

Evening Primrose Oil as a Cervical Ripening Agent

The composition of the cervix is fairly complex. It is primarily composed of fibrous connective tissue and also contains smooth muscle, fibroblasts, blood vessels, epithelial tissue and mucus-secreting glands. The connective tissue is formed by collagen fibers and elastin held together by ground substance (extracellular matrix). Ground substance is primarily composed of glycoproteins that coat the collagen fibers in the extracellular matrix and modify their physical properties, including determining the water content of the tissue. There are two elements involved in cervical softening – increased vascularity and water content. At term, 90% of the cervix is water. Structural changes in the connective tissue in the last weeks of pregnancy are also greatly involved in the softening of the cervix. One of the glycoproteins found in the ground substance is hyaluronic acid. It normally provides stiffness and resilience with some lubricating properties, but it has a greater ability to bind large amounts of water and a lesser ability to bind collagen. Eventually, it will weaken the binding between the collagen fibers and another glycoprotein called fibronectin (which protects collagen and stabilizes the ground substance during the majority of the pregnancy). As the bonds between the collagen and fibronectin weaken, the increased levels of the hyaluronic acid activate macrophages and neutrophils in the cervical tissue to secrete a substance called interleukins. Interleukins increase prostaglandin activity and the neutrophil migration and degranulation of the cervical tissue, which result in the release of enzymes (collagenase and elastase) which break down collagen and elastin fibers. This results in an increased production of prostaglandins.

Prostaglandins promote myometrial contractions, cervical dilation and membrane rupture and are normally present in low concentrations in the maternal circulation. They can be synthesized as a consequent of tissue trauma (including labor itself and manipulative or tactile stimuli). In late pregnancy, they are synthesized by coitus, vaginal examination, sweeping of membranes or amniotomy. Exogenous prostaglandins can be used therapeutically to ripen the cervix and induce uterine contractions and labor. The hormone, relaxin, which is produced and secreted in greater quantities towards the end of pregnancy also appear to promote cervical ripening by enhancing prostaglandin production during labor. Corticotrophin releasing hormone (CRH) is important in initiating labor by establishing the positive feedback mechanisms. CRH increases prostaglandin production which in turn, increases the synthesis of CRH. Levels of prostaglandins are usually 200 times lower during pregnancy than at any other stage of the menstrual cycle but these increased levels (due to CRH) occur rapidly in maternal circulation after week 36 gestation. Also, the release of CRH exposes decidual cells in the uterine endometrium to oxytocin. This also increases the release of prostaglandins. This, in turn, increases uterine responsiveness to oxytocin, further enhancing the positive feedback mechanisms needed in labor. The most important forms of prostaglandins are PGF_{2α} and PGE₂. PGE₂ is involved in cervical ripening.

Essential fatty acids play a role in the process of cervical ripening. These necessary fatty acids are required by the body and must be taken from our diet. They are needed for many body functions such as immunities, vision, the transport of lipids and formation of cellular membranes but they are also necessary for the production of hormone-like compounds, such as prostaglandins. *Omega-3 Fatty Acids*, such as linolenic acid, EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), and *Omega-6 Fatty Acids*, such as linoleic and arachidonic acid, are responsible for the production of eicosanoids.

Eicosanoids are a group of hormone-like compounds. One of their roles is regulation of childbirth in the form of prostaglandins. These hormone-like compounds act more locally and are produced in small quantities but are very potent. They are not stored in cells. They are synthesized just before they are released into the area where they are needed. They do not circulate through the entire body as hormones do.

Evening Primrose Oil (Oenothera biennis) contains gamma-linolenic acid (GLA – an Omega-3) and linoleic acid (and Omega-6). In optimum conditions, linoleic acid is converted to GLA by an enzyme called delta-6-desaturase. The GLA produced is further converted to dihomogamma-linolenic acid, which in turn leads to arachidonic acid. Arachidonic acid is the precursor of prostaglandin, specifically the prostaglandin 2 series. Since PGE₂ is responsible for cervical ripening and prostaglandin is an eicosanoid or hormone-like compound released ONLY in an area where action is necessary, it makes sense that EPO used for a cervical ripening agent would have its best effect when applied locally or directly on the cervical tissue!

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