

SUPPLEMENTS USED IN PREVENTION OF PREECLAMPSIA AND FOR LABOR PREPARATION

Historically, a number of supplements have been used for preeclampsia and preparation for labor. This Whole Health tool highlights some of those most commonly used, focusing on the research related to their use.

PREECLAMPSIA PREVENTION

Note: Please refer to the [Passport to Whole Health](#), Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

CALCIUM

A Cochrane review of 13 trials involving 15,730 pregnant women reported that the risk of preeclampsia and hypertensive disorders was reduced in those receiving calcium supplements compared to placebo.[1] The effect was greatest in high-risk groups (e.g., those with prior history of preeclampsia) and those with a low baseline calcium intake, which is, unfortunately, a large number of women in the United States. Calcium, as well as magnesium, is essential for maintaining a healthy blood pressure and may prevent leg cramps women experience in the latter half of pregnancy. Calcium is considered safe for use in pregnancy. A dietary history that assesses intake of calcium-rich vegetables and dairy products can provide helpful information to guide supplementation. All calcium intake from diet and supplementation should be taken into consideration, so as to avoid excessive intake. The World Health Organization recommends an intake of 1.5–2.0 gm elemental calcium/day with the total daily dosage divided into three doses (preferably taken at mealtimes) from 20 weeks' gestation until the end of pregnancy.[2]

Dose: Start a dose of 600 mg per day and increase dietary intake.

VITAMIN D

Hypovitaminosis D has been associated with an increased risk of preeclampsia.[3] Vitamin D plays a role in the development of preeclampsia by affecting blood pressure through calcium homeostasis and/or modulating inflammation and immunity.[3] Insufficiency has also been linked to other adverse maternal and fetal outcomes, including poor fetal and infant bone mineralization, hypocalcemia, and rickets in neonates.[4] A number of prospective observational studies have shown a high prevalence of hypovitaminosis D during pregnancy across ethnic groups and nationalities.

Vitamin D is considered adequate when 25(OH)D levels are above 50 nmol/L, as defined by the Institute of Medicine. A level between 30 and 50 nmol/L is considered insufficient, and less than 30 nmol/L, deficient.[5] Supplementing with a combination of vitamin D and calcium during pregnancy may lead to a lower risk of preeclampsia, but data on the use of vitamin D alone for this purpose is mixed.[6,7] Women who supplement with vitamin D in pregnancy have been shown to decrease the risk of low birth weight in their infants.[8] While more research needs to be done, the evidence suggests that screening women in the first trimester for vitamin D deficiency is warranted.

Women can increase vitamin D by obtaining nonburning sun exposure daily (typically about 10 minutes) and by eating foods high in vitamin D, such as mushrooms, milk, fish, and egg yolks. Due to the common use of sunscreen and high amounts of time spent indoors, even women who live in sunny parts of the country may be deficient in vitamin D. A good rule of thumb is that 1,000 International Units (IUs) of D3 taken orally will raise serum 25-OH vitamin D levels by about 8-10 points.

Dose: Because of a huge variability in both sun exposure and dietary intake, it is perhaps best to individually dose supplementation based on a 25-OH vitamin D level.

CHOCOLATE (*THEOBROMA CACOA*)

What pregnant woman does not want an excuse to eat more chocolate? A study of 1,681 pregnant women found those who reported eating chocolate five or more times a week, or who had the highest levels of theobromine (a compound in cocoa) in their cord blood, had the lowest risk of preeclampsia. The scientists speculate that flavonoids in chocolate may provide cardiovascular protection.[9] This is an interesting correlation, especially given our growing understanding of the effects of dietary flavanols on vascular nitric oxide, which can benefit blood pressure control.[10]

Dose: As chocolate can be high in calories, it is probably best to encourage women, if they enjoy chocolate, to eat 1-2 oz of dark chocolate (70% cacao or greater) three to four times per week. For the blood-pressure-lowering effects, the dose is one-fourth of a regular chocolate bar (70% cacao or greater) daily.

OMEGA-3 FATTY ACIDS

Omega-3 fatty acids have potential beneficial effects on preeclampsia. Higher blood concentrations of arachidonic acid in preeclamptic women were noted more than 20 years ago, and high-dose omega-3 fatty acid intake has been shown to reduce maternal thromboxane A2 synthesis and enhance maternal refractoriness to angiotensin II. However, despite some promising early observational data, there is little evidence from randomized, placebo-controlled trials of a significant effect on the incidence or severity of preeclampsia.[11] A recent systematic review did not show any benefits in prevention of preeclampsia, but the doses of omega-3s used in the studies may have been too low to achieve a therapeutic response.[12] This review did, however, show a reduction in low birth weight infants and in preterm births. Of note, several studies have looked at a link

between omega-3 intake and development in the fetus. One large systematic review found that higher docosahexaenoic acid (DHA) intake in pregnancy prolonged the gestation in high-risk pregnancies, increased birth weight, and enhanced visual acuity and problem solving in the child.[13] One small randomized-controlled trial suggested that maternal omega-3 supplementation during pregnancy may reduce the risk of allergic disease in the child and may reduce the risk of preterm birth.[14] Another review looked at five randomized-controlled trials and found that omega-3 supplementation during pregnancy decreases the risk of childhood asthma in the offspring.[15] Other studies have not shown these benefits, so the data is overall inconclusive. Again, this may be related to the variable dosages used in the different studies. More research is needed.

Good dietary sources include cold-water fish, nuts (especially walnuts), ground flaxseed, avocado, and vegetables. Although cold-water fish are a good source of omega-3 fatty acids, the pregnant mother should avoid fish high in mercury. Information on fish safety can be found at the [U.S. Food and Drug Administration](https://www.fda.gov/food/food-safety) website.

Dose: 1,000 mg omega-3 fats (DHA + EPA) daily

FOLIC ACID

One systematic review showed that maternal consumption of folic acid supplementation in pregnancy reduces the risk of preeclampsia.[16] Most pregnant women already take folic acid in their prenatal vitamin for the prevention of neural tube defects. The prevention of preeclampsia is another reason to stress the importance of a daily prenatal vitamin.

Dose: 400 mcg of folic acid daily

PARTUS PREPARATORS: SUPPLEMENTS TO PREPARE FOR LABOR

It is important to stress to women that their bodies know how to give birth. There is no substance that needs to be ingested or used topically in order to have a successful delivery. That being said, there is a rich tradition of the use of herbs and foods to aid labor preparation, and many women may inquire about their use.

BLUE COHOSH

Blue cohosh (*Caulophyllum thalictroides*) has a long history of use as a labor aid. Indigenous North American women used blue cohosh to induce labor or stimulate sluggish, ineffective contractions. It was included in the United States Pharmacopeia as a labor-inducing agent from 1882 to 1905. Today, blue cohosh is found in many formulations marketed to women as partus preparators. Many physicians are unfamiliar with its use, but a survey of nurse midwives in 1999 found that 64% used blue cohosh, often in combination with black cohosh, to augment labor during delivery.[17] While many used blue cohosh, midwives also reported having the least comfort with its use during pregnancy. A significant number reported observing increased rates of meconium, tachycardia in the neonate, and need for resuscitation in the neonate with its use.

There have been a small number of case reports implicating blue cohosh, often in combination with black cohosh and/or other herbs, with myocardial infarction,[18] multi-organ failure, congestive heart failure,[19] and perinatal stroke[20] in infants born to mothers taking the herb several weeks before birth. While the published case reports are not conclusive, blue cohosh contains some potentially dangerous compounds including caulosaponin, a glycoside that has been shown to constrict coronary vessels and likely accounts for its oxytocic effects. It also contains N-methylcytisine, an alkaloid with action similar to nicotine, known to cause coronary vasoconstriction, tachycardia, hypotension, and respiratory depression. In vitro studies show that extracts of blue cohosh rhizome (the lateral root) or pure N-methylcytisine (at 20 parts per million [ppm]) induce major malformations in cultured rat embryos.[21] The concentration of N-methylcytisine in dietary supplements containing blue cohosh ranges from 5-850 ppm.[22]

Despite the shortcomings of published case reports, the chemistry and pharmacology of blue cohosh are reasonably well known. The human case reports, as incomplete as they are, paint a picture that is consistent with the evidence provided by in vitro and animal studies. At this time, it is wise to err on the side of caution and **advise pregnant women not to use this plant.**

(X) Do not recommend.

BLACK COHOSH

Black cohosh (*Actaea racemosa*; *Cimicifuga racemosa*) is probably best known for its use in menopause, though it was traditionally used for rheumatic pain, uterine cramping, and to support mood. The German health authorities also recognize its use for dysmenorrhea. It is unrelated to blue cohosh, but the two herbs are often used in combination as a partus preparator. Studies on other *Cimicifuga* species failed to show teratogenicity in female rats at doses up to 2,000 mg/kg per day; however, similar studies in *Actaea racemosa* have not been published. Both the British Herbal Pharmacopoea and American Herbal Products Association recommend against the use of black cohosh during pregnancy.[23] **It is best to advise patients against its use**, as reproductive toxicology studies are needed for this herb. An analysis of 69 cases shows little, if any, supportive evidence for a significant hepatotoxic risk of black cohosh.[24]

(X) Do not recommend.

EVENING PRIMROSE OIL

Evening primrose oil (*Oenothera biennis*) is used widely during the last month of pregnancy by midwives in the United States for cervical softening. It is a rich source of omega-6 fatty acids. It is typically administered as two capsules intravaginally at bedtime. Five studies have been done indicating the safety of evening primrose oil, three of which were randomized controlled trials. When used orally as a cervical ripening agent, it has not been shown to reduce the risk of post-dates presentation.[25] This is not surprising, since oral administration during pregnancy was never a traditional use. One randomized-controlled

trial did not show any benefit on cervical ripening or length of labor.[26] Anecdotally, there is concern that it may increase the risk of the premature rupture of membranes. More trials assessing efficacy and safety are needed.

(X) Do not recommend.

RASPBERRY LEAF

Raspberry leaf (*Rubus idaeus*, *R. occidentalis*) can be found in many popular "pregnancy teas" in conventional stores across the country. It is often promoted to prevent miscarriage, ease morning sickness, and ensure a quick birth. A survey of 172 certified nurse midwives found that 63% of midwives using herbal preparations recommended red raspberry leaf.[17]

A double blind, placebo-controlled study randomized 192 low-risk, nulliparous women to receive raspberry leaf tablets (two tablets of 1.2 gm per day) or placebo, from 32 weeks gestation until delivery.[27] Raspberry leaf was not associated with any adverse effects in mother or baby, but it has not been shown to shorten the first stage of labor. Clinically significant findings were a shortening of the second stage of labor (mean difference, 9.59 minutes) and a lower rate of forceps deliveries between the treatment group and the control group (19.3% versus 30.4%). No contraindications for use in pregnancy or lactation are found in the literature; therefore, it is considered reasonable for pregnant women to use this plant.

Dose: Raspberry leaf tablets 1.2 gm orally daily, or as a tea, 1-3 cups daily

CASTOR OIL

In one national survey 93% of midwives reported using castor oil to induce labor.[17] Despite this prevalence, there has been little research into the use of castor oil. Only one study looking at safety was included in a recent Cochrane review which, unfortunately, was small and of poor methodological quality.[28] Outcomes which were evaluated in this study included c-section rate, meconium staining of amniotic fluid, and APGAR scores. All women who ingested castor oil had nausea; otherwise, outcomes were no different than for women who did not ingest it. One randomized-controlled trial of 81 women did show it to be effective in inducing labor in post-date multiparous women, although benefit was not seen in primiparous women. [29] No difference in obstetrical complications or in the rates of neonatal outcomes were seen. One systematic review did find that use of castor oil may increase the risk of meconium-stained fluid and the risk of C-section.[30] Patients should be counseled on these potential risks, if they choose to use castor oil.

Dose: 60 mL orally once

OTHER HERBS

Many herbs have historically been used to induce labor. These include blue cohosh (*Caulophyllum thalictroides*), cotton root bark (*Gossypium herbaceum*), partridge berry

(*Mitchella repens*), cramp bark (*Viburnum opulus*) and black cohosh (*Cimicifuga racemosa*). As little to no research has been conducted on the safety of these herbs for labor induction, their use by those without training in herbal medicine is **not recommended**. [31]

DATE FRUIT

A randomized-controlled trial of 154 nulliparous women looked at the consumption of dates in pregnancy. [32] Date fruit consumption was not associated with an expedited onset of labor, but did appear to decrease the risk of needing labor augmentation. Another prospective study showed lower need for induction or augmentation of labor when dates were consumed in the last 4 weeks of pregnancy. [33] Dates are a safe and low-cost option for women who choose to consume them.

Dose: 6 date fruits per day starting at 36 weeks gestation

RESOURCE LINKS

- [Passport to Whole Health:](https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf) https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf
- [U.S. Food and Drug Administration:](https://www.fda.gov/food/consumers/advice-about-eating-fish) <https://www.fda.gov/food/consumers/advice-about-eating-fish>

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