

**Topics:** Evening primrose oil (EPO), omega-6 fatty acids, gamma-linolenic acid (GLA), atopic eczema, atopic dermatitis (AD), skin, delta-6-desaturase (D-6-D)

**Objective:** To determine the effect of GLA supplementation on skin barrier function in subjects with dry skin and mild atopic eczema.

**Background:** Synthesis of the long chain omega-6 fatty acids involves alternating steps of desaturation and elongation with serial conversion of linoleic acid (LA) to GLA, dihommo-gammalinolenic acid (DGLA) and arachidonic acid (AA). Over twenty years ago, scientists at the Efamol Research Institute found that blood levels of LA were higher and all its metabolites were lower than normal in people with atopic eczema; a condition where skin barrier function is compromised resulting in increased trans-epidermal water loss (TEWL) and epidermal hyper-proliferation. They proposed there was a defect in fatty acid metabolism that contributed to the development of atopic eczema. However, the exact mechanisms whereby deficiencies of GLA, DGLA and AA contributed to the condition was unclear.

**Method:** This randomised, double-blind, placebo controlled trial included 130 males and females with dry skin and mild to moderate atopic eczema (dermatitis) as diagnosed according to the Japanese Dermatological Association 2009 Guidelines for Management of Atopic Eczema criteria. Subjects consumed either a test food (cream sandwich wafer) providing **200 mg of GLA** daily (roughly the same amount of GLA in 4 Efamol Evening Primrose Oil capsules per day) or a placebo wafer containing a mixture of rapeseed and soybean with no GLA for 12 weeks. Four week observation periods preceded and followed the study. Throughout the study, patients recorded their food consumption, daily physical condition including nocturnal and diurnal itching and any special activities (i.e. intense exercise or sunburn).

**Exclusion Criteria:** AD patients taking steroids, using a specific health food regularly other than the test diet, showing an allergic reaction to the test diet, being continuously treated by a physician, having severe renal dysfunction, severe liver dysfunction, severe anemia, endocrine disorders, planning pregnancy and nursing during the study period, planning to undergo anesthesia during the study period, or having a concern about developing pollinosis.

The following assessments were taken before treatment and following 4, 8, 12 and 16 weeks of treatment.

1. **Skin hydration** by corneometry
2. **TEWL** of the cheek and forearm using a TEWA-Meter TM 300
3. **Skin condition** (desquamation and crusting) diagnosed by a dermatologist
4. **Itch** evaluated by intensity, range and frequency using a visual analogue scale (VAS)
5. **Plasma fatty acids** including GLA, DGLA and AA
6. **Hematological tests** including white blood cell count, red blood cell count, hemoglobin, hematocrit, and platelets.
7. **Biochemical tests** including aspartate transaminase (AST, GOT. Glutamic oxalic transaminase), alanine transaminase (ALT, GPT, glutamic-pyruvate transaminase), lactate dehydrogenase, alkaline phosphatase, gamma-glutamyltransferase, total bilirubin, albumin, total protein, blood urea nitrogen, creatinine, uric acid, total cholesterol, high density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, glucose, glycosylated hemoglobin, sodium, potassium, and chloride.
8. **Urinalysis** for specific gravity, pH, sugar, occult blood, protein, urobilinogen and ketone bodies.

TEWL, hydration and VAS of itch was compared before and after treatment using unpaired or paired t-test. Physician assessed skin condition and itch intensity and frequency was compared before and after treatment using Mann-Whitney U test and Wilcoxon signed-ranks test.

Patient's fatty acid composition was used to divide the population into two main groups as follows and the tests before and after treatment were repeated.

- A) **Pro-inflammatory Group** having GLA < 0.3 %, DGLA  $\leq$  1.2%, AA > 6.2%
- B) **Anti-inflammatory Group** having GLA  $\leq$  0.3%, DGLA > 1.2%, AA  $\leq$  6.2%

**Findings:**

1. TEWL of the cheek and forearm was lower in the GLA and the placebo group at week 4 (P=0.070 and P= 0.077, respectively).
2. In subjects whose plasma DGLA was 1.2% or less, the change in cheek TEWL of the GLA group was significantly lower than the placebo group at week 8 (p=0.08). The change in the forearm TEWL of the GLA group was also lower than that in the placebo group at week 8 in the group of subjects stratified by plasma AA over 6.2% (P=0.068). These statistically significant differences attributable to the test diet were only seen between pro-inflammatory groups and were absent in the anti-inflammatory groups, indicating that the efficacy of GLA is stronger in subjects with high levels of pro-inflammatory substances.
3. The VAS of nocturnal itching in the GLA group was significantly improved at week 8. The scores of pruritus intensity and frequency of nocturnal itching were also reduced at weeks 4 and 8 in the GLA group. However, no such statistically significant changes were seen in the placebo group during this same time period.
4. There were no clinically significant changes in results of any of the haematological, biochemical or urine tests following treatment. There were no adverse events attributable to the GLA treatment.
5. GLA supplementation did not increase plasma AA concentration.

**Conclusion:**

GLA supplementation safely improves skin properties within 4 weeks including TEWL that protects skin barrier function and itch, the most debilitating symptom. Subjects with high levels of pro-inflammatory eicosanoid precursors and/or low levels of anti-inflammatory eicosanoid precursors appear to be more responsive to the beneficial effects of GLA supplementation. Therefore, GLA appears to improve the atopic skin condition at least partly through its anti-inflammatory effects.

**Relevance to:**

Efamol Evening Primrose Oil

**Reference:**

Kawamura A, Ooyama K, Kojima K, Kachi H, Abe T et al. Dietary supplementation of gamma-linolenic acid improves skin parameters in subjects with dry skin and mild atopic dermatitis. J Oleo Sci 2011;60 (12):597-607.

**PRESS RELEASE****GLA Proven Once Again to Improve Skin <sup>1</sup>.**

A new independent study published in the Journal of Oleo Science has duplicated results reported previously in a meta-analysis of randomized, double-blind, placebo-controlled trials which demonstrated that Efamol evening primrose oil improved skin condition and significantly reduced itch in people with atopic eczema. Atopic eczema is a skin condition affecting up to 30% of children in Westernized countries<sup>2</sup> and is a non-infectious, chronically relapsing inflammatory condition causing scaliness, dryness, redness, cracks, sores and severe itching, which from the patient's perspective is the most troublesome symptom. It starts in infancy or early childhood, continues throughout life and runs in families. An associated abnormality in fatty acid metabolism was first proposed in the early 1930s and a study at the Efamol Research Institute in the early 1980s confirmed that people with atopic eczema had lower than normal blood levels of linoleic acid (LA) metabolites including GLA and other fatty acids derived from it including dihommogamma-linolenic acid (DGLA) and arachidonic acid (AA)<sup>3,4</sup>.

The newly published independent study included 130 males and females with dry skin and mild to moderate atopic eczema who ate either a test food (cream sandwich wafer) providing **200 mg of gamma-linolenic acid (GLA)** daily (roughly the same amount of GLA in 4 Efamol Evening Primrose Oil capsules per day) or a placebo wafer containing a mixture of rapeseed and soybean with no GLA for 12 weeks. Throughout the study, patients recorded their food consumption, daily physical condition including day and night-time itching and any special activities including intense exercise or sunburn. A number of assessments were completed before treatment and following 4, 8, 12 and 16 weeks of treatment including skin hydration, skin barrier function as determined by trans epidermal water loss (TEWL) on the cheek and forearm, skin condition as assessed by a dermatologist, itch intensity, range and frequency, and a number of safety related tests including various hematological tests, numerous biochemical tests and urinalysis. Plasma fatty acids were also determined and subjects were identified as either being prone to inflammation or not according to their plasma concentration of GLA, DGLA and AA.

Following 4 weeks of supplementation, there was an improvement in TEWL and itch in the GLA group without any negative impact on safety parameters. In addition, the patients with the highest likelihood of inflammation were significantly more responsive to the treatment as assessed by TEWL in both cheek and forearm skin than the patients with lower risk of inflammation. These results confirmed that GLA safely improves atopic skin at least partly through its anti-inflammatory effects and it is particularly effective to enhance skin barrier function and relieve itch.

In 2008, a group of researchers in Taipei looked at the relationship between omega-6 fatty acid deficiency, TEWL and immune response in children with atopic disorders<sup>5</sup>. The study included 35 children with atopic eczema, 35 age matched children with allergic rhinitis, asthma or both and 31 nonatopic controls. Results showed that atopic children had higher levels of LA and lower levels of its metabolites including GLA, DGLA and AA. Furthermore, it showed that the more deficient they were in GLA, DGLA and AA, the more severe was their atopic dermatitis and the greater was the loss of water through their skin. Those with the highest LA had the worst TEWL and atopic eczema.

Dietary GLA supplementation can partially correct the deficiency of GLA, DGLA and AA in people with atopic eczema<sup>3</sup>. A study in India reported a 96% response rate using evening primrose oil (EPO) as a source of GLA to treat atopic eczema in an East Indian population<sup>6</sup>. Results of this study also agree with those of two meta-analyses using Efamol EPO as the active reported in 1989 and 2007. The 1989 investigation including 10 clinical studies showed that EPO was particularly effective for relieving itch and those patients who had the greatest increase in their blood levels of GLA, DGLA and AA also had the greatest improvement in their skin condition<sup>7</sup>. The 2007 meta-analysis including 26 studies with more than 1200 patients confirmed that Efamol EPO is a safe and effective remedy for symptomatic relief of atopic eczema with simultaneous benefits on itch, crusting, oedema and redness that become apparent between 4 and 8 weeks after treatment is initiated<sup>8</sup>.

Results of this latest independent study reflect those of the previously mentioned studies which further substantiates the use of GLA supplementation for skin health. This study also helps to explain how GLA improves skin condition in people with atopic eczema.

## References:

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