# Building the Skin Care Regimen: Choosing the Right Ingredients

Four primary product types provide the basis for a skincare regimen that ensures the health and optimized function of the skin.

**By Vivian W. Bucay, MD**

When I first entered private practice in 1991, my primary concern was that I would be able to make the correct diagnosis, which, in turn, would allow me to make the appropriate treatment recommendations. It did not occur to me then that recommending skin care regimens would occupy such a large part of clinical time. In fact, today one of the most common "chief complaints" that prompts a patient to schedule an office visit is for recommendations for skin care. Anyone who has ever navigated the skin care aisles of a drugstore or the cosmetics counter at a department store or even the many websites devoted to skin care can understand the feeling of being overwhelmed by the plethora of choices. Clever marketing can make it very difficult to separate hype from fact. Ironically, the typical dermatology residency program does not devote time to the area of skin care, and we are often left to learn this on our own time. This irony is unfortunate because, as dermatologists, our focus should not be limited only to diseases of the skin, hair, and nails, but to their health and well being as well. Carrying this one step further, health and well being are often equated with beauty. It would be difficult to deny that beauty and cosmetic concerns have a place in the daily practice of our specialty.

As physicians devoted to treating the diseases of and ensuring the well being of the skin, patients seek our advice regarding the best skin care options available. Given the vast array of skin care products available today, patients are no longer willing to believe that all creams are the same and that, beyond a good sunscreen, nothing else matters. It is our responsibility to be as familiar as possible with the various topical agents available so that we can make the appropriate skin care recommendations.

At the conclusion of the first office visit, whether it is for acne, a skin cancer check, or psoriasis, I will typically ask the patient if there is anything else they would like to discuss. More often than not, the answer goes something like this, "Why, yes, can you recommend a good skin care regimen?" Despite the

**Take-Home Tips.** Dermatologists should be prepared to recommend skin care—beyond cleansers and moisturizers—for all patients. Four categories are key: 1) sunscreen, 2) topical antioxidants, 3) retinoids, and 4) DNA repair. When devising a skin care regimen, consider the individual's particular skin type and any dermatologic problems such as acne, melasma, rosacea, as well as other factors such as work/school schedules, lifestyle habits, and willingness to adhere to a skin care routine. Keeping the skin care regimen as simple as possible will increase the probability of compliance.

fact that I know that this will put me even further behind schedule, I prefer not to miss this opportunity to review the skin care products that are most compatible with that individual's skin type and needs. For the purposes of this paper, I am not referring to the usual skin care regimen consisting of a cleanser, toner, and moisturizer. I think of skin care in the following categories: 1) sunscreen, 2) topical antioxidants, 3) retinoids, and 4) DNA repair. Patients often ask about collagen boosters, such as growth factors and peptides. Although there are many excellent products on the market containing some of these novel agents, these products also frequently contain retinol and/or antioxidants, the benefits of which have been well established as supported by extensive research.

When devising a skin care regimen, I take into consideration the individual's particular skin type (Leslie Baumann's *The Skin Type Solution*[1] is an excellent resource) and any dermatologic problems such as acne, melasma, rosacea, as well as other factors such as work/school schedules, lifestyle habits, and willingness to adhere to a skin care routine. Keeping the regimen as simple as possible will increase the probability of compliance.

## Sunscreen

I tell patients that the daily use of sunscreen is nonnegotionable. Period. Adequate sun protection is at the core of every skin care regimen. As dermatologists, we understand the importance of sun protection, but our challenge lies in conveying the role that sunscreen plays in maintaining skin health. Once a patient understands the need for daily sunscreen use, the next hurdle to overcome is finding a sunscreen that she/he will want to use on a daily basis. There are a number of reasons why a patient will not use sunscreen. Complaints include: 1) the product feels oily, heavy, or sticky; 2) it causes acne; 3) the sunscreen makes the patient feel hot and sweaty; and 4) incompatibility with makeup or other skin care products.[2] All of these issues can be addressed simply by selecting the right sunscreen for the individual's skin type. Sunscreens come in a variety of formulations including lotions, creams, gels, sprays, and powders, which makes it relatively easy to find a product suited to a patient's skin type and needs.

The purpose of sunscreens is to protect the skin from the harmful effects of ultraviolet radiation (UVR). For any patient who doubts that chronic sun exposure leads to aging of the skin, I tell them to look at the skin on a covered area, like the buttocks, and compare it to skin on the arms or upper chest. The majority of patients are unaware of ultraviolet immunosuppression.[3] As a matter of fact, most patients are surprised to learn that the skin even plays a role in immune surveillance.

When patients bring up the issue of sunscreen safety, I explain to patients that sunscreens are classified as over-the-counter drugs and can only contain ingredients that have been approved by the US Food and Drug Administration as listed in the FDA's Sunscreen Monograph final Rule.[4] Currently, there are 17 UV filters (Mexoryl SX was added to the initial list of 16 based on a new drug application submitted to the FDA) on this list, and all permitted UV filters can be combined with other approved UV filters, with the exception of avobenzone.[5] Like any other drug, the efficacy of a sunscreen is dose-dependent, and it is important to apply an adequate amount of sunscreen in order to reap its benefits. The dose of sunscreen used in testing by the FDA and the recommended dose for regular use is 2mg/cm$^2$. Using this amount as a

guideline, 10ml or two teaspoons of an SPF 15 sunscreen are needed for the face alone; for a SPF 30 product, it takes about one ounce or 30ml to cover the average adult from head to toe.[6]

A sunscreen should offer broad UV protection to include UVA (320-400nm) and UVB (290-320nm). Active ingredients are often combined in order to obtain broader UV coverage. Sunscreens are generally divided into two classes: chemical (organic) and physical (inorganic). Chemical sunscreens (e.g. benzophenone, homosalate, methyl anthranilate, octylmethoxycinnamate, oxybenzone, avobenzone) work by converting UVB radiation into heat. Physical sunscreens (e.g. zinc oxide, titanium dioxide, kaolin, ichthammol, iron oxide) scatter, reflect and absorb solar radiation across a broad spectrum in the UV and visible ranges. With the development of micronized formulations, physical sunscreens are now cosmetically elegant, non-comedogenic, and invisible, because the finely ground particles do not reflect in the visible spectrum. Another advantage of physical sunscreens is their chemical stability and minimal risk of contact sensitivity.

## Topical Antioxidants

Free radicals are highly unstable and reactive molecules with an odd number of electrons, and those generated from oxygen are known as reactive oxygen species (ROS). These highly reactive molecules can damage cellular membranes, DNA, and cellular proteins. Free radicals can be produced by normal cellular metabolism or can be triggered by external factors, including UVR and cigarette smoking. Skin aging is generally attributed to a combination of intrinsic/chronologic aging and extrinsic/ environmental aging, and ROS play a key role in both types of aging, a concept first published by Harman, et al. in 1956.[7] Free radicals can also lead to inflammation, another factor that has been implicated in aging.[8]

Endogenous mechanisms that protect the body from ROS generated by normal cellular metabolism include enzymes such as superoxide dismutase, glutathione peroxidase, and catalase, as well as other antioxidants including glutathione, vitamin C, and vitamin E, carotenoids, and ubiquinone (CoQ10). Studies have shown that UVR can affect both enzymatic and nonenzymatic antioxidant levels.[9,10,11] These decreased levels of antioxidants can lead to cell damage following repeated UV exposure.

Given that ultraviolet radiation is the primary cause of free radical formation, daily sunscreen use is ideal although not often a reality for most of our patients. For this reason, I recommend daily use of a topical antioxidant to scavenge free radicals and decrease cellular damage, in an attempt to prevent photodamage as well as to improve some of the signs of aging, such as wrinkles and solar lentigines. Some antioxidants, such as green tea, also possess anti-inflammatory properties, thereby offering an additional mechanism of protection. There are numerous topical antioxidants available, and the rest of this section will focus on some of the more well known and more studied of these.

***Vitamin C.*** Topically applied vitamin C has been studied extensively and has been shown to prevent UV-induced erythema and sunburn cell formation.[12,13] Vitamin C exists primarily in its reduced form, ascorbic acid, which has a short half life, and many available products that claim to contain vitamin C contain its derivatives, which may not be absorbed as readily[14] or converted to ascorbic acid, the active form.[15] Oxidation renders vitamin C ineffective, and it is important to choose products that are stable and not easily degraded. Not only is vitamin C required for collagen production, its addition to human skin fibroblasts has been shown to stimulate collagen synthesis.[16] Studies have shown that topically applied vitamin C improves the appearance of wrinkles.[17,18] Adding vitamin C to a sunscreen enhances its photoprotective properties when compared to sunscreen alone,[19] and there is a growing market trend to add antioxidants to sunscreens.

In a 12-week double-blind split-face study, Fitzpatrick and Rostan demonstrated the ability of topically applied vitamin C to improve wrinkling due to photodamage.[20] The authors used a combination of water-soluble 10% ascorbic acid and a lipid-soluble analog of vitamin C 7%, tetrahexyldecyl ascorbate, to increase absorption in both water-soluble portions of the cell as well as enhance penetra-

tion through cell membranes (lipid-soluble). Studies by Barnet Products Corporation have shown that tetrahexyldecyl ascorbate (THD) penetrates through the epidermis and reaches the dermis better than ascorbic acid.[21] Penetration rates are dose-dependent, but, at the same concentration, THD surpasses the penetration of ascorbic acid by three-fold, and the rate of penetration is higher even when the concentration of ascorbic acid is 25 times that of THD.[21]

Finally, it is important to keep in mind that in addition to its function as an antioxidant and its role in collagen production, vitamin C restores vitamin E's antioxidant capacity,[22,23] an important activity given that vitamin E is the body's most potent inhibitor of lipid peroxidation.

***Vitamin E.*** Another popular topical antioxidant is vitamin E, also known as tocopherol. Lipid-soluble, the vitamin E family consists of eight active isomers, which are divided into tocopherols and tocotrienols. Of these, alpha-tocopherol has the strongest biologic activity. Vitamin E reduces the number of sunburn cells, decreases UVB-induced photodamage,[24] and can inhibit UV-induced tumor formation.[25] Alpha-tocopherol, a membrane-bound antioxidant, protects cell membranes from damage caused by phospholipase A, lysophospholipids, and free fatty acids.[26] Vitamin E has been shown to inhibit human macrophage metalloelastase, a matrixmetalloproteinase (MMP) that degrades elastin,[27] and signs of photoaging were shown to improve in a study comparing the use of a vitamin E cream versus placebo.[28] The combined application of vitamins E and C has been shown to provide more potent photoprotection compared to either agent alone,[13] and there are several products on the market that offer this combination. A limitation to topically applied vitamin E is the potential for contact dermatitis.[29,30]

***Green Tea.*** Green tea refers to the antioxidant extracted from the leaves and buds of the plant *Camellia sinensis*. The green tea polyphenols include epicatechin, epicatechin-3-gallate, epigallocatechin, and epigallocatechin-3-gallate (EGCG), the latter being the most abundant and potent.[31] Animal studies have shown that topical application of green tea polyphenols can inhibit photocarcinogenesis[32] as well as prevent UV-induced oxidative damage and induction of matrix metalloproteinases.[33] In vivo application of green tea polyphenols to human backs 30 minutes prior to UV irradiation was shown to reduce erythema, the number of sunburn cells, immunosuppression,[34] and DNA damage.[35] Another study demonstrated that topically applied EGCG was effective in reducing UVB-induced inflammation.[36]

Their ability to act as antioxidants, anticarcinogens, and anti-inflammatories contribute to the popularity of green tea polyphenols in cosmeceuticals. It is important to keep in mind that the concentration of green tea polyphenols varies from product to product and that controlled clinical trials are lacking. Notwithstanding, I find the concomitant application of a green tea-containing product to be very helpful in mitigating the skin irritation associated with topical retinoid use.

***Niacinamide.*** Also known as nicotinamide, niacinamide is the biologically active form of vitamin B3. Like the green tea polyphenols, niacinamide functions as an antioxidant and an anti-inflammatory.[37] Another interesting property of this compound is its ability to improve hyperpigmentation by decreasing melanosome transfer to keratinocytes. In a clinical study, topically applied niacinamide was found to reduce fine lines and hyperpigmentation and to improve skin texture and tone.[38] Perhaps not as well known is the beneficial effect of niacinamide on acne. In an eight week double-blind study involving 76 patients, Shalita, et al. found twice daily application of a 4% nicotinamide gel to be of comparable efficacy to twice daily application of 1% clindamycin gel in the treatment of acne vulgaris.[39] Application of 2% niacinamide has been shown to lower sebum excretion rates in facial skin.[40]

From a practical standpoint, I often recommend a niacinamide-enriched sunscreen for my patients, of particular benefit to those suffering from acne and who are prone to post-inflammatory hyperpigmentation.

***Other antioxidants.*** Sylimarin extract consists of three polyphenolic flavonoids (silybin, silydianin, and silychristine) derived from the milk thistle plant, *Sylibum marianum*. Sylibin is considered to be the

most biologically active form and has been shown to have photoprotective properties[41] as well as to decrease the production of skin tumors by 92 percent after UVB exposure in a mouse skin model.[42]

Idebenone is the synthetic analog of ubiquinone (Coenzyme Q10 or CoQ10) and has been shown to be more potent as an antioxidant than CoQ10.[43] Although shown to be effective in the treatment of photodamaged skin, there are reports of contact dermatitis from skin care products containing idebenone.[44] Over the last several years, I have seen many cases of contact dermatitis in patients who have developed sensitivity to this compound.

Genistein, an isoflavone derived from soybeans, is a potent antioxidant that scavenges peroxyl radicals, thereby protecting against lipid peroxidation. It inhibits UV-induced oxidative damage[45] and reduces UVB-induced photodamage in human skin.[46]

Additional topical antioxidants of interest include resveratrol, CoffeeBerry® and pycnogenol, to name a few. It is important to counsel patients that although products containing these compounds may sound appealing, one should keep in mind that controlled clinical studies are lacking and that it may be

**Table 1. Cosmeceutical Recommendations and Notes**

### Sunscreens

**Elta UV Clear SPF 46** (Swiss-American): Oil-free, 9.0% zinc oxide, octinoxate 7.5%, vitamin B3 (niacinamide); Works on acne and photodamage.

**Sunforgettable SPF 30** (Colorescience): Titanium dioxide 12% and zinc oxide 11%; Brush-on, refillable, several shades, portable, water resistant.

**Revision Intellishade SPF 45** (Revision, Inc., Dallas, TX): Tinted moisturizer that evens out skin tone, hydrates and provides sun protection; Octinoxate 7.5%, octisalate 5.0%, zinc oxide 2.0%; An alterantive to foundation.

### Antioxidants

**Glytone Antioxidant Serum** (Pierre Fabre, Dist by Genesis Pharamceuticals): Vitamin C as tetrahexyldecyl ascorbate (THD), Vitamin E as delta-tocopheryl glucoside complex, and red tea flavonoids.

**SkinCeuticals C E Ferulic** (SkinCeuticals, Inc.): L-ascorbic acid, alpha tocopherol, ferulic acid .

**Replenix Power of Three Cream** (Topix): green tea polyphenols, resveratrol, and caffeine; anti-inflammatory.

### Retinoids/Exfoliators

**Refissa** (Spear Dermatology Products/Coria Laboratories): A prescription only 0.05% tretinoin; Highly emollient.

**Retriderm** (Biopelle, Inc.): Retinol available in 0.5%, 0.75%, 1% strengths; Oil-free; Protein-rich, aqueous suspension; Increased absorption and bioavailability; Proteins increase conversion rate of retinol to retinoic acid; Reduced irritation because of vehicle blend.

**Retrinal 0.05% and 0.1%** (Pierre Fabre): Retinaldehyde; Well tolerated.

**Retrinal H.A.F.** (Pierre Fabre): Retinaldehyde with hyaluronic acid fragments; Works well around eyes, mouth and the lips.

**Epionce Purifying Lytic Toner and Lytic Lotion Plus** (Episciences, Inc.): Contains salicylic acid; Great for acne prone skin and for postinflammatory hyper pigmentation; Hydrating, well tolerated by patients with rosacea because of the anti-inflammatory properties of salicylic acid.

**Gly/Sal 10/2 Pads** (Topix): 60 pads presoaked with 10% glycolic acid and 2% salicylic acid; Great for acne, keratosis pilaris, and PIH; Easy to use; Great value.

### DNA Repair and Skin Repair

**CELFIX ™ DNA Youth Recovery™ Serum** (Carefree Skincare): 40-50% decrease in UV spots (Canfield Visia) with BID use for 3 months (unpublished results as seen in my practice in over 100 patients in whom baseline and follow-up Visia scans were performed).

**gloTherapeutics gloRefine Hydrator** (gloTherapeutics): Contains Renovage™ (Sederma), teprenone; Works on telomeres to extend cell life by 1/3; Decreases TEWL, up to 56% decrease in UV spots (Canfield Visia)—references on Sederma website.

**Tensage Intensive Ampoules SCA 40** (Biopelle, Inc.): Secretion of snail Cryptomphalus Aspersa (SCA)- snail growth factor; Contains fibroblast growth factor; Works for photodamage and excellent post-procedure, e.g., chemical peels, ablative and nonablative laser procedures; In Europe indicated for radiation dermatitis.

best to use a product containing antioxidants whose effects have been studied extensively.

## Retinoids

Much has been published about the retinoids, a term that refers to naturally occurring as well as synthetic compounds that exhibit the biological actions typical of vitamin A.[47] The chemical structure of retinol was elucidated in the 1930s, followed by publication in 1943 of the first study of its use in acne.[48] All-trans-retinoic acid (tretinoin) was first used to treat acne in 1959. The publication in 1986 by Kligman, et al.[49] of groundbreaking research examining the effects of tretinoin on photoaged skin heralded an explosion of research regarding the effects of topically applied retinoids as well as the development of new topical retinoids. In keeping with the context of this article, retinoids will be discussed for the indication of photoaging.

For regulatory purposes, photodamage is defined as fine wrinkling, mottled hyperpigmentation, and tactile roughness of facial skin. Only tretinoin and tazarotene (a third generation poly-aromatic retinoid) have FDA approval for the indication of treating photodamaged skin. In clinical practice, adapalene may also be used for photodamage, but this is considered off-label. Nonprescription retinoids, including retinol and its metabolite retinaldehyde, are also used to treat aging skin.

A brief review of retinoid metabolism is helpful in understanding the clinical effects of retinoids on photodamaged skin. In order to exert their effects, retinoids first pass through the cellular membrane by nonreceptor mediated endocytosis,[50] after which they are then transferred to the nucleus by cellular retinoic acid-binding protein (CRABP) or cellular retinol-binding protein (CBRP), both of which influence retinoid bioavailability. Retinoids then bind to retinoic acid receptors (RAR) and retinoid X receptors (RXR), both of which have alpha, beta and gamma subtypes. Receptor binding is selective and leads to the formation of homo- and heterodimer receptor complexes that then bind to DNA in the promoter gene region referred to as retinoid response elements (RRE). Transcription can be regulated by activation through specific DNA sites or by inhibition of transcription factors.

Wrinkle improvement is the result of retinoid mediated effects on dermal collagen. An increase in type I procollagen expression[51] mediated by the inhibition of the UV-induction of c-Jun[52] and an alteration of TGF-β expression,[53] correlate with an increase in collagen synthesis. Additionally, inhibition of dermal collagen degradation is accomplished by inhibition of transcriptional factor activator protein-1 (AP-1) activation of matrix metalloproteinases (MMP) like collagenase.[54,55]

The improvement in dyschromia is most likely the result of retinoid inhibition of tyrosinase activity and a reduction in melanin synthesis, a decrease in melanosome transfer, and increased shedding of keratinocytes.[56,57]

An increase in skin smoothness and a decrease in tactile roughness occur early after initiation of topical retinoid therapy. Increased epidermal proliferation and differentiation, compaction of the stratum corneum, combined with an increase in epidermal and dermal intercellular mucin deposition are the result of retinoid influence on molecular mechanisms.[58,59]

For patients who opt for an over-the-counter retinoid or an office-dispensed nonprescription retinoid, retinol and retinaldehyde are good choices. However, I counsel patients that although retinol is less irritating than its metabolite retinoic acid, studies have shown it to be about 20-fold less potent than retinoic acid.[59] Retinaldehyde is a naturally occurring metabolite of retinol and is the precursor of retinoic acid. It is generally well tolerated[60] and demonstrates efficacy in the treatment of photodamage.[61] A study using profilometric evaluation of photodamaged skin demonstrated efficacy of both topical retinaldehyde and retinoic acid in the reduction of wrinkles and roughness; retinaldehyde was better tolerated compared to retinoic acid.[62]

Counseling patients regarding possible side effects of retinoid therapy is critical in ensuring compliance with treatment. Side effects of skin irritation, dryness, and increased sensitivity can be minimized by showing patients the correct amount to apply, limiting frequency to once daily application or as tolerated, avoid-

ing the use of other skin care products that can cause skin irritation, maintaining the integrity of the skin with a barrier repair cream or similar product, and, of course, daily use of sunscreen. As mentioned previously, I have found the use of a cream containing green tea polyphenols or CoffeeBerry®polyphenols prior to or after the application of the retinoid to be very helpful in reducing skin redness and irritation.

## DNA Repair

Gaining in popularity are products that claim to repair DNA damage. Although controlled clinical trials proving the efficacy of these products are lacking, clinical experience in the last few years leads me to believe that there is some validity to these claims. As a stage IV melanoma survivor, the topic of DNA intrigues me. The concept of DNA repair products was first brought to my attention by way of the Remergent skin care line developed by AGI Dermatics founder and cosmeceutical innovator Daniel Yarosh, PhD, a photobiologist with more than 100 publications on the subject of skin and DNA repair. Yarosh's book *The New Science of Perfect Skin* details the science of skin care and is an excellent reference that includes an ample bibliography.[63]

Although the Remergent line was purchased by Estee Lauder two years ago, there are several products on the market that incorporate many of the ingredients recommended by Yarosh. Many of the products use proprietary names for what appear to be the same active ingredients, making it difficult to compare the ingredient lists on product labels. In clinical practice, I have found a product known as CELFIX™DNA Youth Recovery (Carefree Skincare) to be very similar to the original Remergent DNA repair. An unpublished study performed in my clinic involving approximately 100 patients demonstrated that after three months of twice daily application of a DNA repair cream, a 40-50 percent reduction in UV spots was achieved as measured by the VISIA Complexion Analysis (Canfield Imaging Systems). Patients were instructed to apply the DNA repair cream twice daily after cleansing and to wear an SPF 30 sunscreen daily. Otherwise, they were advised to continue following their current skin care regimen as the baseline VISIA for the purpose of this study took these products into account. Furthermore, I have found that the addition of a topical antioxidant in the morning results in an even greater reduction of UV spots than can be obtained with the use of either product alone.

DNA repair liposomes were shown to reduce the incidence of UV-induced skin cancer in mice.[64] To date, there are no controlled trials in humans demonstrating the same, and we are a long way from knowing whether adding DNA repair products to our daily skin care routine will translate to a reduction in the incidence of skin cancer. On the other hand, there is no harm in exploring this possibility, so for now I recommend a DNA repair product for those patients who have a score higher than 200 on the VISIA Complexion Analysis in the category of UV spots.

## Making the Skincare Regimen Part of Your Daily Practice

First-time patients to the practice are offered a VISIA complexion analysis to assess various parameters: spots, wrinkles, pores, texture, porphyrins (as a measure of bacterial colonization), and UV spots. The baseline image is helpful not only in confirming a patient's concerns; it helps track a patient's progress and response to in-office treatments, such as chemical peels and laser resurfacing, as well as to monitor a patient's response to a skin care regimen. The VISIA Complexion Analysis is a tool—it is not a substitute for physical examination of the skin. On the other hand, it does afford a method for measuring some quantifiable parameters that may not be obvious upon simple inspection of the skin. I find it most helpful for tracking UV damage that may not yet be apparent or, as I tell patients, what is lurking beneath the surface. An added benefit is increased adherence to the skin care regimen because patients know that "the VISIA doesn't lie," as one of my patients so simply put it. In that regard, the skin analysis functions in much the same way as a scale does for the dieter.

With the number of Americans age 65 or older climbing to almost 80 million in 2011, we dermatologists have the unique opportunity to guide our patients in making the right skin care choices to maximize the health and beauty of the skin. As a

whole, we are living longer and healthier lives, and our skin should reflect that. In the introduction of *The New Science of Perfect Skin*, Yarosh writes: "Dermatologists know skin. But I know ingredients." Isn't it time we did, too? ■

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