Clinical Studies on Evening Primrose (*Oenothera biennis* L.)

Breast Pain and PMS Symptoms

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Cheung, 1999	Cyclical mastalgia	P n=32 women with disturbing cyclical mastalgia, median duration of pain 12 months, interfering with lifestyle (mean age 37 years)	3 months if symptoms improved; if symptoms did not completely resolve, additional 3 months (6 months total)	Six, 500 mg capsules/day (240 mg GLA/day)	Efamast® capsules (500 mg EPO providing 40 mg GLA per capsule)	An overall, clinically useful response rate of 97% was observed at 6 months. One-third and one-half of women were pain-free at end of 3 and 6 months, respectively. Side effects greater than expected (12%) though mild and did not interfere with treatment. Authors conclude that EPO should be recommended as first-line specific treatment for women with disturbing cyclical mastalgia.
Gateley *et al.*, 1992b	Cyclical mastalgia	P n=85 women with cyclical mastalgia	17 years (4-month treatment periods)	Two, 500 mg capsules 6x/day (240 mg GLA/day)	Efamast® capsules (500 mg EPO providing 40 mg GLA per capsule)	A clinically useful response was obtained in 51 of 85 patients (54%) at 4 months. An additional 12 of 29 patients (41%) who failed to obtain a useful response from other therapies obtained a useful response from EPO as a second line treatment. EPO was less effective than danazol but showed equivalent efficacy to bromocriptine.
Wetzig, 1994	Cyclical and non-cyclical mastalgia with significant breast pain for more than 3 years	Cm n=170 (EPO group n=39) Australian women with cyclical or non-cyclical mastalgia (mean age 42 years)	3 years	Two, 500 mg capsules 2–3x/day	EPO 500 mg capsules, (brand not stated) or Vitamin B6 50–100mg 2x/day or Danazol 100 mg 2x/day tapering to 100 mg daily after pain control (tamoxifen dose not specified if resistant to danzol and progesterones)	10 out of 39 (26%) had complete pain relief. 70% of women who did not respond to treatment had cyclical pain. Response rates of vitamin B6 and EPO were no better than placebo effect. 67% of women taking danazol had complete response.
Khoo *et al.*, 1990	PMS symptoms	DB, PC, R, CO n=38 women with PMS	6 months (crossover after 3 cycles)	Four, 500 mg capsules 2x/day (360 mg GLA/day)	Efamol® capsules (500 mg EPO providing 45 mg GLA) vs. placebo (500 mg liquid paraffin)	Substantial improvement in PMS symptoms for EPO and placebo suggesting a strong placebo effect. No significant differences in scoring of 10 PMS symptoms or menstrual symptoms between EPO and placebo. Authors conclude the improvement experienced by women with moderate PMS was solely placebo effect.
Ockerman *et al.*, 1986	PMS symptoms	DB, PC n=36 women with severe PMS	3 months	One, 500 mg capsule	Efamol® capsules (500 mg EPO providing 45 mg GLA)	Statistically significant difference ($p<0.01$) between EPO group and placebo for moderate to complete relief of symptoms.

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Clinical Studies on Evening Primrose (*Oenothera biennis* L.) (cont.)

Dermatological

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Gehring *et al.*, 1999	Atopic dermatitis	DB, VC, PC, R n=40	5 weeks (4-week treatment followed by 1 week no treatment)	Topical application to entire flexor side of forearm 2x/day	Amphiphilic oil-in-water emulsion containing 20% EPO vs. placebo (20% miglyol) and water-in-oil emulsion with 20% EPO vs. placebo (20% liquid paraffin)	Statistically significant stabilizing effect on barrier function was observed with EPO in water-in-oil emulsion ($p<0.05$) treatment vs. placebo, documented as a reduction in transepidermal water loss (TEWL). Peak effect not apparent until 5 weeks, including 1-week treatment-free period. Only water-in-oil emulsion proved to be an effective vehicle for EPO, demonstrating that choice in vehicle is an extremely important factor in the efficacy of topically applied EPO.
Yoshimoto-Furuie *et al.*, 1999	Uremic skin symptoms (pruritus, erythema, dryness)	DB, PC, R n=16 male and female patients undergoing hemodialysis (ages 23–79 years)	6 weeks plus 6-week observation	Two, 500 mg capsules 2x/day (180 mg GLA/day)	Efamol® capsules (500 mg EPO providing 360 mg linoleic acid, 50 mg oleic acid, 45 mg GLA) vs. placebo (500 mg linoleic acid)	EPO group had statistically significant overall improvement vs. linoleic acid group ($p<0.05$). EPO group had significant increase in mean lipid plasma concentration of DGLA at weeks 6 and 12 compared to baseline ($p<0.01$). EPO group also had significant increases in plasma GLA levels in cholesterol ester ($p<0.01$) and triglyceride ($p<0.05$) fractions at 6 and 12 weeks.
Whitaker *et al.*, 1996	Chronic hand dermatitis (>1 year duration)	DB, PC, R n=39	8 weeks each, with an 8-week follow-up period	Twelve, 500mg capsules/day for 16 weeks (600 mg GLA/day)	Epogam® capsules (500 mg EPO providing 50 mg GLA) vs. placebo (500 mg sunflower oil)	No statistical difference between orally ingested EPO and placebo groups for any parameters tested. Therapeutic value of EPO for chronic hand dermatitis was not superior to placebo.
Hederos and Berg, 1996	Children (ages 1–16 years) with atopic dermatitis who needed regular treatment with topical steroids (22 patients had asthma)	DB, PC, PG, R n=58	16 weeks	Four or six, 500 mg capsules 2x/day according to age (320–480 mg GLA/day)	Epogam® capsules (500 mg EPO providing 40 mg GLA w/10 mg vit. E) vs. placebo (500 mg sunflower oil with vitamin E)	EPO group had significantly increased plasma concentrations of EFAs ($p<0.001$). Both groups showed significant improvement from baseline symptoms ($p<0.001$–$p<0.05$) without a significant difference between placebo and EPO.
Oliwiecki and Burton, 1994	Chronic stable-plaque psoriasis	DB, PC, PG n=37 (ages 16–70 years)	28 weeks (4 week placebo then treatment, or placebo for 24 weeks)	Six, 500 mg capsules 2x/day (480 mg GLA/day)	Efamol® Marine capsules (430 mg EPO and 107 mg fish oil, providing 40 mg GLA, 20 mg EPA, 11 mg DHA, and 10 mg vitamin E) vs. placebo (paraffin)	No significant difference between EPO and placebo groups in plaque thickness or transepidermal water loss. In the clinical assessment, no significant difference in LAS (linear analogue measurement) was seen in erythema or scaling and overall severity scores. Mean LAS score for overall severity was significantly higher in EPO group at week 8 ($p<0.05$). Authors conclude that EPO combined with fish oil produces no significant improvement in chronic stable plaque psoriasis.
Veale *et al.*, 1994	Dermatological; psoriatic arthritis (PsA)	DB, PC, R n=38	1 year (9-month treatment followed by 3 month placebo)	Twelve, 500mg capsules/day (480 mg GLA/day)	Efamol® Marine capsules (430 mg EPO and 107 mg fish oil, providing 40 mg GLA, 20 mg EPA, 11 mg DHA and 10 mg vitamin E) vs. placebo (paraffin and vitamin E)	EPO and fish oil combination appears to alter prostaglandin metabolism in patients with PsA though this study failed to prove that it could substitute for NSAID therapy. All measures of skin disease activity were unaffected by treatment and did not allow reduction in NSAID requirement. Authors conclude that the study did demonstrate metabolic effects on prostanoid and leukotriene metabolism, suggesting that larger doses might produce a clinical response.

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Dermatological (cont.)

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Berth-Jones and Graham-Brown, 1993	Atopic dermatitis	DB, PC, R, PG n=102 adults and children with 3 treatment limbs	16 weeks	Six, 500 mg capsules 2x/day (480 mg GLA/day) or six, 500 mg EPO & fish oil capsules 2x/day	Epogam® capsules (500 mg EPO, providing 321 mg LA, 40 mg GLA); Efamol® Marine capsules (430 mg EPO, 107 mg fish oil), vs. placebo (paraffin or olive oil)	No therapeutic effect was demonstrated for either EPO or EPO in combination with marine fish oil. No significant difference from placebo in mean improvement of any parameters used to monitor disease, severity including clinical severity scores (both Leicester score and Costa score systems used), percentage of skin affected, topical steroid requirement, and patient diaries.
Oliwiecki *et al*., 1993	Epidermal thinning	Cm, R n=24 healthy volunteers with 2 treatment limbs	3 weeks	Apply a thin layer of cream over an area of forearm 5 X 5 cm in diameter 2x/day	Scotia Cream A (0.1% betamethasone valerate), Cream B (0.1% betamethasone Valerate, 10% EPO), Cream C (10% arachis oil)	Concomitant administration of EPO and beta-methasone valerate did not prevent steroid-induced epidermal thinning, suggesting that steroid-induced epidermal thinning is not mediated by the inhibition of EFA release from cell membranes. EPO did not affect histological changes (e.g., absence of granular layer and flattening of rete ridges).
Schäfer and Kragballe, 1991	Atopic dermatitis	R (3 dose levels) n=15	10 weeks	4, 8, or 12 capsules/day (0.5g oil)	Quest Vitamins EPO capsules (500 mg EPO)	Supplementation at the highest dosage level, 6 g EPO/day, increased n-6 fatty acid level, especially DGLA by 15–60% in neutrophil and epidermal phospholipids ($p<0.05$). A beneficial shift in ratio between n-6 and monounsaturated fatty acids was also observed. Authors conclude that EPO at 6 g/day can effect moderate and favorable fatty acid changes in the epidermis of atopic dermatitis patients.

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Dove and Johnson, 1999	Pregnancy labor	R, PC, RS n=108	7 years, entering at different times (1991–98)	500 mg 3x/day for 1 week at week 37 of gestation, followed by 500 mg/day until labor	Brand not stated	No significant differences between EPO and placebo on age, Apgar score, days of gestation ($p>.05$). There was slight significant difference in birth weight ($p = .043$), with infants in EPO group averaging 156 g larger than those in control group. Women in EPO group had labor averaging 3 hours longer than for the placebo, and an increase in active-phase labor abnormalities including protracted active phase, prolonged rupture of membranes, increased oxytocin, and arrest of descent, some of which may be attributed to larger infant weight.
Jenkins *et al*., 1996	Liver damage due to chronic hepatitis B	PC, R n=20 patients with chronic hepatitis B	1 year	Four, 500 mg capsules 2x/day before meals	Efamol® capsules (500 mg EPO plus 10 mg vitamin E) vs. placebo (liquid paraffin)	EPO treatment showed no improvement over placebo in biochemical or histological indices of liver damage, or in rate of loss of circulating surface or e-antigen.
Chenoy *et al*., 1994	Menopausal hot flash (at least 3x daily)	DB, PC, R n=35 menopausal women (mean age EPO group 53.7 years; mean age placebo group 54.2 years)	6-month treatment periods	Four, 500 mg capsules 2x/day	Efamol® capsules (500 mg EPO with 10 mg natural vitamin E) vs. placebo (500 mg liquid paraffin)	The only significant improvement in EPO group was reduction in maximum number of nighttime flushes ($p<0.05$). Authors concluded that EPO provides no benefit over placebo in treatment of menopausal hot flashes.
Keen *et al*., 1993	Diabetic neuropathy	DB, PC, R, PG, MC n=111	1 year	500 mg capsule 12/day (480 mg GLA/day)	EF4- capsules (500 mg EPO providing 40 mg GLA)	EPO was significantly superior to placebo in relieving 13 of 16 parameters. Both neurological and conduction values improved significantly vs. placebo group. Researchers concluded that EPO may prevent deterioration and reverse the condition in patients with mild diabetic polyneuropathy.

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Other (cont.)

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Brzeski *et al.*, 1991	Rheumatoid arthritis and upper gastro-intestinal lesions due to non-steroidal anti-inflammatory drugs	DB, PC, P, R n=30 (mean age EPO group 60 years; mean age placebo group 61 years)	6 months	500 mg capsule 12/day (540 mg GLA/day)	Efamol® capsules (500 mg EPO plus 10 mg vitamin E) vs. placebo (olive oil)	EPO produced statistically significant reduction in morning stiffness but only small reduction in articular index. Only 23% (3/13) of EPO group could reduce NSAID dose and none could stop, similar to olive oil group. Of EPO group, 77% (10/13) showed a significant rise in plasma DGLA. Authors conclude that EPO cannot be substituted for non-steroidal anti-inflammatory drugs (NSAIDs) in patients with NSAID-induced upper gastrointestinal side effects.
Cant *et al.*, 1991	Effect on milk composition in nursing mothers	DB, PC, R n=36 breast-feeding women	8 months	Four, 500 mg capsules 2x/day (2,800 mg LA/day, 320 mg GLA/day)	Efamol® capsules (500 mg EPO) vs. placebo (liquid paraffin)	Total fat and EFA content in milk declined 17-23% in placebo group and increased an unspecified percentage in EPO group. This study demonstrates that supplementing the maternal diet with EPO changes milk fatty acid composition and may provide other beneficial effects by increasing fat content and energy content of breast milk while also increasing ratio of poly-unsaturated to saturated fats.
Jamal and Carmichael, 1990	Diabetic neuropathy	DB, PC, R n=22 patients with distal diabetic polyneuropathy	6 months	Two, 500 mg capsules 4x/day (360 mg GLA/day)	EPO (500-mg capsules providing 45 mg GLA) (brand not stated)	In comparison to placebo, patients in EPO group showed statistically significant increase in both median ($p<0.01$) and peroneal nerve conduction ($p<0.05$), as well as an improvement in neuropathy symptom scores ($p=0.001$) such as abnormal sensations of heat, cold, numbness, pain, weakness, and paresthesias.
van der Merwe *et al.*, 1990	Liver cancer	DB, PC, R n=62 patients with primary liver cancer	2 years, volunteers entering at different points during this period	500 mg capsule 36/day (1,440 mg GLA/day)	Efamol® capsules (500 mg EPO providing 40 mg GLA) vs. placebo (500 mg olive oil)	Mean survival time for EPO group was 58 vs. 42 days in placebo group. Effect of EPO on survival in primary liver cancer was not significantly better than placebo. In objective and subjective measurements, EPO scored better than placebo, but was not siginificant. EPO had a statistically significant beneficial effect on gamma-glutamyl transferase values, as a measure of liver function ($p=0.0192$).

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