

Inside the Science of Topical Antioxidants



The significance of vitamin C in skin health has long been understood, with scurvy highlighting the lack of mature collagen in vitamin C-deficient patients. Beyond its internal benefits, the revelation that vitamin C, particularly L-Ascorbic acid, could fortify and revitalize the skin externally was a pivotal discovery by the late Sheldon R. Pinnell, MD, SkinCeuticals' founding scientist.

A collagen chemist and dermatologist by training, Dr. Pinnell was among the first scientists to study the role of L-Ascorbic acid in reinforcing connective tissue during wound healing. His patents and research on antioxidant formulations and qualities of L-Ascorbic acid led to landmark studies impacting free radical formation and mitigation of cellular damage.

SkinCeuticals' CE Ferulic serum stands as a testament to this discovery, combining a precise blend of antioxidants that work synergistically to effectively penetrate the outer stratum corneum and protect the extracellular matrix (ECM). Clinical studies demonstrate that adding vitamin E (alpha tocopherol) and ferulic acid to pure L-Ascorbic in a specific ratio provides 8 times the skin's natural protection against atmospheric skin aging.^{1,2} The influential work of Dr. Pinnell spurred more interest and research into the relationship of vitamin C and its beneficial impact on ECM remodeling and cell health.

Each SkinCeuticals vitamin C serum is formulated under The Duke Parameters for effective delivery of vitamin C to the skin and contains specific ingredients to address individual skin concerns of patients. For example, those concerned with fine lines and wrinkles can benefit from C E Ferulic. For patients with uneven skin tone and discoloration, Phloretin CF features 2% phloretin, while Silymarin CF is great for those concerned with blemishes and oil-prone skin.

Dr. Pinnell's research demonstrated there are both aesthetic and skin health benefits of vitamin C. Patricia Farris, MD, goes deeper on the clinical studies to explain our understanding of the mechanism of action of vitamin C within the skin.

— Alison Murakami, PhD, VP and Head, Medical Affairs

Pure L-Ascorbic Acid: The Gold Standard for Environmental Protection



WITH PATRICIA FARRIS, MD

What specific properties of L-Ascorbic acid make it a valuable ingredient in skincare products, and how do these properties contribute to improving skin health?

Dr. Farris: L-Ascorbic acid is a widely studied, multi-tasking cosmetic ingredient that can both protect and repair aging skin. As the most plentiful antioxidant in the epidermis, it neutralizes free radicals and protects skin from oxidative stress, which can damage cell membranes, DNA, and proteins like collagen and elastin. Dr. Pinnell demonstrated that pretreatment of skin with L-Ascorbic acid protects skin from these insults and mitigates sunburn following exposure to solar simulated light. L-Ascorbic acid is also a co-factor for lysyl oxidase and prolyl oxidase, enzymes that are necessary for collagen cross-linking. In addition, L-Ascorbic acid is a potent tyrosinase inhibitor and acts as a skin lightening agent.

There are many varieties of vitamin C on the market, what is important to consider when choosing an antioxidant-containing product?

Dr. Farris: Due to the instability of L-Ascorbic acid, many cosmetic companies use vitamin C derivatives, such as magnesium ascorbyl phosphate (MAP) and tetrahexyldecyl ascorbate (THD) along with other ingredients to achieve skin brightening and cell-turnover. While these are stable forms of vitamin C, they aren't nearly as potent as L-Ascorbic acid and must be converted to L-Ascorbic acid to be biologically active.

Dr. Pinnell is credited with the discovery of how to formulate stable and effective combination antioxidants. He combined pure L-Ascorbic acid with vitamin E and ferulic acid and demonstrated that this combination prevents the formation of cyclobutane pyrimidine dimers (CPDs), sunburn cells, and P 53 up-regulation that is seen following UV light exposure. More recently this triple combination antioxidant has been found to protect skin against pollution-induced oxidative stress and infrared-induced damage. It has also been demonstrated *in vivo* to lessen that damage and to prevent connective tissue breakdown by enzymes in the skin.

So, when choosing a vitamin C serum, consider the source and concentration, solubility of actives, formulation, impact of other ingredients, and what data is available that supports the claims.

THE ANTIOXIDANT AUTHORITY

2005

2008

2014

2021



C E FERULIC LAUNCH
Ferulic acid is added to vitamins C and E, providing 8x skin's natural defense against atmospheric aggressors
(Lin et al., *Journal of Investigative Dermatology*, 2005)

PHLORETN CF LAUNCH
The phloretin molecule is identified and shown to have protective effects when combined with vitamin C and ferulic acid
(Oresajo et al., *Journal of Cosmetic Dermatology*, 2008)

RESVERATROL B E LAUNCH
The first nighttime SkinCeuticals antioxidant is developed with pure, stable resveratrol
(Farris et al., *Journal of Drugs in Dermatology*, 2014)
Research is published on antioxidant protection against infrared-A generated free radicals
(Grether-Beck et al., *Photodermatology, Photoimmunology & Photomedicine*, 2014)

SILYMARIN CF LAUNCH
A combination antioxidant is developed with silymarin and salicylic acid and is clinically proven to help prevent oil oxidation that can lead to breakouts
(SkinCeuticals study, data on file)

What are the scientific mechanisms behind how vitamin C functions as an antioxidant and its role in protecting the ECM from UV damage and environmental stressors?

Dr. Farris: The ECM can be damaged by oxidative stress. UV light, visible light, and infrared are known to increase reactive oxygen species in the skin. Pollutants including ozone and particulate matter also have deleterious effects on skin modulated by oxidative stress. Reactive oxygen species can damage molecules like collagen and elastin directly and indirectly by upregulating redox-sensitive transcription factors that increase collagen-degrading matrix metalloproteinases. Topical L-Ascorbic acid prevents damage to the ECM by neutralizing reactive oxygen species, preventing collagen degradation, and by acting as a co-factor for the enzymes that produce collagen. Vitamin C helps regenerate vitamin E by donating electrons to restore its antioxidant activity.

The effects of L-Ascorbic acid on the dynamics of elastin in the skin are somewhat contradictory. Elastin accounts for 2–4% of the extracellular matrix.³ We know that extrinsic factors like sunlight and smoking can increase elastin production, specifically tropoelastin.⁴ However, these elastin fibers are of poor quality, lack functionality, and contribute to solar elastosis.

Dr. Pinnell explored the idea that in pathological states where photoaged

skin accumulates dysfunctional elastin, it is possible the skin could benefit from L-Ascorbic acid inhibiting the process of elastin synthesis. We need more studies to determine the effect of L-Ascorbic acid on elastin synthesis and solar elastosis.

In addition to benefits of protecting from free radicals, antioxidant-containing vitamin C topicals have also been shown to have an aesthetic benefit. How do vitamin C-containing topicals help skin look healthier and younger?

Dr. Farris: The phenotype of environmentally aged skin includes deep-crease wrinkles, mottled pigmentation, brown spots, and sallowness. L-Ascorbic acid has been shown in numerous clinical studies to improve the appearance of aging skin. It softens fine lines and wrinkles, lightens hyperpigmentation, and promotes a more even skin tone with long term effects demonstrating skin rejuvenation. These skin benefits are due primarily to its ability to improve the collagen content of the extracellular matrix and inhibit tyrosinase effectively lightening hyperpigmentation.

What kind of integrated skincare approaches are complementary to a skincare regimen that contains vitamin C?

Dr. Farris: As a co-factor necessary for collagen production, L-Ascorbic acid helps promote dermal remodeling necessary for wound healing. Studies have demonstrated that application

of a topical containing C+E+ferulic can reduce redness and edema and improve healing time following an ablative laser procedure. Preliminary biopsy studies taken from such patients indicate that healing is mediated through increased expression of basic fibroblast growth factor and enhanced collagen production.⁵

In addition, combining C+E+ferulic acid with non-ablative laser has been demonstrated to enhance and prolong results compared with laser alone.⁶ And, while antioxidant serums don't replace sunscreen, SkinCeuticals' vitamin C serums enhance the effects of SPF. The pairing of the two provides more advanced broad-spectrum UV and environmental protection. ■

1. Lin, Fu-Hsiung et al. "Ferulic acid stabilizes a solution of vitamins C and E and doubles its photoprotection of skin." *The Journal of investigative dermatology* vol. 125,4 (2005): 826-32. doi:10.1111/j.0022-202X.2005.23768.x.

2. Murray, John C et al. "A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation." *Journal of the American Academy of Dermatology* vol. 59,3 (2008): 418-25. doi:10.1016/j.jaad.2008.05.004.

3. Tzaphlidou, Margaret. "The role of collagen and elastin in aged skin: an image processing approach." *Micron (Oxford, England : 1993)* vol. 35,3 (2004): 173-7. doi:10.1016/j.micron.2003.11.003.

4. Chowdhury, Anika et al. "Polyphenol treatments increase elastin and collagen deposition by human dermal fibroblasts: Implications to improve skin health." *Journal of dermatological science* vol. 102,2 (2021): 94-100. doi:10.1016/j.jdermsci.2021.03.002.

5. Waibel, Jill S et al. "Laser-assisted delivery of vitamin C, vitamin E, and ferulic acid formula serum decreases fractional laser postoperative recovery by increased beta fibroblast growth factor expression." *Lasers in surgery and medicine* vol. 48,3 (2016): 238-44. doi:10.1002/lsm.22448.

6. Geronomus, Roy et al. "Enhanced efficacy of a topical antioxidants regimen in conjunction with a home-use non-ablative fractional diode laser in photo-damaged facial skin." *Journal of cosmetic and laser therapy : official publication of the European Society for Laser Dermatology* vol. 18,3 (2016): 154-61. doi:10.3109/14764172.2015.1112408.

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