposed to water and/or sweat, is also important to obtain sustainable sun protection.<sup>32</sup>

CONCLUSION

Sunscreen, vitamin C, and retinol may be used in combination to combat the effects of UV-induced skin damage, as they each exert photoprotective properties via different mechanisms. The following order allows for the most effective absorption of the products: vitamin C or retinol, followed by moisturizer, followed by sunscreen. Educating patients on the correct application and ways to avoid irritation is crucial for adherence to skincare

regimens involving these products in addition to ensuring each product’s efficacy. In this ever-changing arena of products, it is important for family physicians to stay up to date and to make informed recommendations on these, while considering specific benefits and precautions with certain product formulations.

LITERATURE SEARCH AND DATA SOURCES

This literature review was synthesized using a variety of sources from PubMed and WorldCat Discovery databases. Additional sources were the American Academy of Dermatology, the Cleveland Clinic, and other government-regulated dermatology institutions. Peer-reviewed journal articles and studies were searched using specific parameters to ensure accurate and recent information. Keywords used to search for articles were vitamin C, L-ascorbic acid, photoaging, hyperpigmentation, retinoids, topical retinoids, retinol, sunscreen, organic sunscreens, inorganic sunscreens, skin cancer, melanoma, nonmelanoma skin cancer, photoaging, sun protective factors, sunburn, antiaging, mineral sunscreen, chemical sunscreen.

TABLE 4:  
Active ingredients in sunscreens<sup>36,41</sup>

Active Ingredient	Type	Method of Protection Against UV Rays	FDA Recommendation of Maximum Concentration
Avobenzone	Chemical	Absorbs UVA	3%
Octinoxate	Chemical	Absorbs UVB	7.5%
Homosalate	Chemical	Absorbs UVB	15%
Octisalate	Chemical	Absorbs UVB	5%
Octocrylene	Chemical	Absorbs UVB	10%
Oxybenzone	Chemical	Absorbs UVA and UVB	6%
Zinc oxide	Mineral	Absorbs UVB	25%
Titanium dioxide	Mineral	Absorbs UVB	25%

TABLE 5:  
SPF ratings<sup>43</sup>

SPF	% of UV Radiation Blocked	UPF	% of UV Radiation Blocked
15	93%	15	93.3%
30	97%	30	96.7%
50	98%	50+	98%
100	99%		

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