New studies identify ultraviolet A (UVA) (320 to 400 nm) radiation as a key culprit in photoaging and aggressive skin cancers. Unfortunately, UVA protection is not available in all sunscreens, and when such protection is available, the screening agents do not offer complete protection. Under current Food and Drug Administration regulations, a sunscreen can be labeled “broad-spectrum” if it protects skin from any UVA radiation—no matter how small the amount.

UVA is more than 30 times more present in sunlight than ultraviolet B (UVB) (290 to 320 nm). Furthermore, in comparison with UVB, UVA is more evenly present throughout the year. Moreover, it can pass through glass—including home, office, and car windows. UVB is virtually completely absorbed in the top 0.1 mm of skin; UVA can penetrate into deeper layers and through skin. UVA is especially dangerous because it is more effective than UVB at generating reactive oxygen species. Reactive oxygen species are a family of small, oxygen-based molecules that either contain an unpaired electron or are capable of forming one. Reactive oxygen species are generated by not only ultraviolet radiation but also other environmental insults (including smoke, pollutants, pesticides, herbicides, heat, and cold).

Duke University has patented a stable, concentrated solution of L-ascorbic acid that delivers higher doses of vitamin C into skin than can be achieved by diet. New studies show that topical vitamin C (L-ascorbic acid) is an excellent antioxidant for UVA and UVB (290 to 320 nm) protection, making it a useful adjunct to (but not replacement for) sunscreens.1

**Vitamin C (L-Ascorbic Acid)**

Vitamin C is one of the body’s primary protectants from reactive oxygen damage, but it is depleted during ultraviolet injury. Vitamin C serves as the major aqueous phase antioxidant in skin. It not only neutralizes reactive oxygen species destructive to the skin but also actively recycles vitamin E, which serves to protect lipids and cell membranes from these oxidative insults. Human beings cannot synthesize vitamin C; they must ingest it, and body control mechanisms limit absorption and subsequent delivery to tissues. Skin comprises about 8% of body tissues and gets approximately the same amount of oral vitamin C. Half-life after ingestion is 12 to 20 days.

**Topical L-Ascorbic Acid**

The Duke-patented technology solved the problem of how to stabilize the very unstable molecule, L-ascorbic acid, and get it into skin, which usually is an excellent barrier to foreign substances.2 L-ascorbic acid has been formulated in high concentration in a stable aqueous formulation. L-ascorbic acid is un-ionized at acid pH (<3.5). In its un-ionized form, vitamin C applied topically passes into skin in higher concentrations than ever is possible by oral ingestion.

Because body control mechanisms limit the amount of ingested vitamin C available to skin, applying stable L-ascorbic acid topically yields higher concentrations that provide additional protection. And unlike most sunscreens, once vitamin C gets into skin, it cannot be rubbed or washed off or run off with perspiration. The protection seems to last unchanged for days. Topical vitamin C also prevents ultraviolet immunosuppression, a reaction that has been implicated in both melanoma and nonmelanoma skin cancers.

**Photoaging**

Photoaging changes in normal skin have been produced by repeated exposures of modest amounts of UVA light. Studies show that long-wave UVA (340 to 400 nm) alone can cause these changes.3,5 In skin fibroblast culture, UVA rays, but not UVB, generate a family of matrix metalloproteinases, enzymes that destroy connective tissue. Reactive oxygen species, particularly the singlet oxygen produced by UVA exposure, trigger these changes, with a mechanism of action recently identified.6 Similar changes have been generated experimentally in vivo in human skin. Photoaging seems to be the end result of repeated destruction of connective tissue and resulting scarring.

**Photocarcinogenesis**

Several studies have implied that sunscreen use may not protect people from melanoma and may even increase the
likelihood of its development. However, the sunscreens in these studies provided only UVB protection. Lack of both the sunburn signal and UVA protection may explain the increase in melanoma rates reported in these studies.

UVA has been shown to cause melanoma in some animals, including fish and rats. Moreover, psoralen + UVA therapy is known to cause aggressive squamous cell carcinoma and melanoma in human beings. In cell culture, UVA generation of reactive oxygen species can oxidize guanine residues in DNA, which can lead to DNA mutations.7

Sun protection factor (SPF) ratings generate false security because they measure only erythema, mostly generated by UVB. Consumers should think of SPF not as sun protection factor, but as sunburn protection factor. UVA protection is not reflected by an SPF number. In fact, no current measure of UVA protection exists.

Photoprotection

The added levels of L-ascorbic acid achieved by topical application provide photoprotection to skin. Photodamage, which is measured histologically as sunburn cells, can be lessened by L-ascorbic acid (whether produced by UVB or UVA), with protection against UVA damage appearing especially good.8 Because L-ascorbic acid does not absorb UVB or UVA light, its mechanism of action is different from that of sunscreens. L-ascorbic acid seems to protect by neutralizing reactive oxygen species generated by ultraviolet light. Topical ascorbic acid can even be used to treat sunburn, presumably by neutralizing inflammation. Results to date indicate that topical vitamin C is a useful adjunct to sunscreens.

Ultraviolet Immunosuppression

Immunosuppression by ultraviolet light for both contact and delayed-type hypersensitivity occurs in one of three individuals. However, almost everyone with melanoma or nonmelanoma skin cancer has this reaction. In animals, ultraviolet immunosuppression is associated with more aggressive metastatic behavior. Unfortunately, sunscreens don’t protect very well against ultraviolet immunosuppression. In contrast, topical L-ascorbic acid prevents ultraviolet immunosuppression.9

Collagen Synthesis

Vitamin C is the only antioxidant that has been proven to increase collagen synthesis. In human skin fibroblasts in culture, L-ascorbic acid stimulates collagen synthesis without affecting other protein synthesis. L-ascorbic acid is known to be necessary for prolyl hydroxylase, an enzyme essential for producing a stable collagen molecule. In addition, L-ascorbic acid is necessary for lysyl hydroxylase, an enzyme necessary for cross-linking one collagen molecule to another collagen molecule, which is required for tissue strength. Finally, L-ascorbic acid signals collagen genes to synthesize collagen, a reaction that is important in wound healing.

Ascorbic Acid Derivatives

Vitamin C is L-ascorbic acid; this is the molecule that the body uses. Because it is inherently unstable (thereby allowing it to be so effective as an antioxidant), more stable derivatives of ascorbic acid have been substituted in cosmetic formulations. For these derivatives to function, they must first be absorbed into skin and then converted to L-ascorbic acid. Common derivatives include magnesium ascorbyl phosphate and ascorbyl-6-palmitate. Because magnesium ascorbyl phosphate is a charged molecule, it penetrates skin poorly. Ascorbyl-6-palmitate is lipophilic and may prefer the environment of a cream base to skin. Because percutaneous absorption data have not been published for ascorbyl-6-palmitate preparations, it is not clear whether they absorb into skin. However, skin fibroblast studies reveal that this derivative behaves differently from L-ascorbic acid and is toxic at physiological levels (100 μmol/L).

Effective Topical Vitamin C Products

For a topical vitamin C formulation to work, it must first penetrate skin and then remain stable and be available in high enough concentrations to have a biologic effect. Research to date indicates that the gold standard is stable L-ascorbic acid at high concentration (more than 10%) and low pH (<3.5).

Clinical Studies

Topical vitamin C is used for its photoprotective and anti-inflammatory effects. Because L-ascorbic acid is essential for collagen synthesis, it is also used for its wound healing effects. In photoaged skin, anecdotal improvement has been reported; physicians and their patients particularly note improved skin clarity and color. The results of such observations are encouraging; double-blind studies are underway.

Topical vitamin C also has been used in patients undergoing CO2 laser resurfacing. In a published half-face
study, the side receiving topical L-ascorbic acid demonstrated less erythema.\textsuperscript{10}

Summary

A stable aqueous solution of L-ascorbic acid has been developed that delivers higher doses of vitamin C into skin than ever can be achieved by diet. Topical application augments the normal reservoir present in skin and neutralizes reactive oxygen species, adding photo- and anti-inflammatory protection and preventing ultraviolet immunosuppression. Because UVA has been identified as an important photocarcinogen and photaging influence, additional antioxidant protection should be beneficial. Properly formulated, topical vitamin C seems to be a useful adjunct to sunscreens and other forms of sun protection (such as hats, protective clothing, and sun avoidance when feasible). Topical vitamin C also seems to be useful in speeding wound healing, reducing wrinkling, and preventing the erythema associated with laser resurfacing. \textsuperscript{8}

References

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