Received: 21 January 2022 | Accepted: 24 April 2022

DOI: 10.1111/dth.15543

ORIGINAL ARTICLE

DERMATOLOGIC THERAPY WILEY

Ferulic acid – A novel topical agent in reducing signs of photoaging

Kamila Zduńska-Pęciak[1] | Renata Dębowska[2] | Anna Kołodziejczak[1] | Helena Rotsztejn[1]

[1]Department of Cosmetology and Aesthetic Dermatology, Faculty of Pharmacy, Medical University of Łódź, Łódź, Poland

[2]Centre for Science and Research Dr Irena Eris, Warsaw, Poland

Correspondence
Kamila Zduńska-Pęciak, Department of Cosmetology and Aesthetic Dermatology, Faculty of Pharmacy, Medical University of Łódź, Muszyńskiego 1 Street, PL-91-151 Łódź, Poland.
Email: kamila.zdunska@stud.umed.lodz.pl

Funding information
Medical University of Łódz, Grant/Award Numbers: 503/3-066-01/503-31-001, 502-03/3-066-01/502-34-102

Abstract

Continuous production of reactive oxygen species, induced by UV radiation, is one of the main mechanisms contributing to skin photoaging. Therefore, the use of novel superior antioxidants, which ferulic acid belongs to, is an innovative treatment option. The aim of this study was to evaluate the effect of 14% ferulic acid peel on skin hydration, topography, the level of melanin, and the severity of erythema, in people with skin photoaging symptoms. Twenty women aged 45–60, received eight treatments of chemical peeling in 1-week intervals. Efficacy was measured using The Multi Probe Adapter (MPA) Systems (Courage + Khazaka electronic GmbH, Köln, Germany). The measurements were taken before, 8, and 12 weeks after the first treatment. Additionally, the photo documentation was made with Fotomedicus (Elfo) and VISIA® Complexion Analysis System (Canfield Scientific, Inc.). The objective evaluation showed statistically significant improvement in all measured skin parameters $p < 0.05$). The best results of skin hydration and melanin level were observed right after the end of the series ($p < 0.001$). The best improvement in erythema reduction was noted a month after the last treatment ($p < 0.0001$). At the control, untreated point none of the probes showed statistically significant changes. In conclusion, a series of treatments with 14% ferulic acid peel has a significant bleaching, erythema-reducing, and moisturizing activity. The results achieved by apparatus, are reflected by photo documentation. The effects achieved during a series persist over time.

KEYWORDS
antioxidant, chemical peel, ferulic acid, photoaging

1 | INTRODUCTION

Exposure to ultraviolet radiation may contribute to the increase in reactive oxygen species (ROS), which may be connected with all sorts of negative biochemical processes within the skin. The free oxygen radicals are considered to be one of the major causes of elastosis (accumulation of tropoelastin aggregates in photoaging skin).[1] The other signs of photoaging such as wrinkles, dryness, hyperpigmentation, telangiectasia, are also closely related to oxidative stress.[2] On this basis, it is suggested that the strong antioxidant compounds, given either orally or applied topically on the skin, could reduce and prevent the signs of photoaging.

Ferulic acid ([E]-3-[4-hydroxy-3-methoxy-phenyl] prop-2-enoic acid) (Figure 1) is a phenolic antioxidant found in high concentration in plant tissues.[3] In plants, it is biosynthesized from the action of O-methyl transferase on caffeic acid.[4] It has low toxicity and many proven physiological functions (antioxidant,[5] anti-inflammatory,[6] anticancer,[7] antidiabetic,[8] antimicrobial[9]). The most important property of it is its function as an antioxidant. It has been shown to be useful in counteracting skin photoaging because it has the ability to

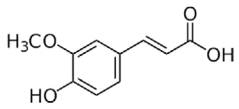

FIGURE 1 Chemical structure of ferulic acid

function as an antioxidant in sunburn cells. Ferulic acid is able to absorb UVA (cis-ferulic acid—peak at 317 nm; trans-ferulic acid—236 and 322 nm).[10] Until recently, this compound was used synergistically together with other antioxidants such as vitamin C and E, increasing their effectiveness and participating in their regeneration processes.[11] After oral administration, the bioavailability of ferulic acid in the skin is relatively low.[12]

Formulas enriched with ferulic acid gain several times higher antioxidant and photoprotective efficacy than those without it. The effectiveness of ferulic acid, as a strong antioxidant reducing UV-induced oxidative skin damage, as well as inhibiting the formation of hyperpigmentation and accelerating skin regeneration, has been proved in numerous studies on cell cultures of fibroblasts, keratinocytes, and melanocytes.[13–16] The results of these studies are promising positive and would qualify ferulic acid as a novel, effective therapeutic agent. However, to our present knowledge, there is a scarcity of studies evaluating the impact of ferulic acid on photoaging skin. The aim of this study is to evaluate the effect of ferulic acid on skin hydration, topography, the level of melanin, and the severity of erythema, in people with skin photoaging symptoms.

2 | MATERIAL AND METHODS

2.1 | Patient selection

The study included a group of 20 patients aged 45–60, with the II and III skin phototypes according to Fitzpatrick's scales. Clinical evaluation of photoaging was done according to Glogau Wrinkle Scale. Fourteen patients were classified as moderate (II type) and six patients as severe (IV type) facial photoaging. Before starting the examination, a detailed interview with each of the patients was conducted. It regarded general health, including information about taken medicines and skin diseases. The patients were qualified for the examination and then instructed about skin care regimen after the treatments. All patients pledged to comply with the recommendations and to resign from other cosmetic and dermatological procedures for the entire duration of the study. Each of the patients completed a full cycle of tests.

2.2 | Treatment protocol

Each patient received a series of eight treatments of chemical peeling based on 14% ferulic acid (Mediderma by Sesderma®), performed once a week. This product contains ferulic acid (in nanosome technology) and propylene glycol. Before applying ferulic peeling, the skin was cleaned with the make-up cleansing milk and then degreased with disinfectant spray based on ethyl alcohol. Next, a special product containing empty nanosomes was sprayed on the face, to enhance the transepidermal permeation of active ingredients. Afterward, in a few minutes intervals, two layers of peeling were applied to the skin. A total of 1.5 ml. Each layer, in accordance with the producer's recommendations, was massaged into the skin until absorbed. Next, patients were asked to wash their faces at home 6 h after the treatment, using a cotton pad soaked in lukewarm water, as the nanosome products had to be left on the skin for a couple of hours. Patients were instructed to use only delicate, moisturizing cream and apply sunscreen with a high Sun Protection Factor (SPF 50) every morning.

2.3 | Measurement

Measurements of selected skin parameters were made with Mexameter (melanin and erythema level) and Corneometer (skin hydration level)—The Multi Probe Adapter (MPA) Systems (Courage + Khazaka electronic GmbH, Köln, Germany). The measurements included 3-time points: before starting a series of treatments, immediately after the end of the series (8 weeks after the first treatment), and 1 month after the end of the series (12 weeks after the first treatment). Three measurement points were designated: 1—on the forehead, 2—on the cheek, and 3—on the jaw. The untreated skin sample behind the ear constituted a control point (point 4), as it is the nearest and most similar skin area to the treated one. All measurements were done three times in each place and the recorded result is their average.

All measurements were made in the same room, with constant temperature conditions (24–26°C) and air humidity (33%–41%), always at a similar time of the day. Before taking the measurements, the patients were asked for 10–15 min acclimatization in the measuring room.

Mexameter MX 18 (Courage + Khazaka electronic) it is a noninvasive device used to measure the concentration of melanin and hemoglobin in the skin by light absorption. The probe emits light at three wavelengths selected to achieve different levels of absorption by the pigment melanin (MEX) and hemoglobin (ERYT). The amount of light emitted is precisely defined, the amount of light absorbed by the skin can be calculated and the receptor measures the light reflected from the skin. Melanin and erythema index were calculated.

Skin hydration was measured with Corneometer CM825, which measurement of skin's electrical capacity, based on the relatively high dielectric constant of water. It is related to the degree of epidermal hydration. Parameters used: skin compressed for 1 s with a force of 7.1 N/cm^2, 20–30 μm deep into the stratum corneum. The measurement result is in the range 0–130. The higher is the value, the better is the hydration of the epidermis.

The topography of the skin was accurately examined with Visioscan® VC 98 (Courage + Khazaka electronic GmbH, Köln, Germany)—a high-resolution UVA camera. The photographs show the

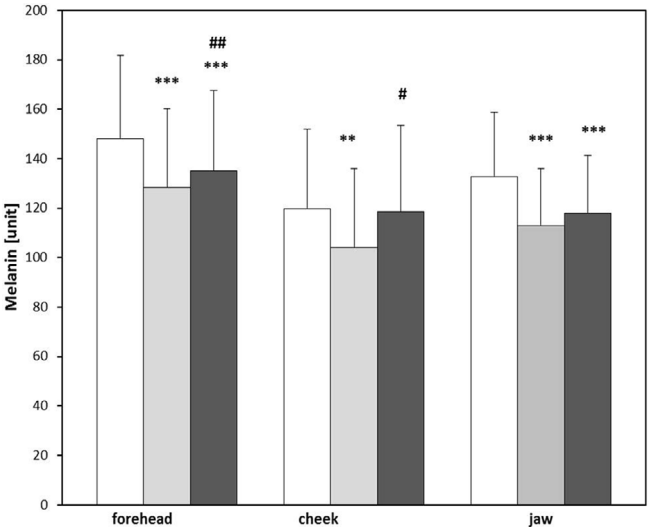

FIGURE 2 Melanin value according to place and time of measurement. White bar—measurement I, light gray bar—measurement II, dark gray bar—measurement III. Data presented as mean ± SD. ***$p < 0.0001$; **$p < 0.01$ versus measurement I; ##$p < 0.01$; #$p < 0.05$ versus measurement II

structure of the skin in multiple magnifications. The SELS® parameters (Surface Evaluation of the Living Skin), developed especially for this camera are SEsc (scaliness)—a value expressed in arbitrary units, showing the level of exfoliation of the stratum corneum, including the value of hydration and SEr—skin roughness. Both values increase with age.

Additionally, before starting the treatment and after its completion, photographs were taken with photographic systems: VISIA® Complexion Analysis System (Canfield Scientific, Inc.) and Fotomedicus (Elfo®).

3 | RESULTS

The results are presented as mean value and standard deviation (SD) mean ± SD. Repeated measures one-way analysis of variance (ANOVA) (with a Greenhouse–Geisser correction where appropriate) followed by Bonferroni's post hoc comparisons tests were used.

3.1 | Skin lightening efficacy

A statistically significant difference in skin melanin level was observed in all measuring points, directly after a series of treatments. The decrease of melanin level was slightly greater on the forehead and on the jaw than on the cheek area ($p < 0.0001$ and $p < 0.001$, respectively) (Figure 2). The last measurement, taken a month after the end of the series, showed still a significant improvement on the forehead and jaw, compared to the baseline ($p < 0.0001$). On the cheek, the level of melanin raised almost to the baseline a month after the series of treatments.

3.2 | Anti-redness efficacy

At the end of the series, the intensity of erythema decreased significantly in all measuring points, showing slightly greater efficacy on the forehead ($p < 0.0001$) than on the cheek and jawline ($p < 0.05$). A month after the series of treatments the improvement was even better, showing statistical significance of $p < 0.0001$ on the forehead and $p < 0.001$ on the cheek and jaw areas (Figure 3).

3.3 | Skin hydrating efficacy

A statistically significant difference in skin hydration level was observed in all measuring points, directly after a series of treatments ($p < 0.0001$). A month after the end of the series, hydration decreased slightly, compared to the second measurement, still showing the statistically significant difference to the baseline ($p < 0.0001$ on the cheek and jaw and $p < 0.001$ on the forehead) (Figure 4).

3.4 | Skin smoothing efficacy

Statistically significant reduction of exfoliation (SEsc) and roughness (SEr) of the epidermis, was observed on the forehead and jaw ($p < 0.05$) (Table 1).

At the control, untreated point none of the probes showed statistically significant changes (Table 2).

Throughout the duration of the study, none of the patients' side effects were noted in the form of irritation, burning, redness of the skin, which proves the safety of using ferulic acid in the form of chemical peeling.

4 | DISCUSSION

Photoaging of the skin is a process that affects both: the epidermis and the dermis. Histologically, in the epidermis, it concerns its thickening and alterations within its cells (i.e. melanocytes and Langerhans cells). However, major changes are observed in the dermis and they relate to the elastosis process, the invalid structure of collagen fibers, changes in the number of proteoglycans, glycosaminoglycans, and inflammatory cells.[2] Therefore, for the treatment of photoaging skin, a substance that penetrates into the deeper tissue is needed.[17] Ferulic acid has been shown to penetrate deeply into the skin, both acidic and neutral pH, in dissociated and non-dissociated forms. Its efficiency is closely related to maintaining a high local concentration and low cutaneous metabolism.[17–19]

This study demonstrated, that ferulic acid peel is an effective therapeutic agent in reducing clinical signs of photoaging such as skin dryness, telangiectasia, erythema, and hyperpigmentation. The results achieved by MPA probes (Mexameter and Cutometer) are reflected by photo documentation (Figures 5 and 6).

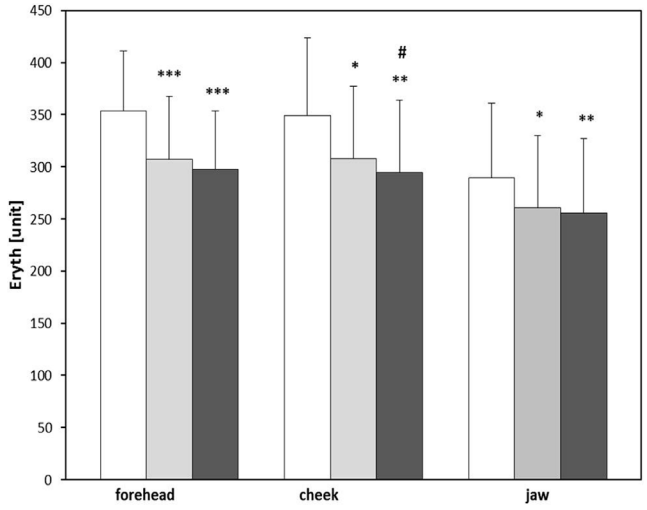

FIGURE 3 Erythema value according to place and time of measurement. White bar—measurement I, light gray bar—measurement II, dark gray bar—measurement III. Data presented as mean ± SD. ***$p < 0.0001$; **$p < 0.01$; *$p < 0.05$ versus measurement I; #$p < 0.05$ versus measurement II

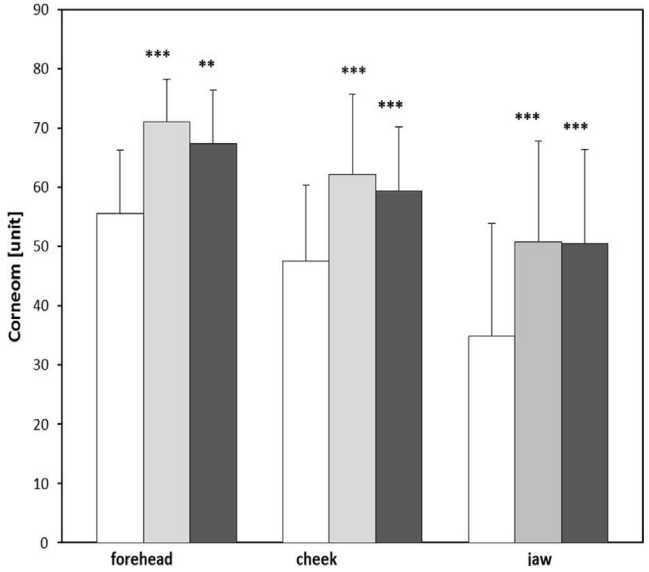

FIGURE 4 Skin hydration level according to place and time of measurement. White bar—measurement I, light gray bar—measurement II, dark gray bar—measurement III. Data presented as mean ± SD. ***$p < 0.0001$; **$p < 0.01$ versus measurement I

Ferulic acid is a well-known compound in the pharmaceutical, food, and cosmetic industries. It is widely used as a preservative,[20] photoprotective agent,[21] and vitamin stabilizer.[22] Its strong antioxidant activity is related to free radical scavenging,[18] inhibiting enzymes that catalyze free radical generation,[23] binding transition metals,[5] preventing lipid peroxidation, enhancing other scavenger enzymes activity.[24,25]

Ferulic acid shows an antioxidant activity due to the phenolic ring and unsaturated side chain.[12] It has the capacity to inhibit a complex reaction of free radicals generation, by forming stable phenoxyl radicals, in the reaction of the radical molecule with the molecule of antioxidant. The phenoxy radical is formed, which is highly resonance stabilized, so it ends its life in condensation and collision with another ferulate radical. It has also the ability to donate atoms directly to the radicals, acting as a hydrogen donor. Another antioxidant mechanism, associated with binding transition metals such as iron and copper, prevents the formation of toxic hydroxyl radicals and in the aftermath autoxidation of lipid acids cell membrane.[5,12,26] Ferulic acid has the ability to inhibit enzymes that catalyze the formation of free radicals and of strengthening scavenger radical enzymes.[12]

Milani et al.[27] showed skin protective effects of an antioxidant and antipollution serum with *Deschampsia antartica* extract, ferulic acid, and vitamin C. The study was conducted on a group of 20 women living in an area of high pollution urban area. The study showed improvement of skin barrier function, to counteract the skin oxidative stress and to reduce hiperpigmentations.

In our research, nanosomal formulations were used (nanosome technology). Gupta et al.[28] states that ferulic acid has problems of poor stability and low aqueous solubility in cosmetics products. The solution obtained in the research was suggested to be an optimal concentration (0.5 wt% ferulic acid in bulk solution) for successful nanoemulsion formulation. In the study formulations of ferulic acid-loaded lipid-based nanoparticle systems, can find various uses in cosmetics.

TABLE 1 Visioscan parameters values: exfoliation (SEsc) and roughness of the epidermis (SEr)

Parameter	Measurement 1	Measurement 2	Significance
Forehead			
SEr	2.98 ± 1.06	2.39 ± 0.82	$p = 0.151$
SEsc	0.45 ± 0.10	0.35 ± 0.07	$p = 0.031$*
Cheek			
SEr	3.87 ± 0.66	2.52 ± 0.18	$p = 0.103$
SEsc	0.54 ± 0.13	0.42 ± 0.06	$p = 0.115$
Jaw			
SEr	3.42 ± 0.82	2.35 ± 0.54	$p = 0.027$*
SEsc	0.49 ± 0.05	0.40 ± 0.11	$p = 0.175$

Note: Data presented as mean ± SD. Values of both parameters (Sesc and Ser) increase with age.
*$p < 0.05$.

TABLE 2 Control point[4] parameter's values according to the time of measurement

Parameter	Measurement 1	Measurement 2	Significance
Melanin	162.3 ± 42.6	159.8 ± 44.7	$p = 0.271$
Erythema	350.1 ± 64.6	349.6 ± 62.1	$p = 0.368$
Corneometer	55.9 ± 13.5	53.2 ± 11.1	$p = 0.162$
PK Vser	1.14 ± 0.19	1.14 ± 0.21	$p = 0.739$
PK Vsesc	0.57 ± 0.12	0.59 ± 0.11	$p = 0.383$

Note: Data presented as mean ± SD.

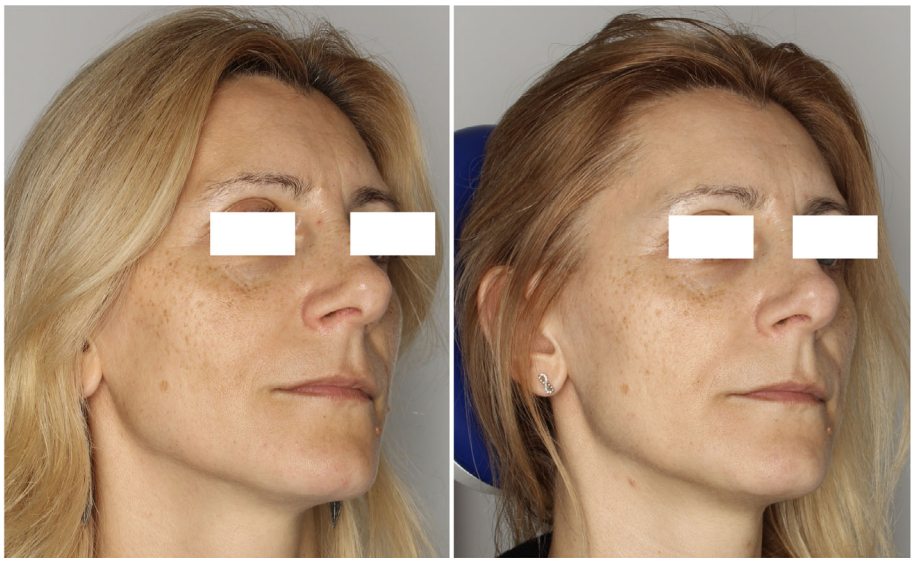

FIGURE 5 Lightening activity of ferulic acid. I photograph—before, II photograph—after the treatment session. Women age 48. II type according to Glogau Wrinkle Scale. The level of melanin at the baseline: 175. The level of melanin after the eight treatments of FA peel: 133

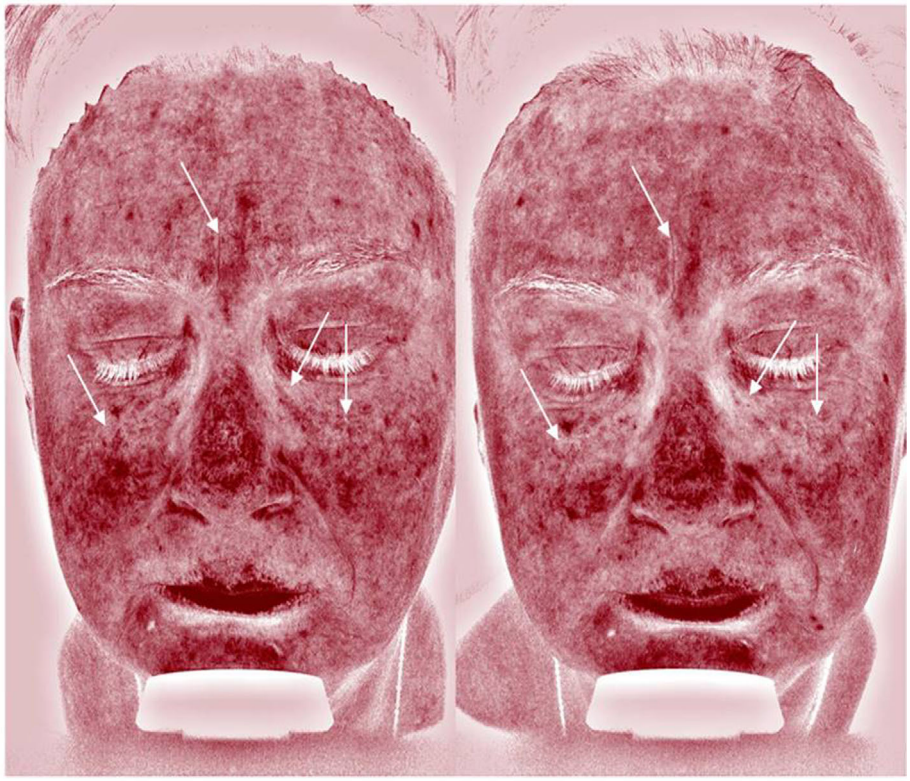

FIGURE 6 The cutaneous superficial network of blood vessels. I photograph—before, II photograph—after the treatment session. The photograph taken by VISIA® Canfield Scientific showing the number and size of vascular lesions. Made in cross polarity in RBX® technology. Women age 58. II type according to Glogau Wrinkle Scale. The level of erythema at the baseline: 470. The level of erythema after the 8 treatment of FA peel: 385

Das and Wong researched to stabilize ferulic acid in topical hydrogel formulation via nanoencapsulation technique and low pH (less than pKa of ferulic acid). They proved that products with ferulic acid with low pH can maintain skin microbiome and homeostasis, may penetrate into skin layers (avoid systemic circulation).[29]

Further pre-treatment studies confirmed the great photoprotective ability of ferulic acid-loaded multiple emulsions (MA), in fact, following a 5 h pre-treatment with ME (W/O/W multiple emulsions), the skin of the volunteers become more protected from a subsequent physical insult and the erythema index remained on lower values than those of the sites pre-treated with the other formulations.[12]

As a result of excessive free radical reactions, the functioning of the skin is disturbed and aging is accelerated. Skin becomes dehydrated, sagging, wrinkled, appears discoloration and vascular spider veins. Treatment with ferulic acid counteracts photoaging of the skin, and also shows depigmenting properties, controlling tyrosinase activity. Because FA has a similar structure to tyrosine, it is believed that it inhibits melanogenesis through competitive inhibition with tyrosine. What else, vitamin E ferulic acid ester exhibited an inhibitory effect on melanin production.[30]

In this research series of treatments with ferulic acid peel, caused a decrease of skin melanin content and thus brightening and evening

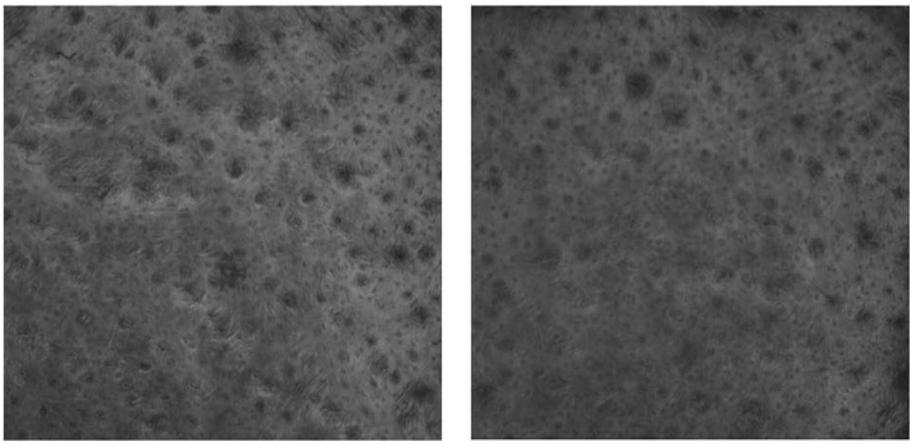

FIGURE 7 Skin surface in a multiple magnification. I photograph—before, II photograph—after the treatment session. The photograph taken by Visioscan® VC98 showing the skin topography using a special UV-A light video camera with high resolution. The images show the structure of the skin and the level of dryness. Accurate analysis of the skin is made with the use of SELS® parameters (Surface Evaluation of the Living Skin)

of skin color. Minor hyperpigmentation has also been lightened and much less visible (Figure 5). Park et al. investigated the mechanism of the skin-whitening action of ferulic acid. It is based on the inhibition of intracellular tyrosinase synthesis in melanocytes. The synthesis of melanin is suppressed by reducing the expression of microphthalmia transcription factor (MITF)—a major transcriptional regulator of the genes for tyrosinase. Ferulic acid affects the synthesis and decomposition of the melanogenic enzyme, by controlling the activity of its transcription factor. Park et al.[31] in their study on B16F10 mouse melanoma cells showed a 19.1% decrease in intracellular tyrosine synthesis, after exposure to 20 μg/ml ferulic acid. The intensity of the melanin synthesis process decreased by 43.6%. Dayal et al.[32] in their study comparing the efficacy of 12% ferulic acid peel with two other common peels, noted good to excellent improvement (according to physician global assessment) in the intensity of periorbital hyperpigmentation (POH) in almost half of the FA group. What is more, 12% ferulic acid was the best-tolerated peel among the three.

Importantly, the effects achieved during a series of ferulic acid treatments persist over time. A month after the end of the series of treatments, the amount of melanin in the skin increased slightly, still showing a significant improvement, compared to the baseline. This may be related to the preventive role of ferulic acid, against changes in the skin caused by UVA and UVB radiation. Pluemsamran et al.[13] proved that there are much smaller photodamages in keratinocytes if ferulic acid is administered prior to UV radiation. Reactive oxygen species' production decreases significantly, endogenous antioxidants, that is, glutathione, and catalase undergo a smaller reduction, and their level returns to the state before exposure. Upon absorption of UV, phenol acids catalyze the stable phenoxy radical formation, ferulic acid terminating free radical chain reactions. Therefore, it can be assumed that ferulic acid not only reduces already existing signs of photoaging but also prevent future photodamage in the skin.[12]

Murray et al.[33] have demonstrated that a stable topical formulation of 15% L-ascorbic acid, 1% alphatocopherol, and 0.5% ferulic acid (CEFer) is able to significantly decrease the expression of immunosuppressive and proinflammatory cytokines that occurs with UV damage. CEFer was applied to separate patches of human skin for 4 days and next the skin was irradiated UV.

Mancuso et al.[12] conducted in vivo and in vitro research which the aim was the evaluation of three types of emulsions with ferulic acid. MA showed the best ability to carry and release ferulic acid and great stability. What is important, in vivo investigation showed that MA has the best capability to treat UV-B-induced erythema.

The study demonstrated that therapy with ferulic acid peel reduced the severity of erythema and visibility of telangiectasia. The best results were achieved on the forehead and cheeks, which is confirmed by the photo taken with the VISIA®, illustrating the cutaneous superficial network of blood vessels (Figure 6). Literature data indicate that ferulic acid has been used for a long time in neurodegenerative and circulatory system diseases. It also improves blood circulation, prevents thrombocyte clumping, and has antithrombotic properties.[34] Lin et al.[35] in their research on human umbilical vein endothelial cells (HUVEC), demonstrated that ferulic acid induces the expression of major angiogenic regulatory factors: vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF). It also increases the amount of hypoxia-inducible factor 1 (HIF-1)—a factor that generates a response to hypoxia. Treatment with ferulic acid leads to significant induction of VEGF, PDGF, and HIF-1α mRNA and protein expression, in a concentration-dependent and time-dependent manner. Due to the angiogenic effect, ferulic acid is supposed to be a new therapeutic agent for microcirculation disorders, also within the skin.

Ferulic acid also significantly increases skin hydration. The increase in hydration of the stratum corneum results in its smoothing, which was confirmed by the photos taken with Visioscan (Figure 7). Chiu et al.[36] demonstrated that topically applied antioxidants reduce transepidermal water loss, support the hydro-lipid barrier, contributing to the increase of water content in the epidermis. What is more, with several applications, they have the ability to cumulate in the epidermis and dermis. In order to achieve optimal results, antioxidant compounds should be used relatively frequently and regularly, which confirms the legitimacy of performing treatments with ferulic acid in the series. Kanlayavattanakul et al.[37] noted satisfactory effects in the form of improved hydration of the epidermis, after using a rice extract-rich in phenolic compounds, including ferulic acid. After 2 months of using the cream with rice extract, the level of hydration of the epidermis increased almost 2-times.

5 | CONCLUSIONS

The topical administration of ferulic acid could ensure activity against UV-induced photodamage.

An objective examination with the use of MPA probes—Mexameter and Corneometer, showed a significant whitening, moisturizing and erythema-reducing effect. The results achieved with apparatus, are reflected in photographic documentation. Within the limits of our study, we found the series of ferulic acid peel treatments, which seems to bring promising effects on photoaging skin. Nevertheless, these initial results need to be further validated on a larger sample size.

AUTHOR CONTRIBUTIONS

Zduńska-Pęciak Kamila is responsible for the study design, collecting the results, statistical analysis, preparing the preliminary version of the manuscript. Dębowska Renata contributed to the collection of results and photodocumentation. Anna Kołodziejczak checked and edited the article in terms of content. Rotsztejn Helena has made an assessment of the overall study design and the correctness of the draft of the manuscript.

ACKNOWLEDGMENTS

This work was supported by statutory research activity of the Department of Cosmetology and Aesthetic Dermatology, Faculty of Pharmacy, Medical University of Lodz, No. 503/3-066-01/503-31-001 and Grant/Award number 502-03/3-066-01/502-34-102.

FUNDING INFORMATION

Statutory research activity of the Department of Cosmetology and Aesthetic Dermatology, Faculty of Pharmacy, Medical University of Lodz, No. 503/3-066-01/503-31-001. Medical University of Łódź, Grant/Award Number: 502-03/3-066-01/502-34-102.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

All participants have given their written informed consent to the procedure. The study protocol has been approved by the Bioethics Committee of the Medical University of Lodz (Protocol No. RNN/81/19/KE). All procedures involving human probands were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

ORCID

Kamila Zduńska-Pęciak https://orcid.org/0000-0002-3012-9054
Anna Kołodziejczak https://orcid.org/0000-0002-7799-9188

REFERENCES

1. Kawaguchi Y, Tanaka H, Okada T, et al. Effect of reactive oxygen species on the elastin mRNA expression in cultured human dermal fibroblasts. *Free Radi Biol Med*. 1997;23:162-165.
2. Augustyniak A, Rotsztejn H, Bartnicka E. Effects of reactive oxygen species on skin photoaging. *Dermatol Rev*. 2016;103:233-239.
3. Mattila P, Kumpulainen J. Determination of free and total phenolic acids in plant-derived foods by HPLC with diode-array detection. *J Agric Food Chem*. 2002;50:3660-3667.
4. Kim JK, Park SU. A recent overview on the biological and pharmacological activities of ferulic acid. *EXCLI J*. 2019;18:132-138.
5. Kiewlicz J, Szymusiak H, Zieliński R. Thermal stability and antioxidant activity of long-chain alkyl esters od ferulic acid. *Zywn Nauk Technol*. 2015;4:188-200.
6. Barone E, Calabrese V, Mancuso C. Ferulic acid and its therapeutic potential as a hormetin for age-related diseases. *Biogerontology*. 2009;10:97-108.
7. Alias LM, Manoharan S, Vellaichamy L, Balakrishnan S, Ramachandran CR. Protective effect of ferulic acid on 7,12-dimethylbenz[a] anthracene-induced skin carcinogenesis in swiss albino mice. *Exp Toxicol Pathol*. 2009;61:205-214.
8. Yasmin S, Cerchia C, Badavath VN, et al. A series of ferulic acid amides reveals unexpected peroxiredoxin 1 inhibitory activity with in vivo antidiabetic and hypolipidemic effects. *Chem Med Chem*. 2021;16:484-498.
9. Fathima S, Shona S, Navamimrajan N, et al. Development and evaluation of ferulic acid loaded chitosan gel for wound healing. *Int J Pharm Res*. 2021;13:2836-2843.
10. Draelos ZD, Yatskayer M, Oresajo C, Fares HS, Hansenne I. Efficacy of ferulic acid in improving the appearance of photoaged skin. *Cosmetic Dermatol*. 2008;21(4):195-198.
11. Lin F-H, Lin J-Y, Ravindra D, et al. Ferulic acid stabilizes a solution of vitamins C and E and doubles its photoprotection of skin. *J Invest Dermatol*. 2005;125:826-832.
12. Mancuso A, Cristiano MC, Pandolfo R, Greco M, Fresta M, Paolino D. Improvement of ferulic acid antioxidant activity by multiple emulsions: in vitro and in vivo. *Eval Nanomater*. 2021;11(2):425.
13. Pluemsamran T, Onkoksoong T, Panich U. Caffeic acid and ferulic acid inhibit UVA-induced matrix metalloproteinase-1 through regulation of antioxidant defense system in keratinocyte HaCaT cells. *Photochem Photobiol*. 2012;88:961-968.
14. Zhou B, Yin H, Xu Y, et al. Baicalin protects human skin fibroblasts from ultraviolet a radiation-induced oxidative damage and apoptosis. *Free Radic Res*. 2012;46:1458-1471.
15. Hahn H, Kim K, Bae S, et al. Pretreatment of ferulic acid protects human dermal fibroblasts against ultraviolet a irradiation. *Ann Dermatol*. 2016;286:740-748.
16. Oresajo C, Stephens T, Hino P, et al. Protective effects of a topical antioxidant mixture containing vitamin C, ferulic acid, and phloretin against ultraviolet-induced photodamage in human skin. *J Cosmet Dermatol*. 2008;74:290-297.
17. Bezerra G, Pereira M, Ostrosky E, et al. Compatibility study between ferulic acid and excipients used in cosmetic formulations by TG/DTG, DSC and FTIR. *J Therm Anal Calor*. 2017;127:1683-1691.
18. Saija A, Tomaino A, Lo Cascio R, et al. Ferulic and caffeic acids as potential protective agents against photooxidative skin damage. *J Sci Food Agric*. 1999;79:476-480.
19. Mathew S, Abraham ET. Ferulic acid: an antioxidant found naturally in plant cell walls and feruloyl esterases involved in its release and their applications. *Crit Rev Biotechnol*. 2004;24:59-83.
20. Yuan L, Haixia Y, Yong C, et al. Ferulic acid-β-cyclodextrin inclusion complexes: application on the preservation of hairtail (*Trichiurus lepturus*). *Int J Food Prop*. 2020;23:282-296.

21. Peres DD, Sarruf FD, de Oliveira CA, MVR V, Baby AR. Ferulic acid photoprotective properties in association with UV filters: multifunctional sunscreen with improved SPF and UVA-PF. *J Photochem Photobiol B*. 2018;185:46-49.
22. Romana-Souza B, Silva-Xavier W, Monte-Alto-Costa A. Topical application of a commercially available formulation of vitamin C stabilized by vitamin E and ferulic acid reduces tissue viability and protein synthesis in ex vivo human normal skin. *J Cosmet Dermatol*. 2020;19:2965-2973.
23. Nile SH, Ko EY, Kim DH, Keum YS. Screening of ferulic acid related compounds as inhibitors of xanthine oxidase and cyclooxygenase-2 with anti-inflammatory activity. *Rev Bras Farmacogn*. 2016;26:50-55.
24. Lodovici M, Guglielmi F, Meoni M, Dolara P. Effect of natural phenolic acids on DNA oxidationin vitro. *Food Chem Toxicol*. 2001;39:1205-1210.
25. Masella R, Vari R, d'Archivio M, et al. Extra virgin olive oil biophenolsinhibit cell-mediated oxidation of LDL by increasing the mRNA transcription of glutathione-related enzymes. *J Nutr*. 2004;134:785-791.
26. Scharffetter-Kochanek K, Brenneisen P, Wenk J, et al. Photoaging of the skin from phenotype to mechanisms. *Exp Gerontol*. 2000;35:307-316.
27. Milani M, Hashtroody B, Piacentini M, Celleno L. Skin protective effects of an antipollution, antioxidant serum containing *Deschampsia antartica* extract, ferulic acid and vitamin C: a controlled single-blind, prospective trial in women living in urbanized, high air pollution area. *Clin Cosmet Investig Dermatol*. 2019;29(12):393-399.
28. Gupta KM, Das S, Shan Chow P, Macbeath C. Encapsulation of ferulic acid in lipid nanoparticles as antioxidant for skin: mechanistic understanding through experiment and molecular simulation. *Nano Mater*. 2020;3(6):5351-5361.
29. Das S, Wong ABH. Stabilization of ferulic acid in topical gel formulation via nanoencapsulation and pH optimization. *Sci Rep*. 2020;10(1):12288. doi:10.1038/s41598-020-68732-6
30. Kumar N, Pruthi V. Potential applications of ferulic acid from natural sources. *Biotechnol Rep*. 2014;16:86-93.
31. Park HJ, Cho JH, Hong SH, et al. Whitening and anti-wrinkle activities of ferulic acid isolated from *Tetragonia tetragonioides* in B16F10 melanoma and CCD-986sk fibroblast cells. *J Nat Med*. 2018;72:127-135.
32. Dayal S, Sangal B, Sahu P. Ferulic acid 12% peel: an innovative peel for constitutional type of periorbital melanosis—comparing clinical efficacy and safety with 20% glycolic peel and 15% lactic peel. *J Cosmet Dermatol*. 2020;19:2342-2348.
33. Murray JC, Burch JA, Streilein RD, Iannacchione MA, Hall RP, Pinnell SR. A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. *J Am Acad Dermatol*. 2008;59(3):418-425.
34. Yogeeta SK, Hanumantra RB, Gnanapragasam A, et al. Attenuation of abnormalities in the lipid metabolism during experimental myocardial infarction induced by isoproterenol in rats: beneficial effect of ferulic acid and ascorbic acid. *Basic Clin Pharmacol Toxicol*. 2006;985:467-472.
35. Lin CM, Chiu JH, Wu IH, Wang BW, Pan CM, Chen YH. Ferulic acid augments angiogenesis via VEGF, PDGF and HIF-1 alpha. *J Nutr Biochem*. 2010;217:627-663.
36. Chiu A, Kimball AB. Topical vitamins, minerals and botanical ingredients as modulators of environmental and chronological skin damage. *Br J Dermatol*. 2003;149:681-691.
37. Kanlayavattanakul M, Lourith N, Chaikul P. Jasmine rice panicle: a safe and efficient natural ingredient for skin aging treatments. *J Ethnopharmacol*. 2016;193:607-616.

How to cite this article: Zduńska-Pęciak K, Dębowska R, Kołodziejczak A, Rotsztejn H. Ferulic acid – A novel topical agent in reducing signs of photoaging. *Dermatologic Therapy*. 2022;e15543. doi:10.1111/dth.15543