Appendix 1 (part 1 of 3): Sample monograph from the www.herbalckd.com website. Reproduced by permission of the authors.

Evening Primrose Oil

Safety

CKD-ND	HD/PD	Transplant
		

Dosing

CKD-ND

No dose adjustment was found in the literature

HD/PD

2 capsules po twice daily x 6 weeks (1 capsule = 360 mg linoleic acid, 50 mg oleic acid 45 mg gamma-linoleic acid)[1] was used in 1 study. Long term safety of this dose has not been studied.

Transplant

4 capsules at time of transplant then 2 capsules three times daily for 6 months was used in 1 study (1 capsule = 0.6 mL of oil that was 73-74% linoleic acid + 8-9% gamma-linoleic acid)[2] Long term safety of this high dose has not been studied.

Adverse Effects

Common Adverse Drug Reactions

- Nausea, dyspepsia, headache[3],[4]
- Oral supplements of evening primrose oil has been used safely in the general population for up to 1 year with no reports of significant adverse reactions[5]-[7]
- *In vivo*, gamma-linoleic acid has been shown to increase bleeding time by 40%[8]

Nephrotoxic effects

No nephrotoxic effects were reported in the literature

Supplementary material for Leung S, Shalansky K, Vashisht P, Leung M, Marin JG. Creation of a natural health products database for assessing safety for patients with chronic kidney disease or renal transplant. *Can J Hosp Pharm*. 2017;70(5):343-8.

Appendix 1 (part 2 of 3): Sample monograph from the www.herbalckd.com website. Reproduced by permission of the authors.

Interactions

General

Evening primrose oil contains gamma-linoleic acid, which can inhibit platelet aggregation and prolong bleeding time. Evening primrose oil should be used with caution in patients taking antiplatelet (including non-steroidal anti-inflammatory agents) or anticoagulant medication due to increased risk of bleeding and/or bruising.[8],[9]

CYP Metabolism

In vitro research suggests that CYP2C9 is inhibited by evening primrose oil constituent *cis*-linoleic acid[10]

Immunomodulatory

In vitro and clinical commentary for the general population suggest that the build up of gamma-linoleic acid metabolite, arachidonic acid, may lead to immunosuppression[11],[12]

Pharmacokinetics

Molecular Weight

No data was found in the literature

Volume of Distribution

No data was found in the literature

Protein Binding

No data was found in the literature

Metabolism

No data was found in the literature

Renal Clearance

No data was found in the literature

Literature Review

- Nephron. 1999 Feb;81(2):151-9.[1]
- Transplantation. 1977;24(4):263-7.[2]

References

1. Yoshimoto-Furuie K, Yoshimoto K, Tanaka T, Saima S, Kikuchi Y, Shay J, et al. Effects of oral supplementation with evening primrose oil for 6 weeks on plasma essential fatty acids and uremic skin symptoms in hemodialysis. *Nephron.* 1999;81(2):151-9.
2. McHugh MI, Wilkinson R, Elliott RW, Field EJ, Dewar P, Hall RR, et al. Immunosuppression with polyunsaturated fatty acids in renal transplantation. *Transplantation*. 1977;24(4):263-7.
3. Roemheld-Hamm B, Dahl NV. Herbs, menopause, and dialysis. *Semin Dial.* 2002;15:53-9.

Supplementary material for Leung S, Shalansky K, Vashisht P, Leung M, Marin JG. Creation of a natural health products database for assessing safety for patients with chronic kidney disease or renal transplant. *Can J Hosp Pharm*. 2017;70(5):343-8.

Appendix 1 (part 3 of 3): Sample monograph from the www.herbalckd.com website. Reproduced by permission of the authors.

4. Kleijnen J. Evening primrose oil. *BMJ* .1994;309:824-25.
5. Evening Primrose Oil. In: Natural Standard: the authority on integrative medicine. Cambridge (MA): Natural Standard;2014.
6. Khoo SK, Munro C, Battistutta D. Evening primrose oil and treatment of premenstrual syndrome. *Med J Aust*. 1990;153:189-92.
7. Van Gool CJ, Zeegers MP, Thijs C. Oral essential fatty acid supplementation in atopic dermatitis-a meta-analysis of placebo-controlled trials. *Br J Dermatol.* 2004;150:728-40.
8. Guivernau M, Meza N, Barja P, Roman O. 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 Leukot Essent Fatty Acids*. 1994;51:311-6.
9. Halat KM, Dennehy CE. Botanicals and dietary supplements in diabetic peripheral neuropathy. *J Am Board Fam Pract.* 2003;16(1):47-57.
10. Zou L, Harkey MR, Henderson GL. Effects of herbal components on cDNA-expressed cytochrome P450 enzyme catalytic activity. *Life Sci.* 2002;71(13):1579-1589.
11. Phinney S. Potential risk of prolonged gamma-linolenic acid use. *Ann Intern Med.* 1994;120:692.
12. Kinsella JE. Lipids, membranee receptors, and enzymes: effects of dietary fatty acids. *J Parenteral Enteral Nutr*. 1990;14:200s-17s.

November 2015

Disclaimer: The content of this website is intended for informational purpose only. It is not intended to replace clinical judgement or to be used as a substitute for professional advice for an individual patient.

Supplementary material for Leung S, Shalansky K, Vashisht P, Leung M, Marin JG. Creation of a natural health products database for assessing safety for patients with chronic kidney disease or renal transplant. *Can J Hosp Pharm*. 2017;70(5):343-8.