Intervention with flaxseed and borage oil supplements modulates skin condition in women

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Ingestion of selected nutrients modulates dermal properties. In the present study, two groups of women ingested flaxseed or borage oil for 12 weeks. The control group received a placebo containing medium-chain fatty acids. Dose was 2·2 g total fatty acids/d with α-linolenic acid and linoleic acid as major constituents in the flaxseed oil group; in the borage oil group linoleic and γ-linolenic acid were predominant. In the flaxseed oil group, the contribution of α-linolenic acid to total fatty acids in plasma was significantly increased on weeks 6 and 12, whereas there was an increase in γ-linolenic acid in the borage oil group (P<0·05). Skin irritation was performed by nicotinate treatment, and changes in skin reddening and blood flow were monitored. Compared to week 0, skin reddening was diminished in both groups; blood flow was also lowered. Skin hydration was significantly increased after 12 weeks of treatment compared to week 0, with flaxseed or borage oil (P<0·05). Transepidermal water loss was decreased in both oil groups by about 10 % after 6 weeks of supplementation. A further decrease was determined after 12 weeks in the flaxseed oil group. Surface evaluation of living skin revealed that roughness and scaling of the skin were significantly decreased with flaxseed and borage oil comparing week 0 and week 12 (P<0·05). Except for hydration, none of the parameters was affected in the placebo group. The present data provide evidence that skin properties can be modulated by an intervention with dietary lipids.

Lipids: Skin: Human studies: Hydration: Blood flow

Basic skin functions like that of a shielding barrier, homeostasis of water, temperature regulation and photoprotection respond to supplementary or dietary intervention with selected nutrients(1,2). Modulated functions are accompanied by changes in cutaneous structure and texture which affect the appearance of the skin. Studies in man have shown that an increased intake of carotenoids such as β-carotene or lycopene, carotenoid-rich food or flavanol-rich cocoa strengthens the basal protection against UV-induced erythema, increases cutaneous blood flow, and modulates skin structure and hydration(3,4).

Some PUFA are essential for the human organism and serve several biological functions. Supplementation with certain fatty acids can influence the fatty acid pattern of the skin and affect its sensitivity towards photooxidation(5) and may contribute to prevention of non-melanoma cancers(6). PUFA, like linoleic acid (LA) or α-linolenic acid (ALA), GLA, γ-linolenic acid (GLA), play a role in cellular signalling interfering with eicosanoid pathways or influencing the regulation of gene expression(2,7). Both n-3 as well as n-6 long-chain PUFA are important components of cellular membranes, contributing to their fluidity, rigidity, permeability and function(8,9). Epidermal lipids are known to play an important role in mediating normal desquamation and deficiency of essential fatty acids has been reported to be involved in cutaneous scaling disorders such as senile xerosis, psoriasis and atopic dermatitis(10).

The organism has a limited activity to generate higher PUFA from C18 fatty acids via desaturation–elongation reactions. Thus, the n-6 PUFA LA can be metabolized to GLA. However, it has been reported that cutaneous tissue lacks such activity(11).

Based on structural effects and signalling processes, PUFA affect macroscopic properties of the skin essential for cutaneous health. Supplementation with LA and GLA from borage oil over a 2-month period leads to decreased transepidermal water loss (TEWL) and itching. Dry skin appearance was diminished significantly, but no alteration of skin hydration was measured(12). LA deficiency results in deformation or absence of the lamellar bodies, giving way to water passing the epidermis(13). Consumption of flaxseed oil rich in ALA or DHA/EPA-rich fish oil is associated with lower levels of proinflammatory eicosanoids(14). In the present study we investigated the effects of 12-week oral supplementation with flaxseed or borage oil on human skin properties.
Materials and methods

Subjects and study design

Forty-five female healthy non-smoking women, between 18 and 65 years, with sensitive and dry skin were recruited by the Institute of Experimental Dermatology, and selected according to their skin type: dry skin; Corneometer value <40 au\(^{(15)}\). Exclusion criteria were: pregnancy and breast-feeding, history of fat malabsorption, liver diseases, diseases regarding lipid metabolism or any photosensitizing disorder. BMI of the participants was between 18 and 25 kg/m\(^2\), they did not take lipid or vitamin supplements or any other medication.

The study was performed as a monocentric, randomized, double-blind placebo-controlled application test, in three parallel treatment groups, consisting of fifteen persons each. Age distribution was comparable between the three groups. Four capsules with different oils were taken every day, two at breakfast and two at dinner. Daily doses amounted to 2·2 g flaxseed or borage oil; in both groups, intake of tocopherol was 10 mg/d. Daily intake of the placebo was also 2·2 g. Every test subject had to submit a written declaration of information listing every single parameter relevant to the study.

Subjects with a skin type of dry skin and BMI between 18 and 25 kg/m\(^2\) were treated under nitrogen to a final volume of 350 μl and transferred to an injection vial sealed with a metal cap. Fatty acid methyl esters were separated by GC on a FFAP column (Crossbond Carbowax PEG for acid compounds; 30 m, 250 μm) and detected by flame ionization (Clarius 500 PE AutoSystem with built-in autosampler; Perkin Elmer, Shelton, USA). The injector temperature was 240°C, the oven temperature programme started at 150°C and increased continuously to 190°C at a rate of 20°C/min and from 190 to 235°C at a rate of 1°C/min with a final hold of 35 min. Nitrogen was used as carrier gas at a pressure of 70 kPa. Detector temperature was 260°C. Peak identification was with authentic fatty acid methyl ester standards (Supelco, Deisenhofen; Fluka; Sigma, St. Louis, MO, USA). With this procedure all esterified fatty acids are detected and referred to as ‘total fatty acids’. The relative amount of each fatty acid was calculated from the ratio of the area under the signal and total area of all identified fatty acid methyl esters (100% method).

Skin hydration and transepidermal water loss

Skin hydration (arbitrary units) was determined by corneometry (Corneometer CM 825; Courage & Khazaka Electronics, Cologne, Germany); TEWL (g/h per m\(^2\)) was measured using a Tewa-Meter TM 300 (Courage & Khazaka Electronics). Skin surface profiles were evaluated with the surface evaluation of living skin method (Visioscan; Courage & Khazaka Electronics) in a 15 × 17 mm area. Four different parameters are applied to characterize skin surface: roughness, scaling, smoothness, wrinkles\(^{(19)}\).

Statistics

For all parameters and all time-points (week 0, week 6, week 12) descriptive statistics (means and standard deviations) were

### Table 1. Fatty acid composition of the supplements (% of total fatty acids)

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Flaxseed oil</th>
<th>Borage oil</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:0</td>
<td>0.0</td>
<td>0.0</td>
<td>36.9</td>
</tr>
<tr>
<td>10:0</td>
<td>0.00</td>
<td>0.00</td>
<td>21.8</td>
</tr>
<tr>
<td>14:0</td>
<td>4.73</td>
<td>1.87</td>
<td>0.24</td>
</tr>
<tr>
<td>18:0</td>
<td>4.12</td>
<td>2.82</td>
<td>0.00</td>
</tr>
<tr>
<td>18:1n9</td>
<td>19.0</td>
<td>15.0</td>
<td>0.60</td>
</tr>
<tr>
<td>18:2n6</td>
<td>16.0</td>
<td>38.7</td>
<td>0.00</td>
</tr>
<tr>
<td>18:3n6</td>
<td>0.00</td>
<td>21.6</td>
<td>0.18</td>
</tr>
<tr>
<td>18:3n3</td>
<td>52.8</td>
<td>0.38</td>
<td>0.00</td>
</tr>
<tr>
<td>20:0</td>
<td>0.16</td>
<td>0.21</td>
<td>0.00</td>
</tr>
<tr>
<td>20:1</td>
<td>0.20</td>
<td>3.96</td>
<td>0.00</td>
</tr>
<tr>
<td>22:0</td>
<td>0.00</td>
<td>0.23</td>
<td>0.00</td>
</tr>
<tr>
<td>22:1</td>
<td>0.00</td>
<td>2.23</td>
<td>0.00</td>
</tr>
<tr>
<td>24:0</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>24:1</td>
<td>0.00</td>
<td>1.30</td>
<td>0.00</td>
</tr>
<tr>
<td>Non-identified fatty acids</td>
<td>2.39</td>
<td>11.7</td>
<td>40.3</td>
</tr>
</tbody>
</table>

With 500 μl methanol–sodium chloride (0-9 %)–chloroform (48:47:3). The solution was dried under a stream of nitrogen. For base-catalyzed transesterification to yield fatty acid methyl esters the fat extract was incubated 1 h at 60°C with 3 ml water-free methanol containing sodium methoxide (3 % m/v). Chlorogenic acid (1 ml) was added, and fatty acid methyl esters were extracted twice with 3 ml hexane, concentrated under nitrogen to a final volume of 350 μl and transferred to an injection vial sealed with a metal cap. Fatty acid methyl esters were separated by GC on a FFAP column (Crossbond Carbowax PEG for acid compounds; 30 m, 250 μm) and detected by flame ionization (Clarius 500 PE AutoSystem with built-in autosampler; Perkin Elmer, Shelton, USA). The injector temperature was 240°C, the oven temperature programme started at 150°C and increased continuously to 190°C at a rate of 20°C/min and from 190 to 235°C at a rate of 1°C/min with a final hold of 35 min. Nitrogen was used as carrier gas at a pressure of 70 kPa. Detector temperature was 260°C. Peak identification was with authentic fatty acid methyl ester standards (Supelco, Deisenhofen; Fluka; Sigma, St. Louis, MO, USA). With this procedure all esterified fatty acids are detected and referred to as ‘total fatty acids’. The relative amount of each fatty acid was calculated from the ratio of the area under the signal and total area of all identified fatty acid methyl esters (100% method).
calculated. For all parameters pre–post differences were calculated and analysed descriptively.

Separately for each of the two pre–post differences ‘week 6 – week 0’ and ‘week 12 – week 0’ an ANOVA with the parameter treatment as the independent variable was performed. Tests for the treatment effect and the contrasts were performed. The least square means for the pre–post differences and the respective 95% CI were calculated. These CI were used to assess whether the pre–post difference was significantly different from zero.

Results

Fatty acid analysis

Fatty acid patterns of the supplements are shown in Table 1. In flaxseed oil, ALA is predominant; also considerable amounts of LA are present. The latter is the major fatty acid in borage oil followed by GLA. Thus, in flaxseed oil n-3 fatty acids contribute more than 50% to total fatty acid content, whereas more than 50% of fatty acids in borage oil are of the n-6 type. Additionally, both supplements contained similar amounts of tocopherol. Medium-chain fatty acids were present in the placebo; caprylic and capric acid were dominating. Volunteers were divided into three groups, flaxseed, borage oil and placebo, ingesting four capsules of the supplement per day over a period of 12 weeks. Daily doses amounted to 2.2 g flaxseed or borage oil; in both groups, intake of tocopherol was 10 mg/d. Daily dose of the placebo was 2.2 g.

Blood samples were collected on day 0, week 6 and week 12 and fatty acid composition of plasma lipids (total fatty acids) was analysed by GC. Results for the different groups are shown in Tables 2–4. In the flaxseed oil group, only the contribution of ALA to total fatty acids was significantly changed. From day 0 to week 6 it increased from 0.58% to 0.83% and remained constant until week 12. Upon supplementation with borage oil, the relative amount of GLA was significantly increased on weeks 6 and 12 compared to day 0. A marginal increase was detectable for di-homo-gamma-linolenic acid (DGLA) from 2.09% in week 0 to 2.44% in week 6 and 2.33% in week 12. Upon supplementation with flaxseed, the relative amount of GLA was significantly increased from weeks 6 and 12 to baseline, values are indicative for anti-inflammatory effects. Compared to baseline, Δ values were significantly lower on weeks 6 and 12 in the groups treated with flaxseed and borage oil; after 12 weeks the decrease was 45 and 35%, respectively (P<0.05).

No changes were observed in the placebo group. However, it has to be noted that the basal value in the placebo group was lower than in the other groups. Values are a measure for skin reddening. The resulting erythema was evaluated by chromametry where a values are a measure for skin reddening. The difference in a values (Δa values) before and after exposure to nicotinate is shown in Table 5. Decreasing Δa values are indicative for anti-inflammatory effects. Compared to baseline, Δa values were significantly lower on weeks 6 and 12 in the groups treated with flaxseed and borage oil; after 12 weeks the decrease was 45 and 35%, respectively (P<0.05).

Mean values were significantly different from those of week 0: *P<0.05.

† For details of procedures and supplements, see Materials and methods section and Table 1.

Skin sensitivity

Exposure of skin to nicotinate leads to chemically induced inflammation. The resulting erythema was evaluated by chromametry where a values are a measure for skin reddening. The difference in a values (Δa values) before and after exposure to nicotinate is shown in Table 5. Decreasing Δa values are indicative for anti-inflammatory effects. Compared to baseline, Δa values were significantly lower on weeks 6 and 12 in the groups treated with flaxseed and borage oil; after 12 weeks the decrease was 45 and 35%, respectively (P<0.05). No changes were observed in the placebo group. However, it has to be noted that the basal value in the placebo group was lower than in the other groups. Changes in the flaxseed oil group were significantly different from the placebo group (weeks 0–6, P=0.01; weeks 0–12, P=0.006). Also the changes in the borage oil

Table 2. Fatty acid composition of plasma lipids (% total fatty acids) in the group treated with flaxseed oil (n 15)† (Mean values and standard deviations)
Flaxseed and borage oil modulate skin conditions

Table 5. Sensitivity of skin to nicotinate-induced irritation in women supplemented with flaxseed or borage oil: intensity of erythema and cutaneous blood flow (arbitrary units; n 15)†

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flaxseed oil</td>
<td>4.3</td>
<td>1.3</td>
<td>2.9*</td>
<td>0.9</td>
<td>2.4*</td>
<td>1.0</td>
</tr>
<tr>
<td>Borage oil</td>
<td>4.2</td>
<td>1.5</td>
<td>3.0*</td>
<td>1.6</td>
<td>2.7*</td>
<td>1.2</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.4</td>
<td>1.0</td>
<td>3.4</td>
<td>1.3</td>
<td>3.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Cutaneous blood flow

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flaxseed oil</td>
<td>75.0</td>
<td>22.0</td>
<td>50.0*</td>
<td>23.0</td>
<td>14.0*</td>
<td>12.0</td>
</tr>
<tr>
<td>Borage oil</td>
<td>71.0</td>
<td>20.0</td>
<td>51.0*</td>
<td>30.0</td>
<td>47.0*</td>
<td>20.0</td>
</tr>
<tr>
<td>Placebo</td>
<td>70.0</td>
<td>22.0</td>
<td>63.0</td>
<td>26.0</td>
<td>64.0</td>
<td>29.0</td>
</tr>
</tbody>
</table>

Mean values were significantly different from those of week 0: *P<0.05.
† For details of procedures and supplements, see Materials and methods section and Table 1.

Discussion

In women supplemented with flaxseed or borage oil, skin hydration was significantly increased after 12 weeks of treatment compared to day 0 (Table 6). In the flaxseed oil group the effect was already seen after 6 weeks. A significant increase in skin hydration was also observed in the placebo group but only after 12 weeks. The increases observed for the plant oils were not significantly different from the placebo group.

TEWL was decreased in both plant oil groups by about 10% after 6 weeks. A further decrease was determined after 12 weeks in the flaxseed oil group, whereas there was only small difference in TEWL values between weeks 6 and 12 in the borage oil group. No statistically significant differences between day 0 and weeks 6 and 12 were measured in the placebo group. The change in the flaxseed oil group from weeks 0 to 12 was significantly different to the placebo group (P=0.00006) and to the borage oil group (P=0.001).

Skin profiles were analysed using the surface evaluation of living skin method which provides parameters associated with roughness, scaling, smoothness and wrinkling of the skin. Upon intervention for 12 weeks with flaxseed oil, roughness, scaling and smoothness were improved (Table 7). Supplementation with borage oil caused modifications in the same parameters, but only the decrease in scaling from week 0 to week 6 was statistically significant. No changes were determined in the placebo group except for a small but statistically significant decrease in the parameter smoothness. None of the treatments affected wrinkling.

Comparing groups, there was a significant difference between flaxseed oil and placebo for the parameter roughness (weeks 0–12, P=0.0006) and smoothness (weeks 0–6, P=0.002; weeks 0–12, P=0.02).

Table 7. Parameters related to skin structure determined by surface evaluation of the skin at weeks 0, 6 and 12 of the study (arbitrary units; n 15)†

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoothness</td>
<td>54.7</td>
<td>0.40</td>
<td>54.8*</td>
<td>0.42</td>
<td>54.8*</td>
<td>0.40</td>
</tr>
<tr>
<td>Borage oil</td>
<td>54.7</td>
<td>0.40</td>
<td>55.3*</td>
<td>0.42</td>
<td>55.3*</td>
<td>0.40</td>
</tr>
<tr>
<td>Placebo</td>
<td>54.7</td>
<td>0.40</td>
<td>55.3*</td>
<td>0.42</td>
<td>55.3*</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Mean values were significantly different from those of week 0: *P<0.05.
† For details of procedures and supplements, see Materials and methods section and Table 1.
sources of n-3 fatty acid. With more than 50 % of total fatty acid, ALA is predominant but also the n-6 LA (16 %) and the monounsaturated oleic acid (20 %) are major constituents (Table 1). The flaxseed oil supplemented used in the present study is typical with respect to its composition of fatty acids(20). Borage oil is produced from the seeds of the borage plant (Borago officinalis) and is rich in the n-6 fatty acids GLA (22 %) and LA (39 %); oleic acid (15 %) is also present in quite high amounts (Table 1). Also this supplement is typical regarding its fatty acid pattern(12).

Ingestion of ALA-rich flaxseed oil or GLA-rich borage oil led to increases in the contribution of the respective fatty acid to total plasma lipids (Tables 2–4). Changes in other fatty acids were not observed, apart from increases in DGLA in the group supplemented with borage oil. DGLA is likely formed from GLA by an elongase-catalysed two-carbon chain elongation. In addition to elongases, desaturases are required for the synthesis of arachidonic acid and higher homologues of the n-6 family as well as for C20 PUFA of the n-3 family. Increases of C20 PUFA in plasma and different lipid fraction in the blood have been shown after application of high doses of ALA(21). In the present study the total dose of ALA and GLA was quite low and thus changes in the levels of longer-chain fatty acids may have been too small for detection. It should be further noted that the pattern of plasma lipids does not necessarily reflect the lipid composition of tissues such as skin. Some major effects observed here are likely due to more significant changes in skin lipids. However, dermal punch biopsy would be required to analyse the fatty acid pattern at the target site.

The irritating effects of nicotine were ameliorated by long-term intake of either flaxseed or borage oil (Table 5). Reddening of the skin after the chemical challenge was lower in both groups after 6 and 12 weeks of intervention. Similar effects have been described after intake of long-term intake of either flaxseed or borage oil (Table 5).

Inflammation induction of skin parameters has been shown for several other nutrients(3,4), indicating that dietary intervention is a way of improving skin conditions and providing protection. Stabilizing effects and improvements of cellular membranes may be responsible for changes of macroscopic skin properties related to water homeostasis. Again, with both supplements skin hydration was increased after 12 weeks of intervention, whereas TEWL was lower than control. Improvement of skin moisture and TEWL as well as firmness, indications for an improved barrier function, have been described after the intake of GLA-rich primrose and borage oil(22). Skin hydration slightly increased in the placebo group. However, this was not accompanied by a decrease in TEWL. External factors maybe responsible for this minor effect.

There have been several approaches to modulate skin parameters with respect to influencing skin appearance under cosmetic aspects. With the surface evaluation of living skin method one can evaluate the skin structure and obtain information on roughness, scaling and wrinkling. Intervention with flaxseed or borage oil led to changes in roughness and scaling, which might be in part explained by the observed modulation of skin hydration and firmness. However, a parameter such as wrinkling, which results mainly from changes in the molecular structure of extracellular components, was not affected by any of the treatments.

It has been shown that under conditions of LA deficiency, LA is substituted by oleic acid in epidermal acylceramides(26), which has been associated with an increased TEWL, perturbations of the intercellular membranes and an altered epidermal homeostasis(27). Thus, an increased LA supply may contribute to improved skin parameters. ALA and GLA may also affect skin homeostasis along this line. Modulation of skin properties has been shown for several other nutrients(3,4), indicating that dietary intervention is a way of improving skin conditions and providing protection. It should be stated that effects are moderate and develop over a long-term period.

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References