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ORIGINAL ARTICLE

Efficacy of dietary hempseed oil in patients with atopic dermatitis

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Abstract
Background: Hempseed oil is a rich and balanced source of omega-6 and omega-3 polyunsaturated fatty acids (PUFAs). Anecdotal evidence indicated that dietary hempseed oil might be useful in treating symptoms of atopic dermatitis. *Patients and methods*: Dietary hempseed oil and olive oil were compared in a 20-week randomized, single-blind crossover study with atopic patients. Fatty acid profiles were measured in plasma triglyceride, cholesteryl and phospholipid fractions. A patient questionnaire provided additional information on skin dryness, itchiness and usage of dermal medications. Skin transepidermal water loss (TEWL) was also measured. *Results*: Levels of both essential fatty acids (EFAs), linoleic acid (18:2n6) and alpha-linolenic acid (18:3n3), and gamma-linolenic acid (GLA; 18:3n6) increased in all lipid fractions after hempseed oil, with no significant increases of arachidonic acid (20:4n6) in any lipid fractions after either oil. Intra-group TEWL values decreased ($p=0.074$), qualities of both skin dryness and itchiness improved ($p=0.027$) and dermal medication usage decreased ($p=0.024$) after hempseed oil intervention. *Conclusions*: Dietary hempseed oil caused significant changes in plasma fatty acid profiles and improved clinical symptoms of atopic dermatitis. It is suggested that these improvements resulted from the balanced and abundant supply of PUFAs in this hempseed oil.

Key words: Cannabis, *hemp, SDA, stearidonic acid, desaturase, eczema*

Introduction

Dietary fatty acids can influence symptoms of atopic dermatitis (1,2) and other aspects of health (3). Seed oils that are rich in both essential fatty acids (EFAs), i.e. linoleic acid (18:2n6) and alpha-linolenic acid (18:3n3), and particularly seed oils that contain gamma-linolenic acid (GLA, 18:3n6), have been studied in patients with atopic dermatitis (4–9), with varying degrees of success, and more recently in regard to immune response (10).

The seed oil from some varieties of *Cannabis sativa* L. can have over 80% polyunsaturated fatty acids (PUFAs). Hempseed oil, pressed from non-drug varieties of the *Cannabis* seed, is an especially rich source of both EFAs (Table I), in addition to their immediate biologic metabolites, GLA and stearidonic acid (SDA; 18:4n3) (11). Moreover, these PUFAs are present in hempseed oil at a metabolically favourable omega-6 to omega-3 ratio (n-6/n-3), in addition to tocopherols (12,13).

The EFAs were already recognized as being essential to human health by the 1930s (14,15). In human metabolism, both EFAs must compete for access to the same rate-limiting enzyme, delta-6 desaturase; a metabolic point at which the transformation of omega-6 and omega–3 fatty acids bifurcate into a cascade of bioactive metabolites (16). Moreover, delta-6-desaturase has a higher affinity for alpha-linolenic acid than linoleic acid (17). Thus, metabolic competition between the EFAs for access to delta-6 desaturase suggests some optimal balance between dietary omega-6 to omega-3 fatty acids (16–19). Recent research indicates this optimal n-6/n-3 dietary ratio to be somewhere between 2:1 and 3:1 (20). By contrast, evening primrose and borage oils are totally lacking in omega-3 PUFAs, i.e. alpha-linolenic acid and SDA, which may account for their poor or inconclusive performance in some clinical studies with these seed oils (6–9,21–23). This idea is supported by effective increases in immunologic vigour from blackcurrant seed oil (10), which has an

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Table I. Fatty acid profiles of the hempseed oil and olive oil used in this study.

Fatty acid (code)	Hempseed oil	Olive oil	Class
Palmitic acid (16:0)	6%	15%	Saturated
Stearic acid (18:0)	2	0	Saturated
Oleic acid (18:1n9)	9	75	MUFA, omega-9
Linoleic acid (18:2n6)	54	7	PUFA, omega-6
alpha-Linolenic acid (18:3n3)	22	<1	PUFA, omega-3
*GLA (18:3n6)	4	0	PUFA, omega-6
*SDA (18:4n3)	2	0	PUFA, omega-3
% PUFA	82%	7%	omega-6 + omega-3
n6/n3 ratio	2.2:1	>7:1	omega-6/omega-3

*GLA and SDA are abbreviations for gamma-linolenic acid and stearidonic acid, which are the biological metabolites of linoleic acid and alpha-linolenic acid, respectively. MUFA=monounsaturated and PUFA=polyunsaturated fatty acids.

excellent n-6/n-3 balance and PUFA profile that is remarkably similar to hempseed oil (11–13,22).

Hempseed oil has been used as a food and medicine for at least 3000 years in China (24), and has recently become available in specialty food shops throughout Europe and North America (25). The recent availability of hempseed oil in Western cultures has led to anecdotal reports of improved health after its oral administration (e.g.26,27). In most cases, noticeable healing of chronic skin problems begins within 2 weeks after initiating regular use of hempseed oil. Thicker, and thus stronger, hair and nails have also been observed after longer periods of regular use (unpublished observations).

Atopic dermatitis, more commonly known as eczema, is a chronic skin condition that can result from various allergenic challenges, but its precise aetiology remains unknown. Several likely factors have been investigated, such as diet (3,19,28), decreased delta-6-desaturase activity (21,29,30), decreased ceramide function (31,32,33), problems in sphingomyelin metabolism (34), bacterial skin flora (35), skin lipid profiles (2), use of alcohol (36) and environmental influences; such as sodium lauryl sulfate (SLS, a detergent found in many body care products) and light (37), in addition to age, season, temperature and humidity (38–40). None of these factors are mutually exclusive, and it seems that dietary fatty acids play some fundamental role in the manifestation of this complex metabolic system, which is more or less dysfunctional in patients who develop symptoms of atopic dermatitis (41). Considering the fatty acid profile of hempseed oil (Table I) with the frequency of subjective reports that claim improvement in skin conditions, its seemed worthwhile to investigate the possibility that hempseed oil might have functional benefits that could also be measured objectively in a clinical trial.

The aim of the present study was to compare the effects of dietary hempseed oil and olive oil on plasma lipid profiles, transepidermal water loss (TEWL), skin quality and dermal medication usage in patients with atopic dermatitis in a randomized crossover design.

Patients and methods

Study design

This was a controlled, randomized single-blind crossover study. The two intervention periods were 8 weeks in duration, with a 4-week washout period in between (Figure 1). A group of 20 patients with atopic dermatitis were included, divided into two groups by electronically generated random digits and instructed to orally consume 30 ml (2 tbsp) of the assigned study oil during each day of the intervention period. Only one member for the study team (US) was privy to patient and sample identity, and this information was not available during the study period or data analysis.

The study was conducted at latitude 63°N, beginning in early January and ending in late May. The patients visited the research unit at the beginning of each intervention period, after 4 weeks and at the end of each intervention period, for a total of six visits. Body weight was measured using the same calibrated electronic scale throughout the study. Patients also met with a nutritionist at the beginning of each study period to receive their intervention oil and detailed information for incorporating the oils into their daily diet. The same

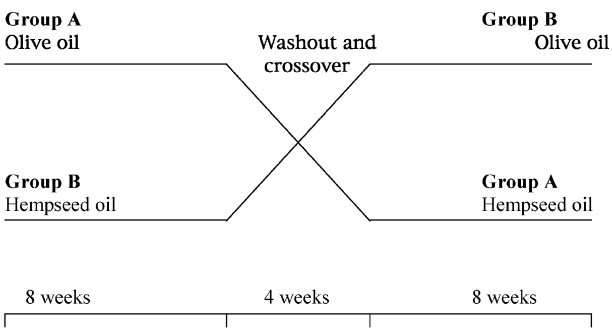

Figure 1. The crossover study design for comparing the study oils in atopic patients, who visited the clinic at 4-week intervals for a total of six visits.

dermatologist (IH) examined and cared for all patients throughout the study. All participants gave their prior written informed consent, and the study protocol was approved by the Ethics Committee of Kuopio University Hospital.

To monitor the diet, all patients kept a 7-day food record (consecutive days) during the third week of each intervention period, and a 4-day food record (consecutive days; 3 weekdays plus one weekend day) during the third week of the washout period. Data from the food records were compiled using the Micro-Nutrica® dietary analysis software version 2.5 (42).

Patients

Inclusion criteria were a body mass index (BMI) <30 kg/m^2, age between 25 and 60 years and a diagnosis of atopic dermatitis, as previously described (43). Patients who were concurrently taking lipid-lowering medications were excluded from the study, and none of the patients were taking antihypertensive medications. The patients were instructed to continue any other medication as needed, such as common skin creams or the occasional use of anti-inflammatory agents, and to maintain their normal level of physical activity during the study period. Patients were also instructed to avoid nutrient supplements, steroids (e.g. in skin creams), oral cyclosporine, asthma medications or solariums during the study or 1 month prior.

Intervention oils

Hempseed oil for this study was cold-pressed from hempseed that was cultivated in Finland during 2001. Olive oil was cold-pressed extra virgin, and obtained from a commercial source in Southern Europe. Both oils were bottled without any additives, in unlabelled 200-ml brown glass and stored at +5°C until use. The peroxide value was below 5 mmeqv/L and the level of free fatty acids was below 1% for both oils at the time of use. Fatty acid profiles and other important properties are presented in Table I for each of the intervention oils.

Patient questionnaire and measurements of transepidermal water loss (TEWL)

All patients responded to a simple questionnaire to determine their perception of changes in skin dryness and itchiness throughout the study period, using a rating scale from 0 (no dryness or itching) to 5 (severe dryness or itching, sleep disturbance). Use of any dermal medication was also rated on a similar scale: 0 (no medication) and 5 (regular usage). The permeability barrier function of skin was determined by measuring transepidermal water loss (TEWL) with a VapoMeter SWL-3 (Delfin Technologies Ltd, Kuopio, Finland), as previously described (44).

Plasma fatty acid analyses

All blood samples were drawn after an overnight fast (12 h). Plasma lipid fractions were isolated and their fatty acid methyl esters (FAMEs) were analysed by capillary gas chromatography (Hewlett-Packard 5890 series II, Hewlett-Packard Company, Waldbronn, Germany) using an FFAP-column (length 25 m, inner diameter 0.2 mm and film thickness 0.33 μm, Hewlett-Packard), with flame ionization detection with helium as the carrier gas, as previously described (45). Heptanoic acid (17:0) was used as an internal standard and individual fatty acid concentrations were calculated as molar percentages of the FAME profile by an eight-point external calibration curve for each FAME, using a 37 component FAME standard (Supelco). Verification of each FAME signal was made by gas chromatography with mass spectrometric detection (Agilent Technologies 6890N Network GC System + 5973 Network Mass Selective Detector).

Statistical analyses

Data were analysed by the SPSS software package for Windows, Release 10.0 (Chicago, IL, USA). Before further analyses, the normal distribution of variables was checked by the Shapiro-Wilk's test. Variables with non-symmetrical distributions were log-transformed and these values were used in further analyses. Repeated measures analysis of variance (ANOVA) was used to test changes within time and possible interactions between time and the intervention period. In cases where the result of an analysis was significant, a paired t-test was used for two-tailed comparisons to identify significant interactions between time and intervention period. Bonferroni corrections were made for all plasma fatty acid results. Wilcoxon matched pairs signed ranks tests were used to analyse patients' reported usage of dermal medication and their perceptions of both skin dryness and itchiness. All data are expressed as the mean $\pm$ standard deviation (SD). A p value <0.05 was considered to be statistically significant.

Results

A total of 20 patients were recruited for this study, but only 16 (1 male, 15 females) completed the entire course. Three patients dropped out within the first week for personal reasons, and another dropped out during week 13, due to the taste of the hempseed oil. No patients experienced any negative side effects or adverse reactions to either oil during the course of this study. Baseline characteristics (mean $\pm$ SD)

Table II. Average dietary intake throughout the study (mean ± standard deviation, $n=16$).

	Hempseed oil	Olive oil	Wash out
Energy (MJ)	7.8 ± 1.4	7.7 ± 1.5	6.9 ± 1.4
Fat (E%)	37.4 ± 7.1	36.3 ± 3.5	30.5 ± 5.3
Saturated	9.6 ± 2.1	10.2 ± 2.1	10.2 ± 2.5
MUFA	9.7 ± 3.8	17.1 ± 1.6	10.5 ± 3.3
PUFAs	15.1 ± 3.2	6.4 ± 2.3	6.1 ± 2.3
18:2n6	10.7 ± 2.6	5.0 ± 1.8	4.7 ± 2.2
18:3n3	3.3 ± 0.6	1.0 ± 0.5	0.9 ± 0.2
Carbohydrates (E%)	45.1 ± 7.5	46.6 ± 4.6	50.8 ± 6.7
Protein (E%)	15.6 ± 3.2	15.6 ± 3.0	17.6 ± 3.6
Alcohol (E%)	2.0 ± 3.5	1.4 ± 2.3	1.1 ± 1.9
Fibre (grams)	21.0 ± 6.2	21.6 ± 5.4	23.5 ± 8.7
(g/MJ)	2.7 ± 0.7	2.9 ± 0.9	3.4 ± 1.3
Cholesterol (mg)	178 ± 67	163 ± 43	162.0 ± 50
(mg/MJ)	22 ± 8	22.0 ± 8	24.4 ± 10

*E%=percent of energy; MUFA=monounsaturated fatty acids; PUFAs=polyunsaturated fatty acids; 18:2n6=linoleic acid; 18:3n3=alpha-linolenic acid.

included age, 38.1 ± 8.5 years; weight, 67.7 ± 13.2 kg; and BMI, 24.9 ± 4.5 kg/m^2.

There were no significant differences in body weight during this study (data not shown), and relatively less 'fat' and energy were ingested during the washout, compared with the intervention periods (Table II). Otherwise, no other remarkable changes were seen in estimated intake of energy, carbohydrates, protein, fibre or cholesterol for either oil. Consumption of oleic acid (as MUFA in Table II) during olive oil intervention was nearly equivalent to the levels of PUFAs (i.e. the two EFAs plus GLA and SDA) ingested during the hempseed oil intervention (Table II).

Statistically significant modifications in plasma fatty acid profiles were observed in all lipid fractions after hempseed oil intervention (Tables III–V). In particular, levels of GLA increased after hempseed oil intervention ($p<0.05$, inter-group comparisons),

Table III. Fatty acid profiles of plasma triglyceride esters at the beginning (0 wk) and end (8 wk) of the oil intervention periods, expressed as mole per cent ($n=16$, mean ± standard deviation); paired t-test, ns=non-significant ($p>0.05$).

	Hempseed oil		Olive oil		
Fatty acid	0 wk	8 wk	0 wk	8 wk	p[a]
Myristic (14:0)	2.71 ± 0.99	2.14 ± 0.66	2.72 ± 1.22	3.06 ± 1.27	0.052
Palmitic (16:0)	24.40 ± 4.72	20.46 ± 3.94 [f,c]	25.19 ± 7.79	25.63 ± 6.04	0.037
Palmitoleic (16:1n-7)	4.26 ± 1.53	3.20 ± 0.97[b]	4.33 ± 1.33	3.71 ± 1.12	ns
Stearic (18:0)	3.16 ± 0.43	2.94 ± 0.47	3.26 ± 0.88	3.40 ± 0.58	ns
Oleic (18:1n9)	33.75 ± 3.02	29.84 ± 4.76[b]	35.12 ± 3.87	35.56 ± 9.53	ns
Linoleic (18:2n6)	23.69 ± 7.48	31.24 ± 7.43[f,g]	22.11 ± 7.46	21.19 ± 5.78	0.000
GLA (18:3n6)	0.43 ± 0.26	0.93 ± 0.46[d,g]	0.40 ± 0.27	0.46 ± 0.25	0.000
alpha-Linolenic (18:3n3)	1.87 ± 0.54	3.95 ± 1.16[f,g]	1.96 ± 0.84	1.84 ± 0.48	0.000
Dihomo-GLA (20:3n6)	1.76 ± 2.96	1.47 ± 2.18	1.18 ± 1.31	1.82 ± 2.53	ns
Arachidonic (20:4n6)	2.38 ± 0.95	2.63 ± 1.10	2.35 ± 0.85	2.14 ± 0.85	ns
Docosahexaenoic (22:6n3)	1.60 ± 1.18	1.20 ± 0.69	1.39 ± 0.69	1.19 ± 0.77	ns

[a]ANOVA probability of interaction between time and intervention period, [b]within a period (intra-group comparison) $p<0.05$, [c]between period ends (inter-group comparison) $p<0.05$, [d]within a period (intra-group comparison) $p<0.01$, [f]within a period (intra-group comparison) $p<0.001$, [g]between period ends (inter-group comparison) $p\leqslant 0.001$.

Table IV. Fatty acid profiles of plasma 1-cholesteryl esters at the beginning (0 wk) and end (8 wk) of the oil intervention periods, expressed as mole per cent ($n=16$, mean ± standard deviation); paired t-test, ns=non-significant ($p>0.05$).

	Hempseed oil		Olive oil		
Fatty acid	0 wk	8 wk	0 wk	8 wk	p[a]
Myristic (14:0)	1.31 ± 0.58	1.42 ± 1.14	1.17 ± 0.30	1.11 ± 0.36	ns
Palmitic (16:0)	12.15 ± 0.23	13.61 ± 6.42	11.60 ± 1.48	10.90 ± 1.78	ns
Palmitoleic (16:1n-7)	3.27 ± 1.60	2.34 ± 0.89[b]	3.21 ± 1.40	2.90 ± 1.35	0.041
Stearic (18:0)	1.57 ± 0.57	2.05 ± 1.95	1.60 ± 0.57	1.43 ± 0.60	ns
Oleic (18:1n9)	17.05 ± 2.34	13.66 ± 2.33[f,g]	17.16 ± 1.92	18.75 ± 2.60[b]	0.000
Linoleic (18:2n6)	54.90 ± 7.21	56.48 ± 11.89	54.30 ± 6.16	55.08 ± 6.69	ns
GLA (18:3n6)	0.67 ± 0.26	0.94 ± 0.32[c]	0.58 ± 0.26	0.61 ± 0.19	0.041
alpha-Linolenic (18:3n3)	0.87 ± 0.16	1.47 ± 1.05	0.85 ± 0.18	0.88 ± 0.16	0.060
Dihomo-GLA (20:3n6)	3.44 ± 5.13	3.19 ± 4.21	3.95 ± 4.32	3.27 ± 5.29	ns
Arachidonic (20:4n6)	4.41 ± 1.20	4.46 ± 1.39	5.18 ± 2.74	4.23 ± 1.24	ns
Docosahexaenoic (22:6n3)	0.35 ± 0.34	0.39 ± 0.47	0.38 ± 0.38	0.41 ± 0.37	ns

[a]ANOVA probability of interaction between time and intervention period, [b]within a period (intra-group comparison) $p<0.05$, [c]between period ends (inter-group comparison) $p<0.05$, [f]within a period (intra-group comparison) $p<0.001$, [g]between period ends (intra-group comparison) $p<0.001$.

Table V. Fatty acid profiles of plasma phospholipid esters at the beginning (0 wk) and end (8 wk) of the oil intervention periods, expressed as mole per cent ($n=16$, mean ± standard deviation); paired t-test, ns=non-significant ($p>0.05$).

	Hempseed oil		Olive oil		
	0 wk	8 wk	0 wk	8 wk	p[a]
Myristic (14:0)	1.34±0.37	1.26±0.22	1.33±0.28	1.38±0.40	ns
Palmitic (16:0)	31.48±4.53	28.92±1.90	31.10±3.23	32.67±8.99	ns
Palmitoleic (16:1n-7)	0.86±0.40	0.64±0.20	0.86±0.33	0.73±0.33	ns
Stearic (18:0)	13.96±5.97	14.56±5.41	13.46±3.33	13.24±3.45	ns
Oleic (18:1n9)	9.92±1.48	8.32±1.40[f,c]	10.21±1.07	11.15±1.71	0.000
Linoleic (18:2n6)	24.32±5.53	27.12±4.17	24.57±4.29	23.59±6.49	0.055
GLA (18:3n6)	0.04±0.06	0.15±0.10[f,e]	0.06±0.09	0.06±0.08	0.000
alpha-Linolenic (18:3n3)	0.43±0.09	0.61±0.13[f,c]	0.43±0.09	0.42±0.12	0.003
Arachidic (20:0)	0.45±0.20	0.51±0.07	0.49±0.11	0.43±0.13	ns
Eicosenoic (20:1n9)	0.42±0.12	0.28±0.09	0.29±0.11	0.27±0.14	ns
Dihomo-GLA (20:3n6)	2.69±1.29	3.80±1.58	3.08±1.51	3.29±1.42	ns
Arachidonic (20:4n6)	6.55±1.51	6.77±1.78	6.77±1.37	6.08±2.10	ns
Eicosapentaenoic (20:5n3)	1.17±0.78	0.99±0.41	1.12±0.82	1.13±0.68	ns
Docosahexaenoic (22:6n3)	4.50±1.27	3.93±0.80	4.49±1.18	4.02±1.50	ns
Behemic (22:0)	0.87±0.17	0.96±0.20	0.92±0.16	0.81±0.28	0.039
Lignoceric (24:0)	1.18±1.43	1.16±1.18	0.83±0.13	0.72±0.24	ns

[a]ANOVA probability of interaction between time and intervention period, [c]between period ends (inter-group comparison) $p<0.05$, [e]between period ends (inter-group comparison) $p<0.01$, [f]within a period (intra-group comparison) $p<0.001$.

Table VI. Patient ratings ($n=16$, mean ± standard deviation) of atopic symptoms (0=no dryness or itching, 5=severe dryness itching, sleep disturbance) and use of dermal medication (0=none, 5=regular usage); Wilcoxon non-parametric t-test.

	Hempseed oil			Olive oil			
	Week 0	Week 8	p*	Week 0	Week 8	p*	p**
Skin dryness	3.19±1.17	2.25±1.18	0.027	3.44±0.81	3.06±1.29	0.380	0.064
Skin itchiness	2.56±1.50	1.56±1.21	0.023	2.44±1.26	2.38±1.59	0.995	0.087
Use of medication	2.69±1.14	1.69±1.08	0.024	2.75±1.00	2.56±1.31	0.734	0.118

Within period changes (p*) are intra-group comparisons of the beginning (week 0) and end (week 8) values for each intervention period. Between period changes (p**) are inter-group comparisons of the end values for each intervention period.

Table VII. Transepidermal water loss (TEWL) values (g/m^{2}h; mean ± standard deviation, $n=16$) for each intervention period; Wilcoxon non-parametric t-test.

Intervention oil	Week 0	Week 8	p*
Hempseed oil	12.2±5.3	9.6±3.7	0.074
Olive oil	12.8±6.3	11.8±7.5	0.813

*Within period changes are intra-group, comparing the beginning and end values of each intervention period. The inter-group comparison at week 8 was not statistically significant ($p=0.274$).

while plasma levels of arachidonic acid (20:4n6) did not change significantly after either oil.

Results from the patient questionnaire are presented in Table VI, and values of TEWL are presented in Table VII. Subjective decreases in both skin dryness and itchiness (Table VI) were statistically significant after hempseed oil intervention ($p=0.027$ and 0.023, respectively, as intra-group comparisons), which were reflected as a trend towards decreased TEWL values ($p=0.074$, intra-group comparison) after hempseed oil intervention (Table VII), while no such improvements were observed after olive oil intervention. A decrease in the usage of dermal medication was also observed after hempseed oil intervention ($p=0.024$, intra-group comparison), with no such improvement after olive oil intervention (Table VI). An inter-group comparison of the TEWL values in Table VII, comparing the end values for both oils, was not statistically significant ($p=0.274$).

Discussion

The two intervention oils differed significantly in their respective fatty acid profiles (Table I). While hempseed oil is over 80% PUFAs, and includes both GLA and SDA, olive oil is a fairly poor source of PUFAs and is totally lacking in either GLA or SDA. The intervention oils also differed in both appearance and taste; the hempseed oil was dark green and nutty in flavour while the olive oil was light green and tasted of olives. The difference in colour was due to more or less chlorophyll, respectively. Other natural components, such as tocopherols, also vary in high quality, cold-pressed oils. Not only do

antioxidants protect dietary oils from oxidation *in situ* but also lipid peroxidation *in vivo* (46,47).

The food oil peroxide value is another important parameter that is typically overlooked, or simply assumed to be low, in studies of unsaturated dietary oils. PUFAs, in particular, will oxidize over time to eventually form varnish. As these peroxides are not known to have any therapeutic value, it is important to demonstrate that intervention oils have low peroxide values, as in the present study (<5 mmeqv/L).

Light can also affect symptoms of atopic dermatitis (37). In the present study, patients avoided the use of solariums throughout the study period, which ran from early January until the end of May. In Finland, ambient outdoor temperatures are too low during this period of time for significant amounts of solar exposure to affected atopic areas of the body. Moreover, the rigorous crossover design employed in this study was intended to compensate for any such changes over time.

Changes in plasma fatty acid profiles were especially significant after hempseed oil in all lipid fractions, particularly for linoleic acid, alpha-linolenic acid and GLA (Tables III–V). Variability in plasma fatty acid values was due to individual heterogeneity in the sample sets, and not the quantitative method. Thus, it is possible that more than one type of atopic patient was included in the present study (48). Dietary GLA (0.48–1.5 g/day) from both borage seed oil and blackcurrant seed oil has been shown to significantly increase levels of its immediate biological metabolite, dihomo-gamma-linolenic acid (DGLA) in healthy humans (49), as measured in polymorphonuclear neutrophils (PMN), where a corresponding decrease in pro-inflammatory leukotriene B4 (LTB_4) was also noted. It has been suggested that dietary GLA is rapidly metabolized in skin to DGLA, which suppresses the ability of PMNs to produce LTB_4(50). The daily amount of GLA in hempseed oil was about 1.2 g/day in the present study, but a slight increase of DGLA in plasma phospholipids (Table V) did not reach statistical significance after hempseed oil intervention. If eicosanoids are involved in atopic dermatitis, perhaps through the production of pro-inflammatory prostaglandins (4,50), then a dietary increase in GLA would provide the requisite substrate in the production of DGLA.

SDA was detected in all plasma samples, but it was below the limit of quantitation and its signal did not always exhibit baseline resolution in all samples. This rare, omega-3 fatty acid is certainly better than alpha-linolenic acid for the *in vivo* production of eicosapentaenoic acid (EPA). A recent study found that 0.75–1.50 g of dietary SDA increased levels of EPA in both erythrocytes and plasma phospholipids (51), but a significant increase in phospholipids for EPA was not seen in the present study, where the daily amount of SDA was about 0.60 g/day. Unfortunately, the present study did not examine fatty acid profiles in erythrocyte membranes.

Decreased levels of ceramides in the stratum corneum may be another important aetiological factor in atopic dermatitis (32). Ceramides may have an important role in skin barrier function, and linoleic acid is metabolically esterified to ceramide 1, while oleic acid is not. Such a metabolite could function as a molecular rivet in the stabilization of lipid lamellar sheets, thus reducing the loss of moisture through skin (31), especially in the elderly (39).

Despite the high levels of oleic acid in olive oil, it is surprising to see how little impact the consumption of this oil actually had on plasma lipid profiles of this fatty acid (Tables III–V). Oleic acid is not essential for health and is clearly not taken up as aggressively into plasma lipids as PUFAs. Overall changes in fatty cholesteryl esters were less robust than those for triglycerides or phospholipids for both oils (Table IV, in relation to Tables III and V, respectively). However, if symptoms of atopic dermatitis were more closely related to membrane function, rather than eicosanoid production, then such a significant increase of PUFAs in phospholipid bilayers (Table V) could effectively increase membrane fluidity and function (3,52).

Patients in the present study reported statistically significant decreases in skin dryness, itchiness and use of dermal medication after hempseed oil intervention (Table VI). A functional skin barrier is essential to maintain skin moisture (53,54). Decreased TEWL values (Table VII) are a good indication that less water was being lost through the skin after hempseed oil, which supports the subjective results from the patient questionnaire in Table VI. Although this trend ($p=0.074$, intra-group comparison) was not statistically significant, it is worth noting in light of the subjective evaluation from the patients, especially in regard to skin dryness. This is important because skin dryness and subsequent itchiness often lead to the use of medication in atopic patients, especially during the dry winter conditions in Finland, where ambient indoor humidity can be <30% moisture for months on end.

It was mentioned in the Introduction that individuals who have used hempseed oil for longer periods of time report increased strength in finger nails (months) and thicker hair (years), in addition to the improvements in skin conditions within weeks. The times required for these varied effects roughly correspond to the amounts of time required for the newly formed cells of each tissue to become physically apparent. These three cell lines are constructed by dermal stem cells from fatty acids that are available in the diet at the time of their formation. Here is yet another interesting facet to consider in the complexity of tissue formation, which

is dependent on dietary fatty acids; i.e. optimal construction of skin, hair and nails at the dermal stem cell level.

The apparent efficacy of dietary hempseed oil in this study could be due to the exceptionally high level of PUFAs in this oil (>80%), which had a metabolically favourable n-6/n-3 ratio of approximately 2:1. These fatty acids are already known to play vital roles in immune response (55). The fatty acid profile of this hempseed oil is remarkably similar to that of blackcurrant seed oil, which has been reported to have a beneficial impact on immunologic vigour (10,22). The presence of both GLA and SDA in hempseed oil (the metabolic products of EFAs linoleic acid and alpha-linolenic acid, respectively) allows the rate-limiting enzymatic step with delta-6-desaturase to be bypassed [e.g. 16], which could be the biochemical mechanism that was responsible for the improvement of atopic symptoms observed in the present study after hempseed oil.

Skin dryness and itchiness, in particular, are very serious problems in atopic dermatitis, which often lead to additional complications, such as opportunistic infections. In any event, it seems that the reduction of atopic symptomology observed in this study is a direct result of ingested hempseed oil. These preliminary results confirm anecdotal observations of improved skin quality after ingesting modest amounts of hempseed oil on a daily basis over a relatively short period of time. From these observations, further study is warranted to determine the value of regular use of dietary hempseed in the treatment of atopic dermatitis.

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