

## EVENING PRIMROSE OIL

Note: Vitamin E is an optional medicinal ingredient in evening primrose oil products. However, no use or purpose statements may be associated with vitamin E. See Appendix 1 for vitamin E proper name, common name, source material, and dose information.

**Date:** July 16, 2008

**Proper name(s):** *Oenothera biennis* L. (Onagraceae) (USDA 2005)

**Common name(s):** Evening primrose (McGuffin et al. 2000), evening primrose oil (Sweetman 2007)

**Source material(s):** Seed oil (Sweetman 2007; WHO 2002)

**Route(s) of administration:** Oral

**Dosage form(s):** Those pharmaceutical dosage forms suited to oral administration, including but not limited to chewables (eg. gummies, tablets), caplets, capsules, strips, lozenges, powders or liquids where the dose is measured in drops, teaspoons or tablespoons, are acceptable. This monograph is not intended to include food-like dosage forms such as bars, chewing gums or beverages.

**Use(s) or Purpose(s):** Statement(s) to the effect of:

- ▶ Source of essential fatty acids (Sweetman 2007; IOM 2006) for the maintenance of good health
- ▶ Source of omega-6 fatty acids (EP 2008; IOM 2006; Mills and Bone 2005; WHO 2002) for the maintenance of good health
- ▶ Source of linoleic acid (EP 2008; IOM 2006; Mills and Bone 2005; WHO 2002) for the maintenance of good health

**Dose(s):** 1,300-6,000 mg, per day (Sweetman 2007; IOM 2006; Keen 1993)

Optional potencies:

- ▶ 7-14% gamma-linolenic/gamolenic acid (GLA) (EP 2008; Mills and Bone 2005; WHO 2002);
- ▶ 65-85% linoleic acid (EP 2008; Mills and Bone 2005; WHO 2002)

**Duration of use:** No statement required.

**Risk information:**

**Caution(s) and warning(s):** No statement required.

**Contraindication(s):** No statement required.

**Known adverse reaction(s):** No statement required.

**Non-medicinal ingredients:**

- ▶ Must be chosen from the current NHPD *List of Acceptable Non-medicinal Ingredients* and must meet the limitations outlined in the list.
- ▶ For products providing vitamin E at doses lower than the minima specified in Table 2 of Appendix 1, vitamin E must be declared as a non-medicinal ingredient.

**Specifications:**

- ▶ The finished product must comply with the minimum specifications outlined in the current NHPD *Compendium of Monographs*.
- ▶ The medicinal ingredient may comply with the specifications outlined in the Refined Evening Primrose Oil Monograph published in the British Pharmacopoeia or the Evening Primrose Oil, Refined Monograph published in the European Pharmacopoeia.
- ▶ For products indicating one or more of the optional potencies listed in the dose section, an assay must be performed in order to confirm the potency(ies).

## References cited:

EP 2008: European Pharmacopoeia, 6<sup>th</sup> edition, Volume 2. Strasbourg (France): Directorate for the Quality of Medicines and HealthCare of the Council of Europe (EDQM).

IOM 2006: Institute of Medicine. Otten JJ, Pitz Hellwig J, Meyers LD, editors. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements. Washington (DC): National Academies Press.

IOM 2003: Institute of Medicine. Committee on Food Chemicals Codex, Food and Nutrition Board, Institute of Medicine. Food Chemicals Codex, 5<sup>th</sup> edition. Washington (DC): National Academies Press.

Keen H, Payan J, Allawi J, Walker J, Jamal GA, Weir AI, Henderson LM, Bissessar EA, Watkins PJ, Sampson M, Gale EA, Scarpello J, Boddie HG, Hardy KJ, Thomas PK, Misra P, Halonen JP. 1993. Treatment of diabetic neuropathy with gamma-linolenic acid. The gamma-Linolenic Acid Multicenter Trial Group. *Diabetes Care* 16(1):8-15.

McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. 2000. *Herbs of Commerce*, 2<sup>nd</sup> edition. Silver Spring (MD): American Herbal Products Association.

Mills S, Bone K. 2005. *The Essential Guide to Herbal Safety*. St. Louis (MO): Elsevier Churchill Livingstone.

O'Neil MJ, Smith A, Heckelman PE, Budavari S, editors. 2001. *Merck Index: An Encyclopedia of Chemicals, Drugs, & Biologicals*, 13<sup>th</sup> edition. Whitehouse Station (NJ): Merck & Co., Inc.

Sweetman SC, editor. 2007. *Martindale: The Complete Drug Reference*, 35<sup>th</sup> edition. London (UK): Pharmaceutical Press.

USDA 2005: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. *Oenothera biennis* L. Beltsville (MD): National Germplasm Resources Laboratory. Available from:

[http://www.ars-grin.gov/cgi-bin/npgs/html/tax\\_search.pl](http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl) [Accessed 16 July 2008].

WHO 2002: World Health Organization (WHO) Monographs on Selected Medicinal Plants, Volume 2. Geneva (CHE): World Health Organization.

## References reviewed:

Barnes J, Anderson LA, Philipson JD. 2007. *Herbal Medicines*, 3<sup>rd</sup> edition. London (UK): The Pharmaceutical Press.

Berardi RR, DeSimone EM, Newton GD, Oszko MA, Popovich NG, Rollins CJ, Shimp LA, Tietze KJ, editors. 2002. Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care, 13<sup>th</sup> edition. Washington (DC): American Pharmaceutical Association.

BP 2008: British Pharmacopoeia, Volume 1. London (UK): British Pharmacopoeia Commission. The Stationary Office.

Brinker F. 2001. Herb Contraindication and Drug Interactions, 3<sup>rd</sup> edition. Sandy (OR): Eclectic Medical Publications.

Guivernau N, Meza N, Barja P, Roman O. 1994. Clinical and experimental study on the long-term effect of dietary gamma-linolenic acid on plasma lipids, platelet aggregation, thromboxane formation, and prostacyclin production. Prostaglandins, Leukotrienes, and Essential Fatty Acids 51(5):311-316.

Hoffmann D. 2003. Medical Herbalism. Rochester (VT): Healing Arts Press.

IOM 2002: Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Washington (DC): National Academy Press.

Lovell CR, Burton JL, Horrobin DF. 1981. Treatment of atopic eczema with evening primrose oil [letter]. Lancet;1(8214):278.

Manku MS, Horrobin DF, Morse N, Kyte Vicki, Jenkins K. 1982. Reduced levels of prostaglandin precursors in the blood of atopic patients: defective delta-6-desaturase function as a biochemical basis for atopy. Prostaglandins Leukotrienes and Medicine 9:615-628.

Manku MS, Horrobin DF, Morse NL, Wright S, Burton JL. 1984. Essential fatty acids in the plasma phospholipids of patients with atopic eczema. The British Journal of Dermatology 110(6):8-643.

McFayden IJ, Forrest AP, Chetty U. 1992. Cyclical breast pain - some observations and the difficulties in treatment. The British Journal Clinical Practice 46(3):161-164.

McGregor L, Smith AD, Sidey M, Belin J, Zilkha KJ, McGregor JL. 1989. Effects of dietary linoleic acid and gamma linolenic acid on platelets of patients with multiple sclerosis. Acta Neurologica Scandinavica 80(1):23-27.

McGuffin M, Hobbs C, Upton R, Goldberg A, editors. 1997. American Herbal Products Association's Botanical Safety Handbook. Boca Raton (FL): CRC Press.

Mills S, Bone K. 2000. Principles and Practice of Phytotherapy. Toronto (ON): Churchill Livingstone.

Morse NL, Clough PM. 2006. A meta-analysis of randomized, placebo-controlled clinical trials of efamol evening primrose oil in atopic eczema. Where do we go from here in light of more recent discoveries? *Current Pharmaceutical Biotechnology* 7(6):24-503.

Morse PF, Horrobin DF, Manku MS, Stewart JC, Allen R, Littlewood S, Wright S, Burton J, Gould DJ, Holt PJ, Jansen CT, Mattila L, Meigel W, Dettke TH, Wexler D, Guenther L, Bordoni A, Patrizi A. 1989. Meta-analysis of placebo-controlled studies of the efficacy of epogam in the treatment of atopic eczema. Relationship between plasma essential fatty acid changes and clinical response. *The British Journal of Dermatology* 121(1):75-90.

Ockerman P, Bachrack I, Glans S, Rassner S. 1986. Evening primrose oil as a treatment of premenstrual syndrome. *Recent Advances in Clinical Nutrition* 2:405-404.

Oliwiecki S, Armstrong J, Burton J, Bradfield J. 1993. The effect of essential fatty acids on epidermal atrophy due to topical steroids. *Clinical and Experimental Dermatology* 18(4):8-326.

Oliwiecki S, Burton J. Evening primrose oil and marine oil in the treatment of psoriasis. 1994. *Clinical and Experimental Dermatology* 19(2):9-127.

Pashby NL, Mansel RE, Hughes LE, Hanslip J, Preece PE. 1981. A clinical trial of evening primrose oil in mastalgia. *The British Journal of Surgery* 68:801.

Puolakka J, Mäkäräinen L, Viinikka L, Ylikorkala O. 1985. Biochemical and clinical effects of treating the premenstrual syndrome with prostaglandin synthesis precursors. *The Journal of Reproductive Medicine* 30:149-153.

Puri BK. The safety of evening primrose oil in epilepsy. 2007. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 77:101-103.

Schäfer L, Kragballe K. 1991. Supplementation with evening primrose oil in atopic dermatitis: effect on fatty acids in neutrophils and epidermis. *Lipids* 26(7):60-557.

Schalin-Karrila M, Mattila L, Jansen CT, Uotila P. 1987. Evening primrose oil in the treatment of atopic eczema: effect on clinical status, plasma phospholipid fatty acids and circulating blood prostaglandins. *The British Journal of Dermatology* 117(1):11-19.

Sharpe GR, Farr PM. 1990. Evening primrose oil and eczema. *Lancet* 335:667-668.

Shuster J. 1996. Black cohosh root? Chasteberry tree? Seizures! *Hospital Pharmacy* 31:1553-1554.

Vaddadi KS. 1981. The use of gamma-linolenic acid and linoleic acid to differentiate between temporal lobe epilepsy and schizophrenia. *Prostaglandins and Medicine* 6:375-379.

Van Gool CJ, Zeegers MP, Thijs C. 2004. Oral essential fatty acid supplementation in atopic dermatitis – a meta-analysis of placebo-controlled trials. *The British Journal of Dermatology* 150:728-740.

Veale D, Torley H, Richards IM, O'Dowd A, Fitzsimons C, Belch JJ, Sturrock RD. 1994. A double-blind placebo controlled trial of Efamol® Marine on skin and joint symptoms of psoriatic arthritis. *British Journal of Rheumatology* 33(10):8-954.

Vericel E, Lagarde M, Mendy F, Courpron PH, Dechavanne M. 1986. Effects of gamma-linolenic acid intake on platelet functions in elderly people. *Thrombosis Research* 42:499-509.

Walker T, Singh PK, Wyatt KM, O'Brien PM. 1999. The effect of prostanoid precursors and inhibitors on platelet angiotensin II binding. *Journal of Obstetrics and Gynaecology* 19(1):56-58.

Wetzig N. 1994. Mastalgia: a 3 year Australian study. *The Australian and New Zealand Journal of Surgery* 64(5):31-329.

Whitaker D, Cilliers J, de Beer C. 1996. Evening primrose (Epogam®) in the treatment of chronic hand dermatitis: disappointing therapeutic results. *Dermatology* 193(2):20-115.

Wiersema J, León B. 1999. *World Economic Plants: A Standard Reference*. Boca Raton (FL): CRC Press LLC.

Williamson EM, Evans FJ, Wren RC. 1988. *Potter's New Cyclopaedia of Botanical Drugs and Preparations*. Saffron Walden (UK): C.W. Daniel Company Limited.

Wright S, Burton JL. 1982. Oral evening primrose seed oil improves atopic eczema. *Lancet* 2(8308):1120-1122.

Yoon S, Lee J & Lee S. 2002. The therapeutic effect of evening primrose oil in atopic dermatitis patients with dry scaly skin lesions is associated with the normalization of serum gamma-interferon levels. *Skin Pharmacology and Applied Skin Physiology* 15:20-25.

Yoshimoto-Furuie K, Yoshimoto K, Tanaka T, Saima S, Kikuchi Y, Shay J, Horrobin DF, Echizen H. 1999. Effects of oral supplementation with evening primrose oil for six weeks on plasma essential fatty acid and uremic skin symptoms in hemodialysis patients. *Nephron* 91:9-151.

## Appendix 1: Vitamin E

### Proper name(s), common name(s), and source material(s)

Table 1: Vitamin E proper name(s), common name(s) and source material(s)

Proper name(s)	Common name(s)	Source material(s)
Vitamin E (Sweetman 2007; IOM 2003; O'Neil et al. 2001)	Alpha ( $\alpha$ )-tocopherol (Sweetman 2007; O'Neil et al. 2001); Vitamin E (Sweetman 2007; IOM 2003; O'Neil et al. 2001)	All <i>racemic</i> (all <i>rac</i> )- $\alpha$ -tocopherol/ <i>dl</i> - $\alpha$ -tocopherol (Sweetman 2007; IOM 2003)  All <i>rac</i> - $\alpha$ -tocopheryl acetate/ <i>dl</i> - $\alpha$ -tocopheryl acetate (Sweetman 2007; IOM 2003)  All <i>rac</i> - $\alpha$ -tocopheryl succinate/ <i>dl</i> - $\alpha$ -tocopheryl acid succinate/ <i>dl</i> - $\alpha$ -tocopheryl succinate (Sweetman 2007)  <i>RRR</i> - $\alpha$ -tocopherol/ <i>d</i> - $\alpha$ -tocopherol (Sweetman 2007; IOM 2003; O'Neil et al. 2001)  <i>RRR</i> - $\alpha$ -tocopheryl acetate/ <i>d</i> - $\alpha$ -tocopheryl acetate (Sweetman 2007; IOM 2003)  <i>RRR</i> - $\alpha$ -tocopheryl succinate/ <i>d</i> - $\alpha$ -tocopheryl acid succinate/ <i>d</i> - $\alpha$ -tocopheryl succinate (Sweetman 2007; IOM 2003)

### Quantity:

The quantity of vitamin E must always be provided in terms of  $\alpha$ -tocopherol (AT) (i.e. mg *RRR*- $\alpha$ -tocopherol), irrespective of the source material used.

IUs may be provided as optional additional information on the PLA form in the "potency" field and on product labels.

Table 2: Dose information for vitamin E presented as dose per day (IOM 2006)

Subpopulation		Vitamin E (mg AT/day)	
		Minimum	Maximum
Adults	$\geq 19$ y	4.5	179

Conversion factors:

Table 3: Conversion of vitamin E source material quantity into vitamin E quantity in terms of alpha-( $\alpha$ )-tocopherol (AT) and vitamin E activity in terms of International Units (IU) (IOM 2006)

Source material (1 mg)	Vitamin E quantity (mg AT)	Vitamin E activity (IU)
<i>RRR</i> - $\alpha$ -Tocopherol	1.00	1.49
<i>RRR</i> - $\alpha$ -Tocopheryl acetate	0.91	1.36
<i>RRR</i> - $\alpha$ -Tocopheryl succinate	0.81	1.21
All <i>rac</i> - $\alpha$ -tocopherol	0.50	1.10
All <i>rac</i> - $\alpha$ -tocopheryl acetate	0.46	1.00
All <i>rac</i> - $\alpha$ -tocopheryl succinate	0.41	0.89

Table 4: Conversion of vitamin E source material activity into vitamin E quantity in terms of alpha-( $\alpha$ )-tocopherol (AT) (IOM 2006)

Source material (1 IU)	Vitamin E quantity (mg AT)
<i>RRR</i> - $\alpha$ -Tocopherol	0.67
<i>RRR</i> - $\alpha$ -Tocopheryl acetate	0.67
<i>RRR</i> - $\alpha$ -Tocopheryl succinate	0.67
All <i>rac</i> - $\alpha$ -tocopherol	0.45
All <i>rac</i> - $\alpha$ -tocopheryl acetate	0.45
All <i>rac</i> - $\alpha$ -tocopheryl succinate	0.45

Examples using the vitamin E conversion factors:

- a) Converting vitamin E activity into quantity of AT (mg)

Convert 400 IU of *RRR*- $\alpha$ -tocopheryl succinate activity into mg AT:  
 $= 400 \text{ IU} \times 0.67 \text{ mg AT/IU}$   
 $= 268 \text{ mg AT}$

- b) Converting vitamin E source material quantity into quantity of AT (mg)

Convert 200 mg of all *rac*- $\alpha$ -tocopheryl acetate into mg AT:  
 $= 200 \text{ mg} \times 0.46 \text{ mg AT/mg}$   
 $= 92 \text{ mg AT}$