Efficacy of Ferulic Acid in Improving the Appearance of Photoaged Skin

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Ferulic acid is a new multifunctional cosmeceutical ingredient with antioxidant and UV radiation (UVR)–protective qualities that was originally isolated in 1866 from the *Ferula foetida* plant, from which its name is derived (Figure 1). Ferulic acid is a phenolic derivative of plant cell walls and is found in lignocellulose, a substance that crosslinks lignin and polysaccharides, conferring rigidity to plant cell walls. Ferulic acid is chemically related to trans-cinnamic acid and is commonly found in foodstuffs, such as rice, wheat, oats, coffee, apples, peanuts, oranges, and pineapples. When used in cosmeceuticals, most ferulic acid is not extracted from foods, but rather synthesized from the action of O-methyl transferase on caffeic acid.

The most interesting property of ferulic acid is its ability to function as an antioxidant (Figure 2). Ferulic acid contains a phenolic oxygen-hydrogen group capable of acting as a hydrogen donor to free radicals. In plants, ferulic acid functions to prevent the oxidation of lipids in the cell wall, since plants must survive in an oxidation-rich outdoor environment. Ferulic acid is remarkably heat stable, retaining 83.8% of its antioxidant capabilities after heating to 160°C and is more thermostable than the common antioxidant preservatives butylated hydroxyanisole and dibutylhydroxytoluene. The ability of ferulic acid to function as an antioxidant was demonstrated in the sunburn cell assay.[1]

Ferulic acid is also able to absorb UVR with a maximal peak at 317 nm for cis-ferulic acid and 236 nm and 322 nm for trans-ferulic acid. This UVR-absorbing capacity is due to the highly unsaturated structure of ferulic acid found in the carbonate-carbonate bond, carbonyl group, and benzene ring. Utilizing the same mechanism of photoprotection as organic sunscreens, after UVR is absorbed it is converted to heat through resonance delocalization.

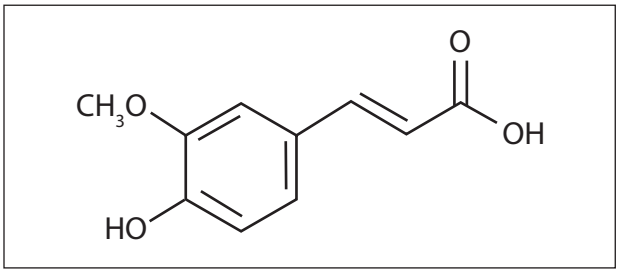

Figure 1. The chemical structure of ferulic acid.

Ferulic acid can be formulated in topical skin preparations with other antioxidant vitamins, such as vitamins C and E, in order to provide a novel topical antioxidant combination. Vitamin C, also known in its reduced form as ascorbic acid and in its active form as L-ascorbate, is an essential oral nutrient requiring daily consumption. It is able to reduce oxidative stress by acting as a substrate for ascorbate peroxidase and an electron donor for 8 different enzymatic functions. Vitamin E is also able to reduce free radicals by donating a hydrogen atom from the hydroxy group contained in the chromanol ring. The antioxidant effect of 0.5% ferulic acid can be enhanced by adding 0.01% of vitamin E. Vitamin E is the most biologically important oral antioxidant, but it also has many topical effects. Vitamin E is frequently used as an emollient in skin care products for its ability to smooth desquamating corneocytes. It aids in imparting a smooth, tactile feel to the skin's surface.

A carefully constructed skin care product contains a combination of complementary ingredients designed to optimize the appearance and texture of the skin. Our research examined the suitability of ferulic acid

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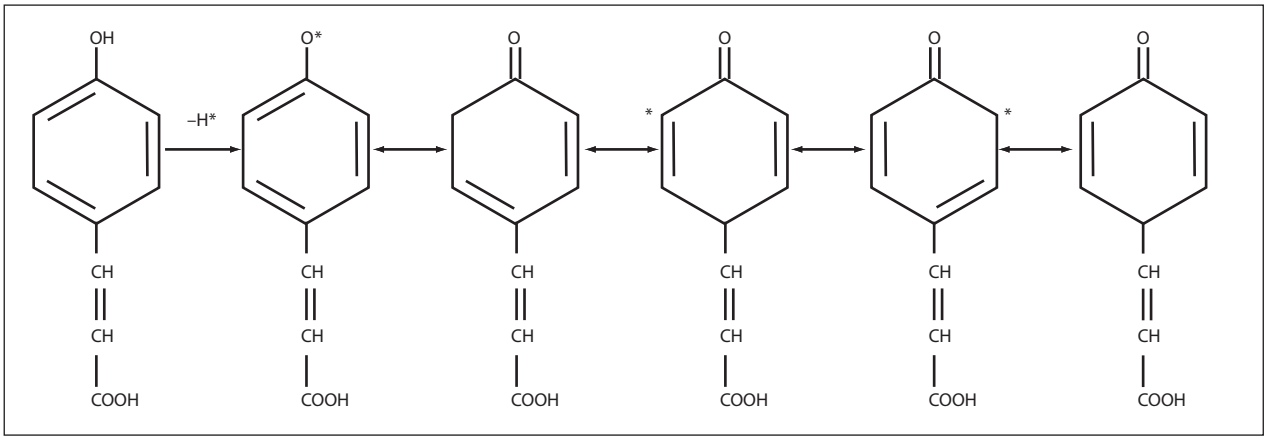

Figure 2. The antioxidant abilities of ferulic acid are related to the phenolic oxygen-hydrogen groups, which release a hydrogen radical to yield phenoxy radicals, forming a stable resonance.

in combination with vitamins C and E in a cleanser and treatment serum when used by individuals with normal and self-perceived sensitive skin. The cleanser and treatment serum were applied twice daily to the face for the purpose of improving the appearance of photoaged skin.

Methods

This single-center study enrolled 35 healthy, nonpregnant females aged 30 to 60 years who signed an institutional review board–approved informed consent form. Half of the subjects possessed normal facial skin and the other half possessed self-perceived sensitive skin and frequent hormonal acne. The goal of the study was to determine the ability of ferulic acid in combination with vitamins C and E to improve facial photodamage, which leads to photoaging in this demographic. Subjects were provided with a treatment serum and a cleanser to use twice daily on the face. A sunscreen with SPF 20 was also provided for at least a once-daily application to the face. The study utilized investigator, subject, dermospectrophotometer, skin elasticity, and profilometry assessments at baseline and weeks 4, 8, 12, 18, and 24. Compliance was determined from subject diaries.

The investigator assessed product tolerability (erythema, desquamation, edema, facial acne flare, itching, stinging, and burning) and efficacy (fine lines, wrinkles, poor skin texture, lack of skin smoothness, and lack of skin firmness) with an ordinal scale defined as follows: 0=none, 0.5=very minimal, 1=minimal, 1.5=very mild, 2=mild, 2.5=moderate, 3=moderately severe, 3.5=severe, and 4=extremely severe. The subjects were also asked to evaluate any facial irritation in terms of redness, facial acne flare, peeling, itching, stinging, and burning on the same ordinal scale.

Noninvasive assessments were also employed to further evaluate the effects of ferulic acid in combination with vitamins C and E on skin tolerability and photodamage leading to photoaging. Dermospectrophotometry measurements for erythema were obtained from the upper left cheek at each visit. The dermospectrophotometer measured red light reflected from the skin's surface with the purpose of determining if ferulic acid in combination with vitamins C and E caused any skin inflammation, as measured indirectly through increased erythema. In addition, skin elasticity was evaluated with an elastometer. The elastometer applied a metered amount of suction to the skin for 5 extension and relaxation cycles. The skin was drawn up into a suction cup until a light beam was interrupted and an elasticity reading was taken. The same operator took measurements from the skin lateral to the right eye at each visit.

Finally, profilometry was used to evaluate the effects of the cleanser and treatment serum containing ferulic acid in combination with vitamins C and E on fine and coarse wrinkling at the left lateral eye. The investigator made silicone replicas of the skin lateral to the left eye by mixing silicone dental-impression material with a catalyst to obtain a polymerized silicone. The polymerizing silicone was applied with a metal spatula to a foam ring and then placed on the skin at the upper outer left eye. The identification tab was consistently placed toward the left ear to allow reproducibility of replica orientation. The replicas were allowed to cure for 72 hours and then placed in plastic 35-mm slide holders for storage. At the conclusion of the study, the replicas were optically analyzed with a scanning laser.

The data were evaluated using a 2-tailed, unpaired Mann-Whitney *t* test with significance defined as $P \leq .05$ based on a 2-sided test.

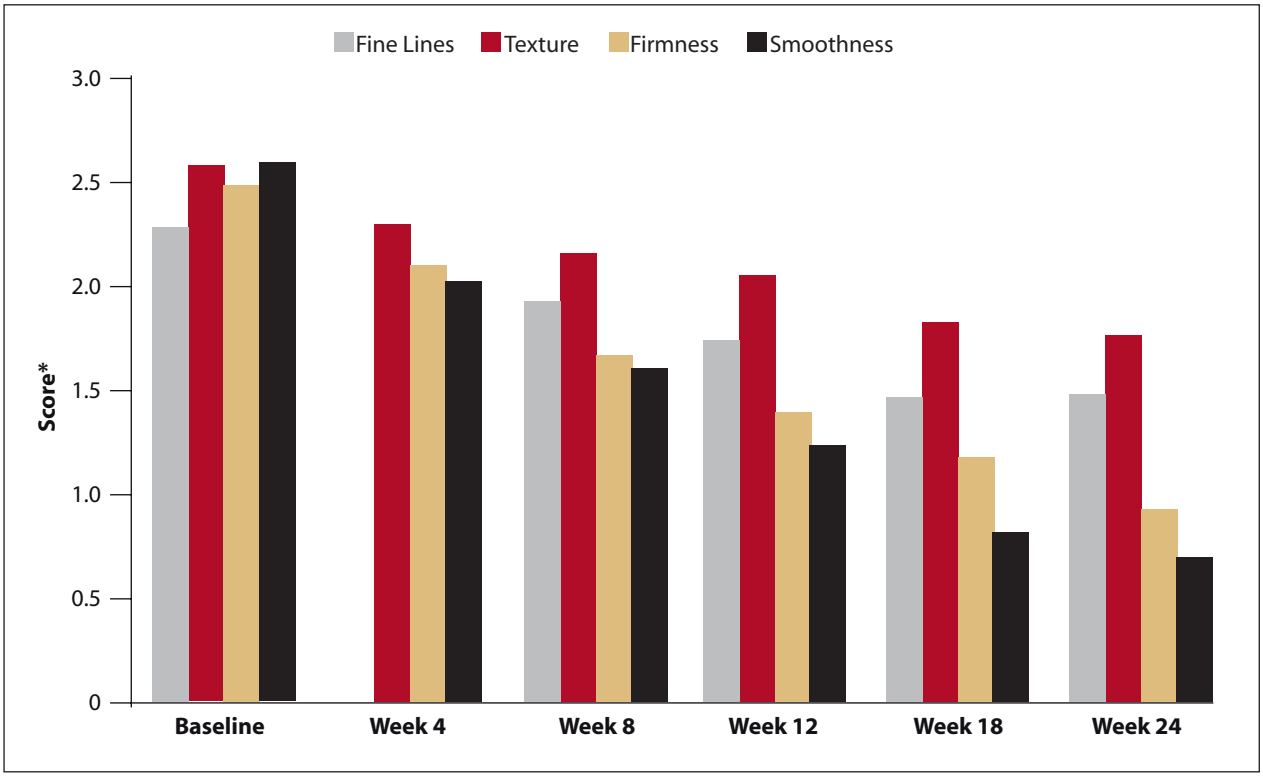

Figure 3. Clinical investigator visual assessments of fine lines, texture, firmness, and smoothness ($P \leq .05$). Asterisk indicates efficacy scale where 0=none, 0.5=very minimal, 1=minimal, 1.5=very mild, 2=mild, 2.5=moderate, 3=moderately severe, 3.5=severe, 4=extremely severe.

Results

Investigator Assessments

All 35 subjects successfully completed the study without any adverse experiences, attesting to the safety of ferulic acid in combination with vitamins C and E in these formulations. The investigator noted statistically significant improvements in skin texture ($P=.049$), firmness ($P=.005$), and smoothness ($P<.001$) after 4 weeks of using the provided cleanser and treatment serum. These effects are directly related to the exfoliant nature of the ferulic acid. At 8 weeks, the investigator noted statistically significant improvements in fine lines ($P=.032$), texture ($P=.006$), firmness ($P<.001$), and smoothness ($P<.001$). It is notable that the improvement in fine lines became apparent at 8 weeks whereas all of the other parameters continued to be significant, as noted at 4 weeks (Figure 3).

The investigator efficacy data continued to improve at week 12. The investigator noted a statistically significant improvement in fine lines ($P=.001$), texture ($P=.001$), firmness ($P<.001$), smoothness ($P<.001$), and erythema ($P=.020$). Investigator assessments continued to improve at weeks 18 and 24. At 18 weeks, the investigator noted a statistically significant improvement in fine lines ($P<.001$), texture ($P<.001$), tone ($P=.027$), firmness ($P<.001$), smoothness ($P<.001$), erythema ($P=.007$), and acne ($P=.004$). At 24 weeks, the investigator noted a statistically significant improvement in fine lines ($P<.001$), texture ($P<.001$), tone ($P=.020$), firmness ($P<.001$), smoothness ($P<.001$), erythema ($P=.003$), and acne ($P=.014$).

Dermospectrophotometer Assessments

The dermospectrophotometer erythema assessments showed no increase in facial redness in subjects with normal or self-perceived sensitive skin at any time during the study. This means that the ferulic acid in combination with vitamins C and E in a cleanser treatment and treatment serum did not produce any vasodilation, which is an indirect sign of inflammation (Figure 4).

Skin Elasticity Assessment

There was no statistically significant change in skin elasticity at any time during the study. However, there was a trend toward improved elasticity, which might have become significant with an increased sample size (Figure 4).

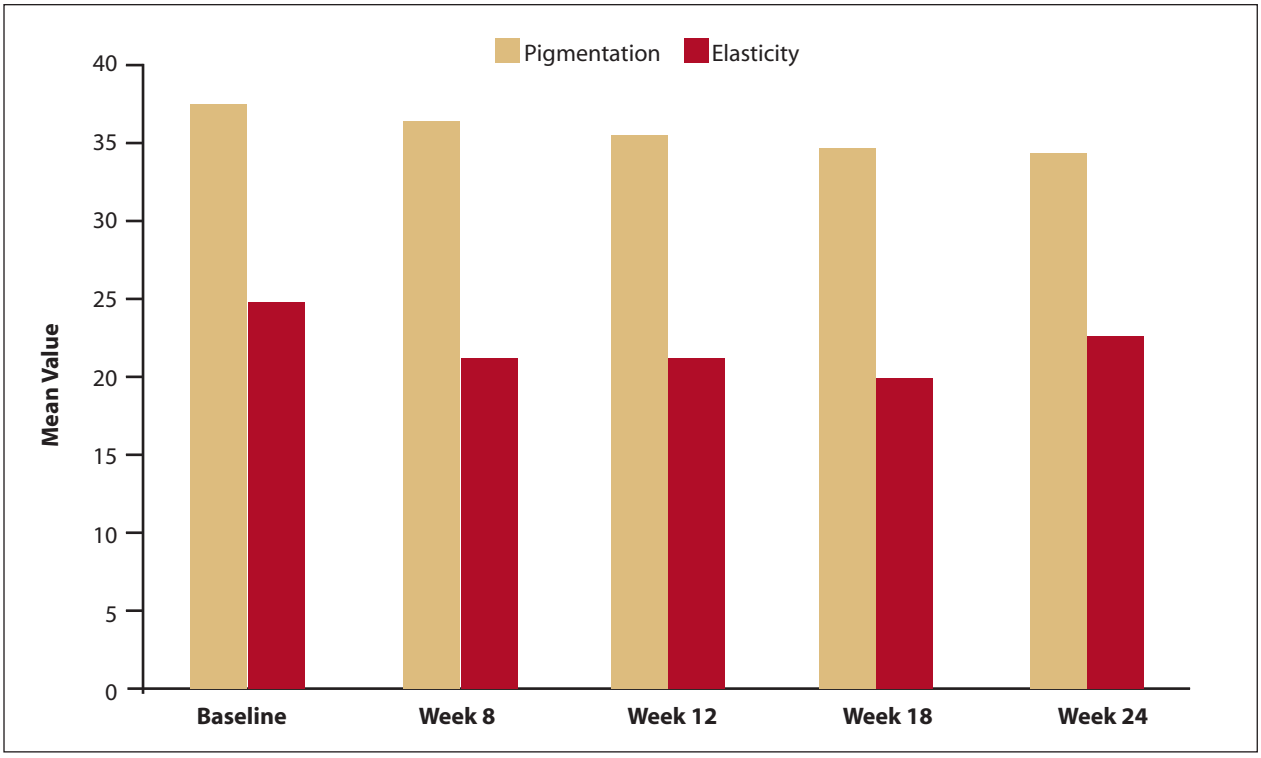

Figure 4. Dermospectrophotometer assessments of pigmentation and elasticity.

Silicone Replica Assessment

There was a statistically significant reduction in wrinkle spacing (the lines that run parallel to the crow's-feet) as compared to baseline at weeks 12 (P=.045), 18 (P=.007), and 24 (P=.042). This indicates a significant conversion of deep wrinkles to fine wrinkles, which is the first step in wrinkle reduction. A statistically significant reduction in wrinkle spacing was also seen in the lines that run at right angles to the crow's-feet at weeks 12 (P=.024) and 18 (P=.040). Again, there was a significant conversion of deep wrinkles to fine lines.

Comment

This research demonstrated the clinical benefits of ferulic acid in combination with vitamins C and E in a cleanser and treatment serum. The noninvasive profilometry confirmed the reduction in wrinkle spacing perceived visually by the investigator. The dermospectrophotometer readings showed no increase in erythema, confirming the lack of investigator-observed inflammation. In summary, the combination of ferulic acid with vitamins C and E in a cleanser and treatment serum demonstrated statistically significant improvement in fine lines, texture, firmness, and smoothness after 24 weeks when used twice daily.

Reference

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Suggested Readings

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