SYNERGIE SKIN
CLEAN SCIENCE

CLINICAL DATA – PURE L ASCORBIC ACID (VITAMIN C)

L Ascorbic Acid: Topical benefits and medically based data

- L ascorbic acid is the most pure bioavailable form of vitamin C in cosmeceutical grade skin care products.
- Vitamin C derivatives must be converted to L ascorbic acid before it can be used by skin cells that can be absorbed and recognized by the skin.
- L ascorbic acid is highly unstable in aqueous solution and exhibits a shelf life of days to weeks. Even before the solution takes on a yellow-brown tone, the solution is oxidising.
- L ascorbic acid is best used immediately and stored in dry crystal form until immediate use.
- L ascorbic acid is highly active and is best used in gradually increasing doses. Gradually increase usage from 3 x weekly for two weeks, to daily as tolerated. Do not exceed 20%-25% crystals in an aqueous solution.
- L ascorbic acid penetrates the skin very well due to its low molecular weight and delivers the Vitamin C directly into the stratum corneum. Vitamin C derivatives must convert in the skin's layers into L ascorbic acid, and only the new derivatives are stable with a high conversion rate to L ascorbic acid. Most common vitamin c derivatives are:
    - Ascorbyl palmitate- Studies show this is not as effective as L ascorbic acid as there is a low conversion rate to L ascorbic.
    - Magnesium Ascorbyl Phosphate- study shows that this derivative can be slightly cytotoxic if not used with sunscreen

L ascorbic and Collagen Production

Studies have shown that vitamin C helps to minimize fine lines, scars, and wrinkles. Vitamin C is the only antioxidant that has been proven to increase collagen synthesis. Collagen synthesis is essential to maintain healthy skin. Collagen decreases with ageing and photoageing accelerates this process. L ascorbic acid serves as a signal, relaying a critical message to collagen synthesising genes to produce collagen. L ascorbic acid is also a cofactor for two important enzymes required in collagen synthesis.

L ascorbic acid and Sun damage protection

UVA and UVB rays cause free radical damage in the deeper layers of the skin. Free radicals attack the cells that produce collagen and elastin resulting in premature ageing of the skin. L ascorbic Acid neutralizes free radicals and prevents cell damage and premature ageing.

Topical vitamin C protects skin against harm caused by exposure to sunlight. It does this by neutralizing reactive oxygen species (free radicals), the highly reactive molecules produced by the interaction of sunlight, cell membranes, and other components of skin tissue. It does not absorb light, and hence, ***is not a sunscreen***, so it should not be used to replace sunscreen, but rather is a good companion to sunscreen products. Plus, once vitamin C gets into the skin, it cannot be washed, rubbed, or perspired off.

Ascorbic acid and skin lightening

Skin pigmentation is influenced by several factors:

- Hemoglobin in the blood vessels
- Carotenoids in the dermis
- Dark pigment/Melanin in the epidermis

Two forms of melanin are produced in the epidermis:

- phenomelanin, which is red to yellow in colour
- eumelanin which is dark brown to black.

The relative proportions of these also influence skin colour. In addition, individuals differ in the number and size of melanin particles.

Melanin Production

Melanin biosynthesis (melanogenesis) is influenced by

- genetics,
- environmental factors
- diet
- medication

The production of melanin by specialized cells called melanocytes (in the basal layer of the epidermis in light skinned people and in the basal as well as horny layer in dark skinned people) occurs through the action of the enzyme tyrosinase. The rate-limiting step in melanogenesis is the conversion of L-tyrosinase to melanin, through the action of tyrosinase. Copper and oxygen act as catalysts.

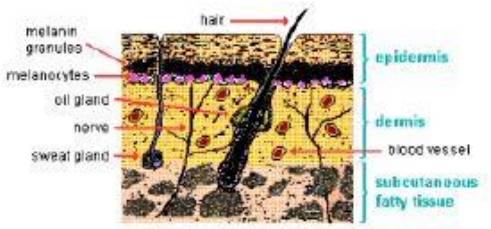
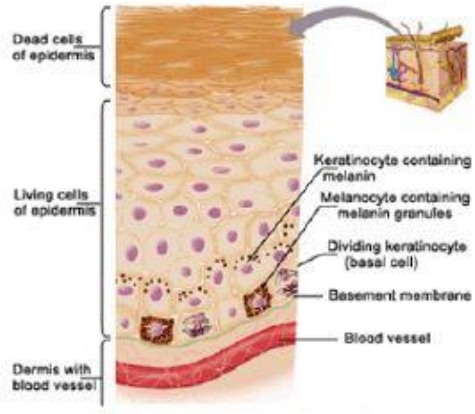


Figure 1: Skin structure and melanin

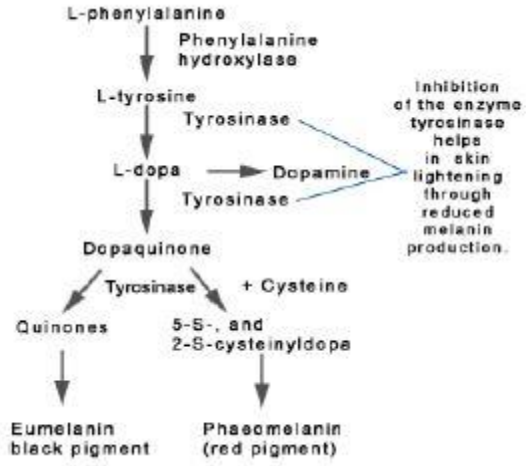


Other enzymes also control melanin production, particularly in the presence of sulphur. These include the following:

- Dopachrome oxidoreductase which controls melanogenesis in the absence of tyrosinase. It helps to convert dopachrome into 5, 6-dihydroxyindole.
- Alpha-glutamyl transpepsidase which helps to maintain the balance in the biosynthesis of eumelanin and pheomelanin.

The currently accepted scheme for melanin biosynthesis is shown in below. Variation in skin pigmentation is attributed to the levels of melanin produced and the number of melanocytes present. Although light skinned, and dark-skinned people may have the

same number of melanocytes present, the rate of melanin production is greater in darker skin tones. Additionally, the melanin present in the epidermal layers of darker skins is resistant to enzymatic degradation. Increased production of melanin on one side of the skin and dramatically reduced decomposition of melanin on the other side results in darker skin tones, and even in light skinned people.



Melanin granules synthesized in the melanocytes are then transferred from the cytoplasm of the melanocytes to the basal cytoplasm of the keratinocytes. They thus form a protective covering in the inner layers of the epidermis, absorbing UV rays and inhibiting their penetration.

Controlling production of melanin

Various types of inflammatory mediators such as leukotrienes and prostaglandins, cytokines and growth factors may influence melanin synthesis by affecting the proliferation and functioning of melanocytes. This explains why inflammatory diseases often induce hypopigmentation or hyperpigmentation. The enzyme, protein kinase C that phosphorylates proteins may also influence the growth and differentiation of melanocytes. Cytokines such as endothelins (also known as vasoconstrictive peptides) are also reported to accelerate melanogenesis.

Thus, the following would all be beneficial in controlling melanin synthesis.

- tyrosinase inhibitors,
- agents that increase keratinocyte turnover,
- agents that inhibit the hormone melanotropin
- physical sunscreens
- reducing agents that convert dopaquinone to DOPA
- indole-blockers that inhibit the formation of intermediates in melanin biosynthesis
- antioxidants that chelate metal ions (which catalyze tyrosinase activity)
- cytokine regulators and genetic manipulation

The toxicity associated with hydroquinone use, induced researchers to identify less dangerous botanicals with comparable activity. The general modes of action include inhibition of the formation of melanosomes, inhibition of tyrosinase biosynthesis, and inhibition of melanin biosynthesis and interference with the transfer of melanosomes into the keratinocytes. Some agents also have a chemical effect on melanin with an increase in the degradation of melanosomes in the keratinocytes. Antioxidants such as L ascorbic acid and others help to decompose preformed melanin. Hyperpigmentation due to UVA and UVB damage may also be addressed with preventive measures such as using antioxidant compounds with sunscreen effect and free radical scavenging action.

Research efforts are generally aimed at achieving one or more of the following effects:

- Regulation/inhibition of tyrosinase, dopachrome oxidoreductase and dopachrome tautomerase involved in melanogenesis
- Regulation of the cytokine network including endothelin
- Regulation of genes related to melanogenesis
- Combinations of the above approaches

Tyrosinase inhibitors such as Arbutin (from the leaves of the common bearberry, (*Arctophylos urva ursi)* and other plants, Glabridin from licorice (*Glycyrrhiza glabra)* roots, L ascorbic acid, Kojic acid (a bacterial carbohydrate metabolite) are all better tolerated than hydroquinone.

Arbutin and Kojic acid inhibit tyrosinase directly, while L ascorbic acid and its derivatives are believed to act as reducing agents on intermediates in melanin biosynthesis at various points in the oxidation chain reaction from tyrosine/DOPA to melanin.

Medical quotes- Research data:

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"In 2002, Fitzpatrick and Rostan 27 applied 10% vitamin C to the cheek of volunteers and compared it with the opposite untreated cheek. At 12 weeks, biopsy specimens revealed an increase in the Grenz zone collagen (the connective tissue immediately beneath the epidermis) and increased gene expression of type I collagen in the skin. There have even been significant changes noted with lower concentrations of vitamin C". Fitzpatrick RE, Rostan EF. Double-blind, half-face study comparing topical Vitamin C and vehicle for rejuvenation of photodamage. Dermatol Surg 2002; 28:231-236

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"In 2004, Sauermann et al investigated the epidermal-dermal junction and depth of dermal papilla in volunteers of all ages and found that as people age, the papillae and its nutritive capillary decrease in density. They then applied topical 3% L-ascorbic acids on the forearm of volunteers and saw that there was an increase in the dermal papillae with new vessel formation after 1 month of treatment, compared with the opposite forearm where placebo was applied. Sauermann K, Jaspers S, Koop U, Wenck H. Topically applied Vitamin C increases the density of dermal papillae in aged human skin. BMC Dermatology 2004; 4:13.

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"Application of a 15% L -ascorbic acid solution to pig skin daily for 4 days protected twofold against solar-simulated UV erythema when compared with vehicle-treated skin." Lin J, Selim M, Shea C et al. UV photoprotection by combination topical antioxidants vitamin C and vitamin E. J Am Acad Dermatol 2003; 48: 866-74.

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