

## RESEARCH

# Evening Primrose Oil for Cervical Ripening

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### *Clinical Question:*

Can evening primrose oil be used as a cervical ripening agent to avoid postdates pregnancy and shorten the length of labour?

### BACKGROUND

Evening primrose (*Oenothera biennis*) is a native North American flower so named because it blooms in the evening. This plant is of special interest to midwives because of anecdotal evidence suggesting that the oil from its seeds can help soften the cervix, preventing postdate pregnancy and shortening the length of labour. Certified Nurse-Midwives in the United States felt that evening primrose oil was the most successful herbal extract preparation for promoting cervical ripening and the stimulation of labour, so it is not surprising that it scored high on their “comfort level in prescribing scale.”<sup>1</sup> The oil extracted from evening primrose seeds contains an unusually high amount of gamma-linolenic acid (GLA), a very active essential fatty acid and a precursor of prostaglandin derivatives. Despite the lack of scientific evidence supporting its use in cervical ripening, in the past two decades, evening primrose oil has been popularized as an alternative remedy for rheumatoid arthritis and atopic dermatitis. Research in both animal and human models have discovered significant changes in serum lipid biosynthesis when evening primrose oil is consumed orally.<sup>2,3</sup> Although the biological effects and biochemical changes that occur due to increases in fatty acids have not been precisely determined, evening primrose oil (theoretically, at least) holds promise for the treatment of some of these systemic diseases.

### THE SCIENCE

The oil extracted from the seeds of the evening primrose is responsible for the therapeutic effect. The oil contains mostly linoleic acid (60%–65%) but is more notably the most important source of GLA (7%–14%).<sup>4</sup> This acid, which is comparatively scarce in most other seed oils, can be metabolized into dihomo-gamma-linoleic acid (DGLA), which is a precursor of prostaglandin E and several other active substances that are thought to mediate its therapeutic effect. The effect of dietary GLA supplementation on prostaglandin biosynthesis has been determined in animal and human models. Macrophages isolated from mice fed diets rich in evening primrose oil for two weeks showed an increased capacity

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to synthesize prostaglandin E1 (PGE1), prostaglandin I2 (PGI2) (also known as prostacyclin), and DGLA.<sup>2</sup> These studies show that macrophage prostaglandin E biosynthesis could be enhanced by the consumption of GLA-rich dietary oils. Similar effects were observed in the serum of patients with rheumatoid arthritis who were treated with oral evening primrose oil for 12 weeks. Evening primrose oil significantly increased the amount of GLA, DGLA, and arachidonic acid (an important precursor in the synthesis of 2-series prostaglandin) in blood serum. These studies suggest that at the least, a 12-week diet rich in evening primrose oil significantly changes the serum fatty acid composition of blood. Whether this leads to any therapeutic effects has yet to be determined.

The increase in prostaglandin precursors seen in these studies may help explain why Certified Nurse-Midwives in the United States anecdotally describe the use of evening primrose oil as a successful therapy for promoting cervical ripening. During pregnancy, prostaglandins are produced mostly by fetal membranes. Synthesis of prostaglandins is low early in pregnancy, and their receptors are furthermore downregulated, dampening signalling from any prostaglandins present. Upregulation and increased prostaglandin production occur near the end of pregnancy

and are stimulated by uterine stretch and the release of maternal corticotropin-releasing hormone, which binds to receptors that are now expressed in the fully mature fetal brain.<sup>5</sup> This produces a chain of events in which cortisol is produced by fetal adrenal glands and feeds back to promote prostaglandin synthesis through estrogen production. Increases in prostaglandin concentrations activate enzymes that start to break down the extracellular matrix of cervical cells, leading to cervical ripening.<sup>5</sup>

Despite the studied effects of dietary evening primrose oil on prostaglandin precursor levels in serum and the well-established role of prostaglandins in remodelling the cervical matrix, no large clinical studies clearly and definitively document the efficacy or safety of this herbal extract in pregnancy. A retrospective study of quasi-experimental design investigating the effect of evening primrose oil on the length of pregnancy and selected intrapartum outcomes<sup>6</sup> showed that the oral administration of evening primrose oil from the 37th gestational week until birth did not shorten gestation or decrease the overall length of labour. However, there was a slight increase in the incidence of prolonged rupture of membranes, oxytocin augmentation, arrest of descent, and vacuum extraction.<sup>6</sup> Conversely, a small randomized double-blind placebo-controlled clinical trial showed a significant improvement in Bishop score and a significant reduction of cervical length in the group treated with evening primrose oil.<sup>7</sup> Although the use of oxytocin was similar in both groups, more women delivered vaginally in the evening primrose oil group (70% versus 51%). These data suggest that the use of evening primrose oil as a cervical priming agent to enhance the success rate for vaginal delivery may be considered for healthy term women awaiting the onset of labour.

#### THE BOTTOM LINE

The use of evening primrose oil during pregnancy is not well supported in the literature, and even though the reported adverse effects are limited simply to gastrointestinal upset and headaches,<sup>4</sup> midwives have a professional responsibility to protect mothers and fetuses under their care from harm. Although some herbal therapies may be relatively safe when used carefully at recommended doses and although evening primrose oil may be considered a dietary supplement rather than a drug, a significant gap in our knowledge relates to the dosage of evening primrose oil. Women report a range of dosages,<sup>1</sup> and no clinical studies document how much should be taken. Well-designed clinical trials that are adequately powered, along with optimal dosing standards,

are necessary before the use of evening primrose oil can be recommended for cervical ripening in pregnancy. Midwives who use herbal extracts with historic functions should be encouraged to report their experiences, participate in and conduct studies to determine the safety and efficacy of such substances, and publish their findings in the literature.

### EFFECTIVE THERAPIES

Effective cervical ripening can be achieved mechanically or pharmaceutically and respectively involves the natural release or the ectopic application of prostaglandins. Foley catheters stretch the lower uterine segment, activating endogenous prostaglandin production, thus ripening the cervix. Pharmacological methods recommended by the Society of Obstetricians and Gynaecologists of Canada to ripen an unfavourable cervix include (1) the use of intravaginal or intracervical PGE2 such as Cervidil, Prostin, and Prepidil (intravaginal application is preferred to intracervical application), and (2) the use of the PGE1 analogue misoprostol.<sup>8</sup> Application of PGE2 will activate matrix metalloproteinases, which degrade collagen and increase the retention of water; this weakens the structure of the cervix and contributes to cervical ripening. Misoprostol likely also works to disintegrate and dissolve collagen bundles in the cervix<sup>9</sup> but also binds to prostaglandin EP1 receptors on uterine muscle, causing calcium release and increased contractile activity. Currently, no herbal preparations have been well studied for their use for the purpose of cervical ripening. Clinical randomized controlled trials that support the use of evening primrose oil to accelerate cervical ripening and shorten labour and that assess adverse effects on both the mother and fetus are needed before evening primrose oil can be confidently implemented during parturition.

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