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THE BENEFITS OF TOPICAL VITAMIN C (L-ASCORBIC ACID) FOR SKIN CARE AND UV PROTECTION

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Summary

Vitamin C (L-ascorbic acid) is one of the body's primary protections from reactive oxygen damage, but it is depleted during ultraviolet (UV) injury. Because body control mechanisms limit the amount of ingested vitamin C available to skin, topical antioxidant therapy becomes an attractive way to target vitamin C directly into skin, provided the unstable L-ascorbic acid molecule can be stabilized and penetrate skin - conditions which have precluded use in topical formulations - until recently.
A new technology for stabilizing high concentrations of L-ascorbic acid that get into skin has been developed. The result: it is now possible to deliver more vitamin C into skin topically than ever can be achieved by diet, thus adding to the body's natural reservoir of antioxidant protection.
Topical vitamin C (L-ascorbic acid) therapies provide several benefits for skin. Topical vitamin C protects against UV radiation, including UVA - an action spectra linked to cause photoaging and some skin cancers, and one that is not protected fully by currently-available sunscreens. Topical vitamin C prevents DNA mutations and UV immunosuppression, a reaction that occurs in over 90% of all skin cancer patients. Topical vitamin C controls inflammation and reduces erythema. Topical vitamin C promotes wound healing and stimulates collagen synthesis.

Riassunto

La vitamina C (acido l-ascorbico) è uno dei principali composti che proteggono il nostro organismo dai danni provocati dai radicali liberi (ROS) ; viene però alterata dai raggi ultravioletti. Poiché il nostro organismo limita e regola la quantità di acido ascorbico usato per via orale, l'utilizzazione della vitamina C per via topica rappresenta un metodo alternativo al suo uso a livello cutaneo. La nota instabilità di questa vitamina ne ha fino ad oggi limitato l'uso.
E' stata perciò messa a punto una nuova tecnologia che, stabilizzando l'acido ascorbico, ne ha reso possibile il suo uso in quantità elevate, aumentando così le riserve antiossidanti della cute.
La vitamina C per uso topico protegge la cute dai raggi UV e può essere inserita in formulazioni solari ad azione antinvecchiamento, per prevenire i danni al DNA e per ridurre i danni da immunosoppressione da irraggiamento che si verificano in più del 90% dei pazienti affetti da tumori cutanei.
La vitamina C per uso topico inoltre controlla i processi infiammatori e riduce l'intensità dell'eritema, promuovendo la riparazione delle ferite e la sintesi del collagene.

ABSTRACT

Topical vitamin C formulated at acid pH can be targeted directly into skin to provide pharmacological levels of protection. It becomes an inherent part of the skin, and is unaffected by bathing, exercise, clothing, or makeup. The benefits of topical vitamin C (L-ascorbic acid) for skin include:

1. Protection from UV radiation - including UVB and UVA;
2. Prevention of UV immunosuppression and DNA mutations;
3. Reduction of inflammation and erythema associated with sunburn;
4. Promotion of wound healing; and
5. Stimulation of collagen synthesis.

Properly formulated, topical vitamin C appears to be a useful complement to sunscreens and other forms of sun protection (such as hats, protective clothing, and sun avoidance).

INTRODUCTION

Vitamin C (L-ascorbic acid) is one of the body's primary protections from reactive oxygen damage, but it is depleted during UV injury. Because body control mechanisms limit the amount of ingested vitamin C available to skin, topical antioxidant therapy becomes an attractive way to target vitamin C directly into skin. By formulating L-ascorbic acid in a stable, acidic, aqueous formulation, it is un-ionized and passes into skin in higher concentrations than ever is possible by oral ingestion (1).

This article first examines the structure and function of vitamin C in skin and then reviews what is known about how ultraviolet light damages skin. Finally, it presents the key benefits of topical vitamin C (L-ascorbic acid) therapies for healthy skin.

B. Why Vitamin C (L-Ascorbic Acid) is Essential for Healthy Skin

The only vitamin C molecule that the body can recognize and use is L-ascorbic acid. However, the body does not synthesize L-ascorbic acid. It must be provided in the diet. Body stores are limited by control mechanisms which allow a maximum of 1200 mg. to be absorbed daily. The half-life of vitamin C is 10-20 days, so that after three weeks, in the absence of further ingestion, vitamin C is mostly depleted. Skin comprises approximately 8% of body tissues and gets about the same percentage of vitamin C through ingestion. The minimum daily requirement for maintaining saturated body stores of vitamin C is 200 mg(2).

L-ascorbic acid is essential to protect skin from oxidative damage and an on-going reservoir is needed to fight free-radical attacks(3). Vitamin C is the major aqueous phase antioxidant in the skin. It not only neutralizes reactive oxygen species destructive to the skin, but also actively regenerates vitamin E(4); vitamin E is the major lipid phase antioxidant in skin and protects cell membranes. Vitamin C protects the aqueous components of skin, including tissue and cell fluids. L-ascorbic acid neutralizes reactive oxygen species including superoxide anion, singlet oxygen and hydroxyl radical.

Reactive oxygen species are stimulated by ultraviolet light and also occur naturally during normal metabolism, since we live in an oxygen-rich atmosphere. Measurements show that when skin is exposed to ultraviolet light, two-thirds of the L-ascorbic acid in skin is destroyed(5). Cigarette smoking also generates reactive oxygen species. Smoking has an even greater effect on premature wrinkling than extensive sun exposure(6). Smoking depletes L-ascorbic acid, resulting in lowered serum levels.

Reactive oxygen species can damage skin constituents including collagen, elastin, proteoglycan, as well as cell membranes and nuclear constituents. In time, it is believed that these changes may result in the breakdown of connective tissue. Visible signs of this destruction encompass intrinsic aging and photoaging changes - including wrinkles, solar lentigines (brown

spots), actinic keratoses - and possibly even skin cancers. It is believed that over 90% of the visible signs of aging are caused by environmental damage.

Topical vitamin C therapies are an attractive way to target additional L-ascorbic acid directly into skin, thereby interfering with environmental oxidative insults, including ultraviolet light, smoking and pollution. The problem has been that what makes L-ascorbic acid such a great antioxidant also makes it a very unstable molecule. In an effort to overcome this inherent problem, formulators have substituted more stable derivatives of vitamin C. But derivatives are not L-ascorbic acid, and L-ascorbic acid is the molecule that the body uses.

Figure 1 compares the L-ascorbic acid molecule with two common derivatives, magnesium ascorbyl phosphate and ascorbyl-6 palmitate.

For a derivative to function in skin, it must first be absorbed into skin and then converted to L-ascorbic acid. The percutaneous absorption of magnesium ascorbyl phosphate is limited because the molecule is charged(7). The percutaneous absorption of ascorbyl palmitate has not been reported, but might be expected to be vehicle dependent; the molecule may prefer a cream vehicle to skin and thus remain outside of skin. Magnesium ascorbyl phosphate is biologically active in fibroblast cell culture and can be shown to stimulate collagen synthesis equal to L-ascorbic acid in a dose dependent manner(8). In comparison, ascorbyl palmitate kills human skin fibroblasts at physiologic concentrations (100FM) by an unknown mechanism9 and is ineffective when compared to L-ascorbic acid against UV photoaging in mice(10).

Stable, topical formulations of L-ascorbic acid, at acid pH, have been developed which deliver pharmacological amounts of L-ascorbic acid into skin, levels that cannot be achieved by diet. (1). Stable preparations of topical vitamin C become an inherent part of the skin, and cannot be washed or rubbed off. Testing shows that they are fully protective for as long as three days after application(1).

To summarize, for a topical Vitamin C formulation to work maximally, it must first get into skin and then remain stable and available in a high enough concentration to have a biologic effect. Studies to date indicate that the gold standard is L-ascorbic acid at high concentration (greater tban 10%) and low pH (less than 3.5).

How Ultraviolet Radiation Damages Skin

The ozone layer protects humans from damage against UVC rays, but not UVB and UVA radiation. UVB radiation causes sunburn. In contrast

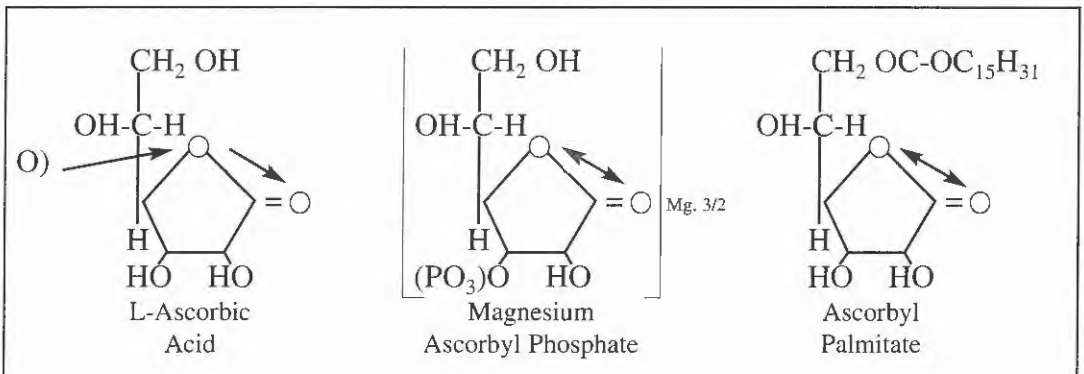

Fig.1 - A Comparison of the Chemical Structure of the L-Ascorbic Acid Molecule with Two Common Derivatives of Vitamin C, Magnesium Ascorbyl Phosphate and Ascorbyl Palmitate.

to UVB, UVA constitutes a severe oxidative stress(11) that may lead to DNA mutations or deletions(12-15). UVA radiation is known to cause photoaging and also is implicated in skin cancers {Lavker, Veres, et al. 1995 ID: 23} {Lowe, Meyers, et al. 1995 ID: 25}(16). Compared to UVB, UVA is thirty times more prevalent. Figure 2 illustrates the relative differences between UVB and UVA, and between short and long UVA in the UV spectrum.

UV radition is implicated in both photoaging and photocarcinogenesis. Recent studies show that it takes relatively small amounts of repeated UVA exposure to cause photoaging in human skin(17-19). Only eight relatively small dosages of UVA are necessary before changes are evident (with a dosage defined as one hour of midday sun); these changes are not prevented by using a sunscreen with a sun protection factor (SPF) of 2218. Studies show that long wave UVA (340-400 nm) alone can cause these changes(20). A recent study reveals details of the photochemistry that may cause photobiologic changes(21). UVA is absorbed by urocanic acid, a natural molecule made by the outermost skin cells, and singlet oxygen is created. The action spectrum peaks at about 355 nm and corresponds to an action spectrum previously shown to cause skin sagging in mice(22).

In skin fibroblast culture, UVA rays, but not UVB, generate matrix metalloproteinases, enzymes that destroy connective tissue(23). Reactive oxygen species, particularly the singlet oxygen produced by UVA exposure, triggers these changes(24). Similar changes have been generated experimentally in vivo in human skin(25). Photoaging appears to be the end result of repeated destruction of connective tissue and resulting scarring.

UVA radiation also may play a role in melanoma formulation. One study detected a correlation

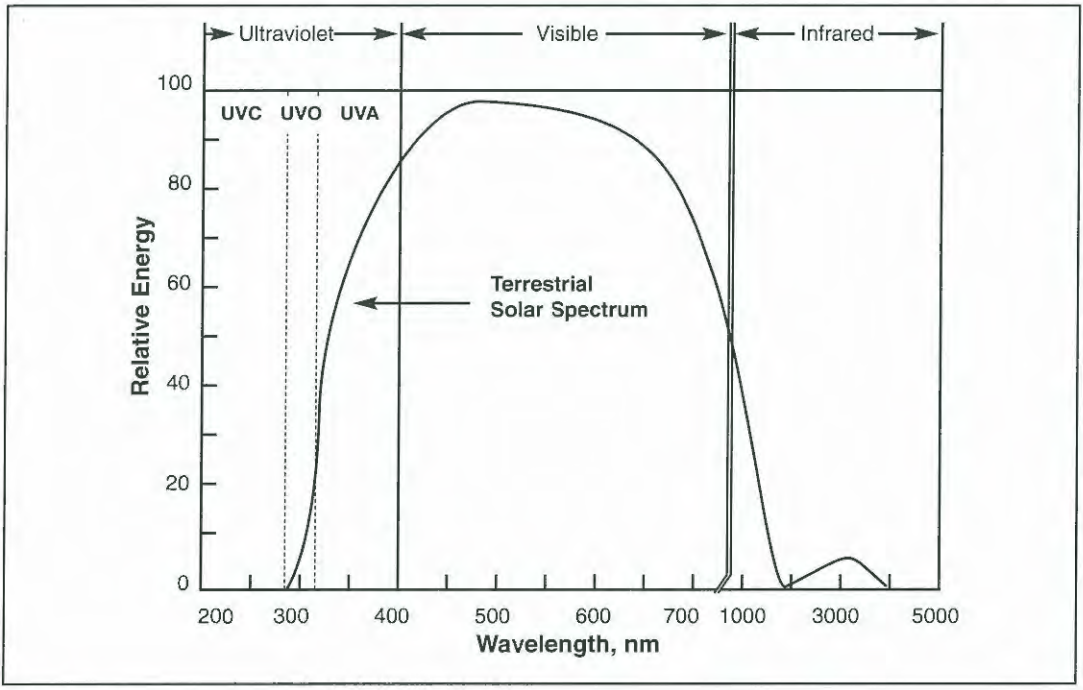

Fig.1 - The Ultraviolet Spectrum

between the use of UVA sunlamps and the development of melanoma, especially in younger individuals(26). PUVA (ultraviolet A radiation plus oral methoxsalen) therapy also is known to increase the incidence of melanoma(27). UVA radiation causes DNA mutations in cell culture12;16 and melanoma in fish(28) and hairless mice(29).

UVA also can promote immunosuppression(30;31), which is associated (with an incidence of 93%) with the development of skin cancer (both non-melanoma and melanoma cancers) in humans(32).

No currently available sunscreen protects fully from UV radiation, with the largest gap in protection occurring in the long-wave UVA range (340-400 nm). Topical vitamin C offers protection against the reactive oxygen species generated by UVA.

KEY BENEFITS OF TOPICAL VITAMIN C (L-ASCORBIC ACID) THERAPIES

Topical vitamin C (L-ascorbic acid) is an excellent antioxidant for skin protection. Topical vitamin C works in two ways: it both protects skin against and reduces harmful effects caused by ultraviolet radiation.

1. Topical Vitamin C Protects Against UV Radiation

Topical vitamin C protects skin against the full UV spectrum, presumably by neutralizing reactive oxygen species before they can damage and destroy DNA and other components of skin(5). Applying L-ascorbic acid topically can lessen photodamage, which is measured histologically as sunburn cells. L-ascorbic acid protects against both UVB and UVA damage; protection against UVA damage is especially good (Darr BJD, 1992 ID77). Because topical vitamin C does not absorb light in the UVB/UVA range, it is not a sunscreen. L-ascorbic acid is a powerful antioxidant and when applied topically, it appears to protect by neutralizing reactive oxygen species generated by ultraviolet radiation.

2. Topical Vitamin C Prevents UV Immunosuppression and DNA Mutations

Topical vitamin C prevents UV immunosuppression(33). This phenomenon, in which the activity of the immune system is stifled following exposure to sunlight, occurs in approximately one-third of individuals. However, it is found in over 90 percent of those who get skin cancers, both melanoma and non-melanoma(32). When skin is immunosuppressed, it is paralyzed in its ability to respond to sensitizers, such as poison ivy. For reasons that are unclear, sunscreens only partially prevent UV immunosuppression. Topical vitamin C prevents UV immunosuppression, specifically the loss of contact hypersensitivity in animals exposed to UV radiation and UVB-induced tolerance(33).

Although it is premature to infer that topical vitamin C protects against skin cancer, scientists do know that mutated cells cause skin cancer and that L-ascorbic acid prevents UV-induced mutations in skin cells. UV-induced reactive oxygen species may change DNA by strand breaks, deletions or mutations. UV light changes guanine into 8-oxoguanine, which may create a DNA mismatch; guanine, when in the 8-oxoguanine state can pair with adenine, rather than cytosine, creating a mutation. The more mutations, the more likely one is to develop skin cancer. Cells in the human body get an estimated 10,000 insults a day, and are able to tolerate and repair the damage(34). However, when cells in the body are subject to more insults in one day (e.g., due to increased sun exposure), they cannot repair themselves fast enough. L-ascorbic acid prevents UV- induced mutations in skin cells in culture (35).

3. Topical Vitamin C Controls Inflammation and Reduces Erythema

Topical vitamin C is capable of controlling the inflammatory response associated with ultraviolet light, including sunburn. Topical vitamin C is protective even when it is applied after sun exposure(5). Topical vitamin C has been used successfully to treat acne rosacea patients(36).

4. Topical Vitamin C Promotes Wound Healing

Topical vitamin C is helpful in speeding the healing process. Topical vitamin C is recommended as a pre- and post-operative regimen for laser resurfacing patients(37). Dermatologic surgeons recommend using it as loug as possible prior to laser resurfacing and beginning again as early as fourteen days following surgery. Topical vitamin C serum (10% L-ascorbic acid) has been shown to decrease the degree and duration of CO2 laser-induced postoperative erythema. Topical vitamin C serum (10% L-ascorbic acid) also has been used successfully to improve the appearance of striae alba following laser treatment(38), possibly by promoting wound healing and stimulating collagen synthesis.

5. Topical Vitamin C Stimulates Collagen Synthesis

Vitamin C is the only antioxidant that has been proven to increase collagen synthesis. This is important because reactive oxygen species destroy skin components - including collagen, which comprises 70% of skin. In human skin fibroblasts in vitro, L-ascorbic acid stimulates collagen synthesis without affecting other protein synthesis(39). L-ascorbic acid also is known to be necessary for prolyl hydroxylase, an enzyme essential for producing a stable collagen molecule(40). In addition, L-ascorbic acid is necessary for lysyl hydroxylase, an enzyme necessary for crosslinking one collagen molecule to another collagen molecule, a reaction which is required for tissue strength(40). Finally, L-ascorbic acid signals collagen genes to synthesize collagen, a reaction that is important in wound healing(41).

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