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Supplementation of Flaxseed Oil Diminishes Skin Sensitivity and Improves Skin Barrier Function and Condition

K. Neukam[a] S. De Spirt[a] W. Stahl[a] M. Bejot[c] J.-M. Maurette[c] H. Tronnier[b] U. Heinrich[b]

[a]Institute of Biochemistry and Molecular Biology I, Medical Faculty, Heinrich-Heine University Düsseldorf, Düsseldorf, and [b]Institute of Experimental Dermatology, University Witten-Herdecke, Witten, Germany; [c]Laboratoire Oenobiol, Paris, France

Key Words
Skin sensitivity · Flaxseed oil · Safflowerseed oil · Transepidermal water loss · Skin hydration · Skin physiology

Abstract
Background: Skin sensitivity is a common problem in the Western population correlated with changes of skin properties like skin barrier function, hydration and skin physiology. Skin properties can be modulated by dietary fatty acids (FA), especially poly-unsaturated FA. The present study was performed to evaluate the effect of daily supplementation with flaxseed oil and safflowerseed oil on healthy volunteers with sensitive skin. ***Methods:*** The study was designed as a randomized, double-blind 12-week intervention with 2 female treatment groups (n = 13). Plasma FA profile, skin sensitivity, skin hydration, transepidermal water loss (TEWL) and skin surface were evaluated on day 0, week 6 and week 12. ***Results:*** Supplementation with flaxseed oil led to significant decreases in sensitivity (after nicotinate irritation), TEWL, skin roughness and scaling, while smoothness and hydration were increased. Concomitantly, the ratio of n–6/n–3 FA in plasma decreased. Upon supplementation with safflowerseed oil, only a significant improvement in skin roughness and hydration was observed; however, the effects were less pronounced and determined at a later point in time than with flaxseed oil. The plasma n–6/n–3 FA ratio increased. ***Conclusion:*** The data provide evidence that daily intake of flaxseed oil modulates skin condition.

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Introduction

Epidemiological studies describe that more than 50% of the Western population consider themselves to have 'sensitive skin'. A recent review summarizes the prevalence of sensitive-skin perceptions in the industrialized world, showing that the numbers of people who claim to have sensitive skin differ between the populations [1, 2]. Although the term 'sensitive skin' is not clearly defined, it is commonly referred to as 'skin whose sensitivity is demonstrated by verifiable, visual and/or quantifiable pathological changes of the skin or by subjective paresthesia (sensation of tension, pruritus)' [3]. These alterations can be due to individual endogenous skin properties but may also be triggered by external stress factors.

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Prof. Dr. Ulrike Heinrich
DermaTronnier, Institut für experimentelle Dermatologie
Universität Witten-Herdecke, Alfred-Herrhausen-Strasse 44
DE–58455 Witten (Germany)
Tel. +49 2302 28 26 300, Fax +49 2302 28 26 326, E-Mail ulrike.heinrich@uni-wh.de

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Sensitive skin has also been defined as hyperreactivity of the human skin to external factors [4, 5].

External stressors influencing skin sensitivity and skin responses are subdivided into physical (e.g. ultraviolet radiation, high/low temperature, wind) and chemical factors (cosmetics, soap, water, environmental pollution). Furthermore, individual characteristics such as psychological (stress) or hormonal (menstrual cycle) constitution have an impact on skin sensitivity [5, 6].

The characteristics of a sensitive skin are altered skin hydration, irritation, inflammatory and immune responses. Apparent cutaneous symptoms are dryness, scaling, erythema, calor as well as changes in skin texture and structure. Patients usually report an itching, stinging and burning sensation. Often it is not possible to identify a single cause for the symptoms, since they are not specific [2, 7].

Accounting for the phenomenon of sensitive skin, the cosmetic industry developed products that lack irritant agents such as perfumes, emulsifiers or preservatives. Additionally, some of these products contain anti-irritant and protective additives. However, due to insufficient absorption, topical application is associated with a low availability of protective agents in the skin cells, especially within the deeper skin layers. To increase the availability of essential dietary compounds, nutritional supplements are discussed as an approach.

It has been demonstrated that the skin condition is influenced by the nutritional status, and an optimal supply of macro- and micronutrients contributes to skin health and appearance [8]. For example, orally taken carotenoids like β-carotene, lycopene, lutein or zeaxanthin can modulate skin conditions or protect the skin against UV irradiation [9–11].

Oils rich in poly-unsaturated fatty acids (FA) play a crucial role in human health. Linoleic acid (LA), α-linolenic acid (ALA) and γ-linolenic acid (GLA) are widely distributed in plant oils such as flaxseed, hempseed, borageseed and evening primrose oil, whereas docosahexaenoic acid and eicosapentaenoic acid (EPA) are mainly found in fish oils [12].

Topical applications of oils containing n–6 FA, LA or GLA are used in the therapy of dry and sensitive skin. Although the literature provides numerous data on the influence of LA and GLA on skin conditions, data on a correlation of plasma FA concentrations and skin function are scarce. The present study investigates the influence of supplementation with flaxseed oil and safflowerseed oil on properties of sensitive skin.

Table 1. FA pattern in flaxseed and safflowerseed oil capsules

FA	Contribution of the FA, %	
	flaxseed oil	safflowerseed oil
Sum of n–6 FA	15.75	72.06
Sum of n–3 FA	48.76	0.64
Myristic acid	n.d.	0.21
Palmitic acid	4.98	7.39
Palmitoleic acid	0.08	0.10
Heptadecanoic acid	0.13	n.d.
Stearic acid	3.70	2.63
Oleic acid	21.24	12.68
LA	15.61	71.98
GLA	0.14	0.08
ALA	48.76	0.64
Arachidic acid	0.16	0.46
Eicosenoic acid	0.49	0.21
Eicosadienoic acid	0.18	0.16
Behenic acid	0.20	0.29
Eruic acid	n.d.	0.56
Lignoceric acid	0.36	0.19
Nervonic acid	n.d.	0.20
Unidentified acids	4.22	1.51
Further components		
D-α-Tocopherol, mg	3.85	n.d.
Rosemary extract, mg	0.83	0.83

n.d. = Not determined.

Materials and Methods

Subjects and Study Design

Twenty-six non-smoking, female volunteers aged 18–65 years with no apparent disease and sensitive skin participated in the study. The subjects had no history of malabsorption diseases, liver diseases or diseases of lipid metabolism, were not pregnant or lactating, had normal nutritional habits (no vegetarians) and a body mass index between 18 and 25. No medication and no cosmetic treatment in the test area (inner forearm) which could influence the study outcome were applied. Subjects were asked to refrain from nutritional supplements, vitamins and extensive sunbathing in the month before and during the study. The study protocol was fully explained to the subjects and they gave their written informed consent. The study design for non-pharmaceutical compounds was approved by the Ethical Committee of the University of Witten-Herdecke, Germany. The study was performed in a double-blind manner with 2 treatment groups consisting of 13 persons each; parts of the design were already described [13]. The volunteers ingested 4 capsules of flaxseed oil (555.32 mg/capsule) or safflowerseed oil (560 mg/capsule) per day. The compositions of the capsules are given in table 1. Duration of the study was 12 weeks, skin parameters were determined on day 0, after 6 weeks and after 12 weeks. Blood samples were drawn at the same time.

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Chemicals and Reagents

Sodium methoxide was purchased from Fluka (Seelze, Germany). FA methyl ester standards were purchased from Supelco (Deisenhofen, Germany) or Fluka. All other reagents were from Merck (Darmstadt, Germany) unless stated otherwise.

Skin Sensitivity

Skin sensitivity was assessed by erythema formation after topical irritation with nicotinate (benzylnicotinate, 0.25 vol% solved in ethanol, 5 $\mu l/cm^2$), which was applied to the test field (2.5 × 2.5 cm^2) on the forearm of volunteers. Erythema (Δa values) was evaluated by chromametry (Minolta CR 300, Ahrensburg, Germany). Capillary blood flow was determined by laser Doppler flowmetry (O2C System, Lea Instruments, Giessen, Germany) [6].

Surface Evaluation of Living Skin

Profilometric examination of the skin surface was conducted with the Visioscan® system and skin visiometer software (Courage & Khazaka Electronics, Cologne, Germany). The surface evaluation of living skin method is based on the evaluation of an image of living skin. A charge-coupled device camera, built into the measuring head, records a picture of the skin, which is then transferred as a grey-value bitmap file by means of the software Skinvisiometer (Courage & Khazaka), which was used for quantitative analysis. In this process, the skin surface is described by 4 different parameters: roughness, scaling, wrinkles and smoothness; parameters are given in arbitrary units [14].

Skin Hydration and Transepidermal Water Loss

The determination of the skin hydration is based on capacitance measurement of a di-electric medium with a Corneometer (CM 825®, Courage & Khazaka Electronics). Any change in the di-electric constant due to changes in skin surface hydration alters the capacitance of a precision measuring capacitor. Skin hydration is given in arbitrary units.

Transepidermal water loss (TEWL) was measured with a Tewameter TM 300® (Courage & Khazaka Electronics). TEWL is given in grams per hour per square metre [15].

All skin measurements were performed according to the International Colipa guidelines for efficacy measurements [16].

FA Analysis

Blood samples were collected into 10-ml S-Monovette tubes (Sarstedt, Nuembrecht, Germany) containing sodium EDTA as anticoagulant. After centrifugation, plasma was collected and stored at –80°C. Plasma FA extraction was performed using the slightly modified method of Folch and Lees [17]. Briefly, plasma samples were mixed with chloroform/methanol containing butylated hydroxytoluene as antioxidant for 45 min at 37°C. After addition of sodium chloride and centrifugation, the lipophilic phase was collected and washed. The solution was dried under a stream of nitrogen. Base-catalysed transesterification of the FA was performed under exclusion of water according to Eder et al. [18]. The dried extract was incubated with water-free methanolic sodium methoxide. After addition of chlorogenic acid, FA methyl esters were extracted with hexane, concentrated under nitrogen and transferred to an injection vial sealed with a metal cap.

FA methyl esters were analysed by gas chromatography/flame ionization detection (Clarius 500 PE Autosystem GC, Perkin Elmer, Shelton, Conn., USA) on a 50% cyanopropylmethyl/50% phenylmethylpolysiloxane column (320 μm/30 m). The injector temperature was set at 230°C, the detector at 260°C. The oven temperature range was set to start at 120°C and increased continuously from 120 to 160°C at the rate of 20°C/min and from 160 to 220°C at the rate of 1°C/min with a final hold for 23 min. Nitrogen was used as carrier gas at a linear pressure of 50 hPa. Peak identification was with authentic FA methyl ester standards. The relative amount of each FA peak was determined by integration of the area under the peak of a selected FA in relation to the sum of areas of all detectable n–3 and n–6 FA. The supplements were analysed accordingly, sparing the extraction step.

Statistics

For all parameters and all measuring points of time, descriptive statistics were calculated; pre-post differences were calculated and analysed descriptively. Within the 2 treatment groups, each combination of 2 points of time was compared using the non-parametric Wilcoxon signed-rank test. For the pre-post differences, each combination of 2 treatment groups was compared using the Wilcoxon rank sum test. Percent changes of all measured parameters were calculated (week 0 vs. weeks 6 and 12, respectively) and the p values were determined at all measuring points. A p value less than 0.05 was considered to be statistically significant.

Results

Sensitivity

Skin irritation, caused by nicotinate exposure, was evaluated measuring skin redness (Δa values) and capillary blood flow in the treated area. Decreasing Δa values are correlated with a diminished inflammatory response to nicotinate irritation (table 2; fig. 1). After intervention for 6 weeks, nicotinate-induced redness in the flaxseed oil group was significantly decreased by 22% and after 12 weeks by 48%. Capillary blood flow was also decreased by 34% after 6 weeks and by 66% after 12 weeks, respectively (fig. 2; table 2). Upon supplementation with safflowerseed oil, Δa values were lowered only marginally after 6 and 12 weeks. Blood flow was increased by 11 and 7%, respectively. The changes were statistically not significant. For the pre-post differences (week 0 vs. week 12), the comparison of the 2 treatment groups showed a statistically significant difference in favour of the flaxseed oil group for the parameter Δa value and capillary blood flow.

Skin Hydration/TEWL

Upon supplementation with flaxseed oil, significant decreases in TEWL were found, by 21% after 6 and by 31% after 12 weeks (table 2), but not for the safflowerseed oil group. Skin hydration was increased in the flaxseed oil group: 7% after 6 weeks, 39% after 12 weeks. In the saf-

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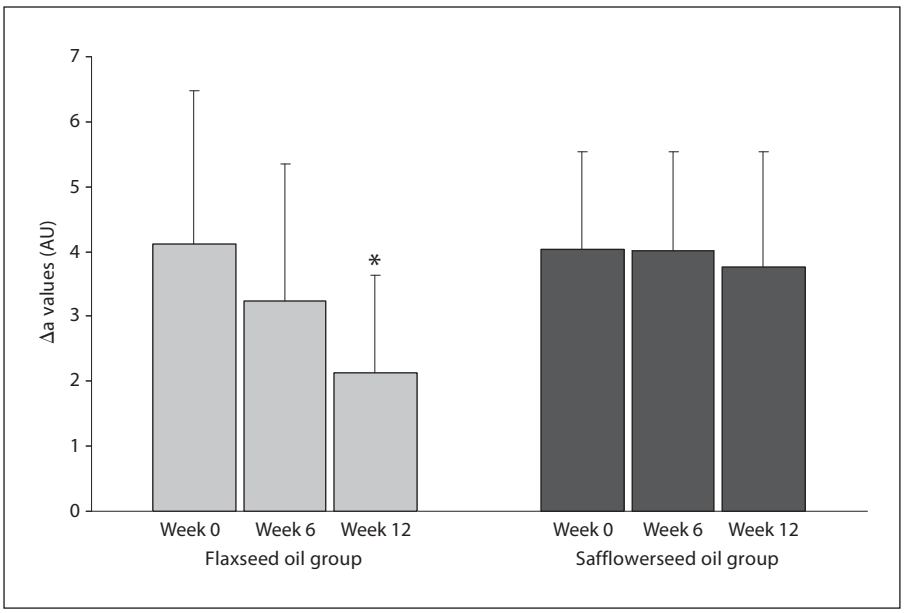

Fig. 1. Decrease in skin reddening (Δa values; arbitrary units, AU) after nicotinate irritation during 12-week oral treatment with flaxseed oil and safflowerseed oil. Data expressed as means ± SD, n = 13/group. * $p < 0.05$: significantly different from week 0.

flowerseed oil group, an increase of 13% was observed after 12 weeks. The improvement of skin hydration after 12 weeks was statistically significant in both groups. However, for the pre-post differences (week 0 vs. week 12), the comparison of the 2 treatment groups showed statistically significant differences in favour of the flaxseed oil group.

Surface Evaluation of Living Skin

Surface evaluation of living skin provides parameters related to the structure of the skin surface, including roughness, scaling, smoothness and wrinkling (table 2). Figure 3 shows typical charge-coupled device pictures of the skin surface before and after treatment of the forearm of 1 volunteer from each group. After supplementation with flaxseed oil, statistically significant differences were measured after 6 and 12 weeks compared to week 0 for the parameters roughness, scaling and smoothness. The parameter roughness decreased by 30%, scaling by 31% and smoothness increased by 7% after 12 weeks; wrinkling was not affected. In the group treated with safflowerseed oil, statistically significant differences were observed after 6 and 12 weeks compared to week 0 for the parameter roughness only. It was lowered at both time points by 10%. A further improvement after 12 weeks was not observed. The pre-post differences (week 0 vs. week 12) comparing both groups showed a statistically significant difference of skin roughness in favour of the flaxseed oil group. Scaling was diminished by 14%; smoothness was increased by 2% after 12 weeks in the safflowerseed oil group.

Table 2. Skin parameters at weeks 0, 6 and 12 after daily treatment (n = 13/group)

Skin parameter	Flaxseed oil group			Safflowerseed oil group		
	0	6	12	0	6	12
Δa value, AU	4.12	3.23	2.13*	4.03	4.02	3.76
Blood flow, AU	86	58*	29*	80	89	85
Hydration, AU	30	32	41*	36	36	41*
TEWL, $g \cdot h^{-1} \cdot m^{-2}$	8.82	6.95*	6.05*	6.95	6.54	6.13
Roughness, AU	1.87	1.45*	1.31*	1.56	1.4*	1.41*
Scaling, AU	0.97	0.83	0.66*	0.95	0.89	0.82
Wrinkling, AU	21.5	21.4	22	22.3	22.9	23.1
Smoothness, AU	25.3	26	27.2*	26.9	22.6	27.4

AU = Arbitrary units; * $p < 0.05$: significantly different from week 0.

FA Analysis

Table 1 shows the FA composition of the capsules, table 3 the FA pattern determined in plasma of the flaxseed oil and safflowerseed oil groups. The following FA were determined by gas chromatography/flame ionization detection: ALA, EPA, docosapentaenoic acid and docosahexaenoic acid (n–3 FA), LA, GLA, eicosatrienic acid and

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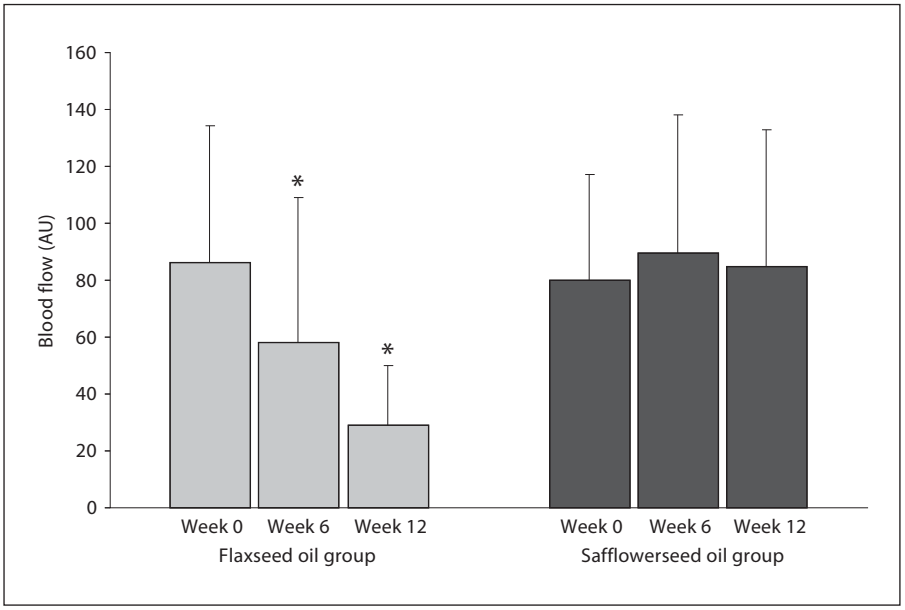

Fig. 2. Decrease in microcirculation (capillary blood flow; arbitrary units, AU) after nicotinate irritation during 12-week oral treatment with flaxseed oil and safflowerseed oil. Data expressed as means ± SD, n = 13/group. * $p < 0.05$: significantly different from week 0.

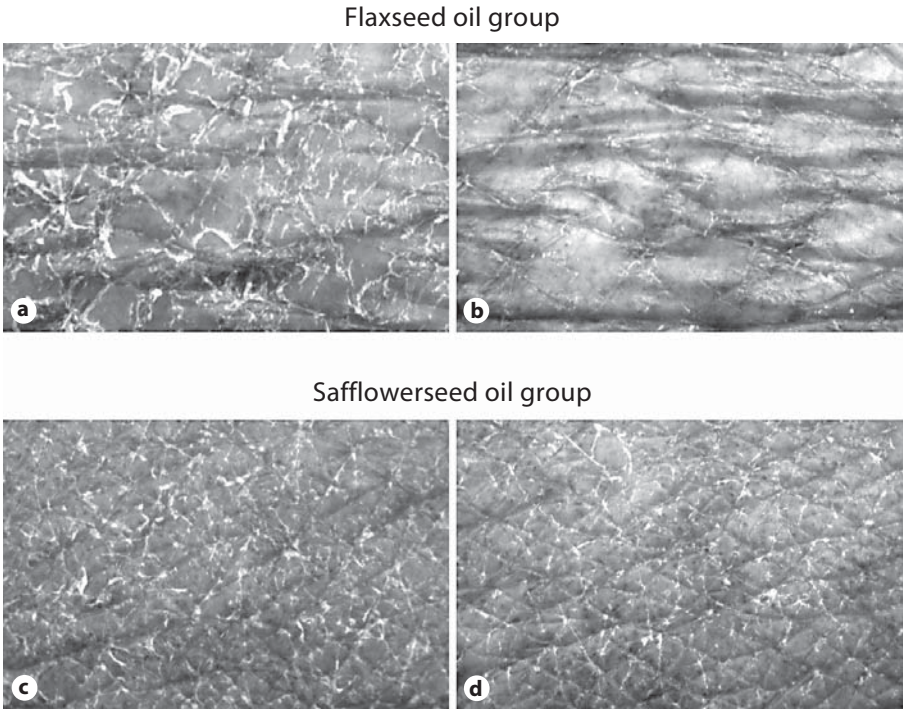

Fig. 3. Skin surface evaluation of the inner forearm by the surface evaluation of living skin method (Visioscan) before treatment (**a**, **c**) and after 12 weeks of supplementation (**b**, **d**) with flaxseed oil and safflowerseed oil.

arachidonic acid (n–6 FA). For further FA determined in the capsules, see table 1. Upon supplementation with flaxseed oil, the percent contribution of all n–6 FA to the FA pattern in plasma slightly decreased, whereas the contribution of n–3 FA increased. This is also reflected by changes in the pattern of single FA. The percentage of LA in plasma lipids decreased, whereas the percent contribution of ALA and EPA increased. Docosahexaenoic acid remained unchanged during supplementation. The sum of n–6 FA slightly increased during treatment with

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Table 3. Flaxseed and safflowerseed oil group composition of plasma FA (n = 13) at weeks 0, 6 and 12

FA	Flaxseed oil group			Safflowerseed oil group		
	0	6	12	0	6	12
Sum of n–6 FA	92.35	90.38	91.54	91.37	92.82	92.62
Sum of n–3 FA	7.65	9.62	8.46	8.63	7.18	7.38
Ratio n–6/n–3	12.1	9.4	10.8	10.6	12.9	12.6
n–6 FA						
LA	67.72	67.31	68.76	68.92	72.62*	71.32
GLA	3.97	1.51	1.90	1.37	1.15	1.16
Eicosatrienoic acid	4.97	4.80	5.11	4.94	4.91	5.08
Arachidonic acid	15.69	16.77	15.77	16.1	14.1	15.1
n–3 FA						
ALA	1.31	2.19*	1.93*	1.36	1.58	1.53
EPA	1.61	2.17	1.86	2.14	1.43*	1.53
Docosapentaenoic acid	1.25	1.70	1.26	1.87	1.68	1.61
Docosahexaenoic acid	3.48	3.56	3.40	3.27	2.49	2.72

Results are expressed as percent contribution to total n–3 and n–6 FA (i.e. sum of LA, ALA, EPA, GLA, arachidonic acid, eicosatrienoic acid, docosapentaenoic acid and docosahexaenoic acid). * $p < 0.05$: significantly different from week 0.

safflowerseed oil, whereas the contribution of total n–3 FA decreased. Corresponding changes were found for LA (increase) and EPA (decrease). Statistically significant were the changes of ALA in the flaxseed oil group and of LA and EPA in the safflowerseed oil group. For the pre-post differences (week 0 vs. week 6), the comparison of the 2 treatment groups showed statistically significant differences for the following parameters: sum of n–6 FA, sum of n–3 FA, ALA, LA and EPA in plasma. For the other pre-post differences and parameters (12 weeks; other FA), no statistically significant differences were found.

Discussion

More than 50% of the Western population claim to have sensitive skin [1], which is often treated by topical application of lotions and creams. New approaches address the modulation of skin properties by dietary intervention or supplementation [9, 19]. This study showed that daily supplementation with flaxseed oil improved skin appearance and led to a decreased skin sensitivity by modulating epidermal barrier function and inflammation response to nicotinate. Nicotinate exposure is a potent model for transcutaneous penetration of chemicals and resulting hyperreactivity of sensitive skin [4, 5, 20]. As a response of the skin, the blood flow increases and an erythema is formed. The reaction is sensitive to the integrity of the skin barrier. Barrier dysfunction can amplify the response to irritating stimuli and their inflammatory potential via a modulation of signal molecules [21]. After supplementation with flaxseed oil, both erythema formation and capillary blood flow were diminished, suggesting that flaxseed oil intake improved epidermal function and modulated inflammation depending on signal molecules.

The determination of the TEWL confirmed the change in the barrier function, as the ingestion of flaxseed oil decreased TEWL. This was also accompanied by a higher skin hydration status, which can be correlated with irritant reaction and skin permeability [22]. In contrast, safflowerseed oil intake did not significantly influence the TEWL; however, a slight increase in hydration was observed. Both methods are used to provide information about the epidermal barrier function of the skin under healthy, diseased or experimentally perturbed conditions [21, 22].

The observed effects were correlated with a shift in the plasma FA pattern. After supplementation with flaxseed oil, ALA concentrations increased, whereas LA concentration increased after safflowerseed supplementation. The changes in the FA pattern following supplementation with either flaxseed oil or safflowerseed oil were in ac-

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cordance with the FA pattern provided with the treatment.

Epidermal lipids play an essential role in water homeostasis, TEWL and sensitivity of the skin. Changes in the lipid organization often result in excessive water loss, seen in dysfunctional skin as in psoriasis, atopic dermatitis, epidermolysis bullosa or burns [23].

Lipids of the stratum corneum are part of the intra- and extracellular matrix. During keratinocyte differentiation, polar lipids, located in lamellar bodies, are secreted and modified into non-polar lipids with a unique composition of 50% ceramide, 25% cholesterol and 15% free FA [24, 25]. C_{12}–C_{24} FA are found free or esterified, and are either synthesized in the epidermis or supplied from the food [25]. A deficiency in essential FA, mainly LA, may result in epidermal changes: the skin gets red, rough, scaly and the barrier can be disturbed [24, 25]; all of this can also be characteristic of a sensitive skin. Improvement of the epidermal barrier function leads to a decreased exsiccation of the skin, resulting in a smoother structure of the skin surface. Accordingly, we observed in our study an improvement in skin surface parameters, like roughness, scaling and smoothness, after supplementation with flaxseed oil. Interestingly, LA ingestion also led to a significant decrease in skin roughness. However, reduction of roughness during ALA-rich flaxseed oil supplementation was significant after already 6 weeks and after 12 weeks; the extent was higher than after LA-rich safflowerseed oil supplementation (30 vs. 10%).

Less is known about the effects of C_{18} FA other than LA, like ALA and GLA. Studies with orally applied oils rich in GLA or ALA have shown the influence of these FA on the epidermal barrier [26–28]. Including this study, all data indicate that essential FA, other than LA, modulate skin conditions. The underlying mechanisms are still unclear.

In the study, we observed a lower inflammatory response of the skin after flaxseed oil intake. Eicosanoids are important signal molecules in the inflammatory pathway, which are synthesized from polyunsaturated C_{20} FA. C_{18} FA are precursors of C_{20} FA. C_{20} n–3 and n–6 FA are precursor molecules for eicosanoids of different series with varied inflammatory potential [29]. However, C_{20} FA in plasma were only slightly modified in both groups of the study. Thus, the effect of eicosanoids cannot be estimated.

Apart from FA, other dietary constituents have been shown to affect skin condition and have potential to reduce skin sensitivity. Lutein and zeaxanthin, two carotenoids with photoprotective activity, increased skin hydration [9]. Supplementation with a mixture consisting of carotenoids, vitamin E and selenium increased skin density and thickness [10]. Epigallocatechin-3-gallate supplementation prevented UVB-induced adverse effects on epidermal thickness and TEWL [30]. Beyond other dietary constituents, oils rich in ALA are further nutrients with impact on sensitive skin.

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Disclosure Statement

The authors declare no conflict of interest.

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