REVIEW

Key Lipophilic Compounds Found in Chlorophyll and Wheat Germ: Preventing Spontaneous Abortion and Miscarriage in At-Risk Women

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The term "threatened abortion" describes the presence of vaginal bleeding or spotting, with or without uterine cramping, during the first 20 weeks of pregnancy.

Incidence and etiology

Approximately one quarter of all pregnant women experience bleeding and/or cramping during the first 20 weeks of pregnancy. About half of the women who experience these symptoms spontaneously abort. Over 90% of women who miscarry do so to reject seriously maldeveloped fetuses.

The degree of difficulty associated with spontaneous abortion is related to the age of the fetus at the time. If the miscarriage occurs during the first 12 weeks of pregnancy, the fetus and placenta remain small enough in size to pass through the vaginal opening without a great loss of blood. Following the 12-week point, a greater risk for complications exists, due to the size of fetal limbs, the lack of natural dilatation of the cervix, and the increased vasculature of the placenta.

Therapeutic Considerations

General nutritional and herbal support to maintain hormonal balance and nourish female reproductive organs may prove helpful when managing a patient at risk of threatened abortion. Before considering any herbal and/or nutritional protocol for this health challenge, the practitioner must rule out and/or address the following conditions:

- Balanced chromosomal translocations in the parents
- Uterine and cervical anomalies
- Infection
- Connective tissue disorders
- Hormonal abnormalities

When managing a patient with a history of miscarriage with complimentary nutritional and herbal support, it is essential to do so at least 3 months before conception (Veal, 1998). Additionally, it is essential that the practitioner address gastrointestinal and liver function to improve bioavailability of key fat-soluble compounds in wheat germ and chlorophyll (through an adequate production of bile salts and pancreatic enzymes, as well as an optimal balance of intestinal microflora) (Figure 1).

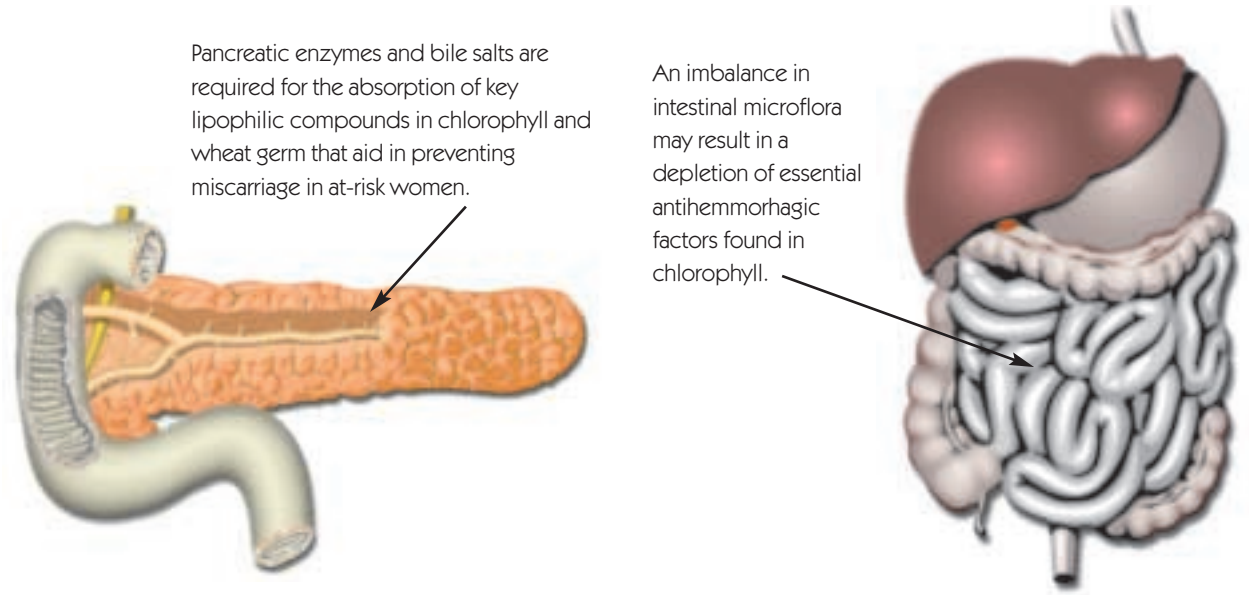

Figure 1 Impact of Digestive Function on the Absorption of Lipophilic Compounds within Chlorophyll and Wheat Germ

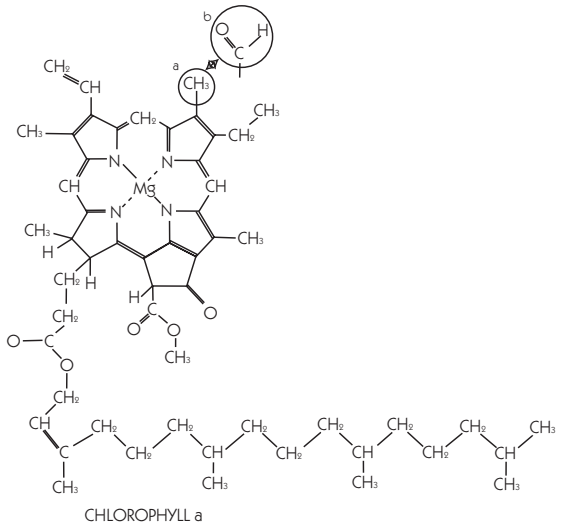

Figure 2 Chemical structure of chlorophylls a and b: Note the tetrapyrole ring around the magnesium atom and the long chain lipophilic phytol tail at the base (Wettstein et al., 1995).

Chlorophyll

Green vegetables such as buckwheat and alfalfa contain a significant amount of chlorophyll, a porphyrin that comprises the primary photoreceptor pigment of plant photosynthesis. Of particular interest with respect to women at risk for spontaneous blood loss are the lipophilic side-chains of chlorophyll. The complete chlorophyll molecule (Figure 2) is made up of four pyrrole rings (made from aliphatic amino acids numbered I through IV) that are ligated to form a tetrapyrrole that forms a ring around a centrally located atom of magnesium (Wettstein et al., 1995).

The fourth ring is esterified and contains a lipophilic side chain made up of one of the simplest diterpene molecules, phytol. This fraction of chlorophyll is fat soluble in its naturally occurring form in green vegetables such as alfalfa, wheat grass, and buckwheat and may prove beneficial for women at risk for hemorrhaging during pregnancy, as well as for preventing hemorrhagic disease of the newborn. It contains the vegetable-derived blood-clotting factor, phylloquinone (K1), found in the vitamin K complex. This antihemorrhagic factor was discovered by a Danish scientist in 1935 who observed that newly hatched chickens developed a hemorrhagic disease, despite receiving a diet that contained all the known essential nutrients. He found the disease to be connected to a fall in prothrombin, a required substance for normal clotting of the blood, and thus named the missed nutrient Vitamin K (for "Koagulationsvitamin").

Until recently, vitamin K1 was considered a less-important vitamin because it was believed that bacteria in the gut could synthesize enough of the related vitamin K2, also referred to as menaquinone. Furthermore, because vitamin K is involved with blood clotting, excessive bleeding was thought to be the only result of deficiency. Now researchers have confirmed that an imbalance in the bacterial composition of the colon dramatically reduces the presence of vitamin K2 in the blood stream. This is primarily caused when there is a relative increase in harmful gut bacteria and the vitamin K-producing beneficial bacteria decrease resulting in a vitamin K deficiency (Igarashi, 1993).

Further, bile and pancreatic juices are necessary for the absorption of the various forms of vitamin K from the upper small intestine for subsequent transport to the liver. If there is an absence of the necessary gastric secretions, this vitamin will not be carried to the liver for further processing. All of these factors highlight the importance of addressing gastrointestinal issues prior to conception.

Chlorophyll is an antagonist of guanidine. Guanidine is a toxin released into the blood as a result of burns, trauma (including pregnancy-associated trauma to the uterine lining), or muscle fatigue in a natural attempt to eliminate dead or defective cell clusters. This is a beneficial and natural phenomenon to the extent that it eliminates "bad" cells. However, a pregnant woman with a history of miscarriage and/or threatened abortion may be predisposed to producing an excess of guanidine that can ultimately cause more damage than repair (Rairigh et al., 2001; Nakatsuka et al., 2000; Farina et al., 2000; Athanassakis et al., 1999).

Wheat Germ

Women with a history of habitual abortion may reveal signs of respiratory alkalosis, which presents as hypoxemia, reduced oxygen saturation, and ketonuria. The vitamin E complex present in wheat germ oil, sometimes referred to as the tocopherols, normalizes acid/base balance thereby improving oxygen transport to maternal tissues (Burlev et al., 1992; Vobecky et al., 1976; Vobecky et al., 1974).

Additionally, the level of free fatty acids (FFAs) in the blood is significantly higher in women with recurring miscarriages (Nicotra et al., 1994; Svetlova et al., 1971). The relative increase in FFA's in the blood may be the result of a continuous discharge of catecholamines from autonomic nerve endings (a natural response to stress)

that can also cause strong uterine vasoconstriction and placental ischemia, leading to eventual miscarriage. Further, abnormal catecholamine discharge causes a relative increase in reactive oxygen species, which can result in DNA damage (Simsek et al., 1998). The fat-soluble compounds naturally occurring in wheat germ suppress oxidative DNA damage that can contribute to abnormal uterine growth. Essentially, these compounds function to re-establish antioxidant levels in the blood that have been compromised due to stress-dependent catecholamine discharge (Chappell et al., 1999; Kukushkina and Dmitrieva, 1991; Davidov et al., 1971). As an added benefit, the vitamin E complex has also been shown to prevent pre-eclampsia in high-risk women (Chappell et al., 1999).

The vitamin E complex, as naturally found in the lipophilic fraction of wheat germ, was originally discovered by Evans and Bishop in 1932. Until then, it had been known that some component in vegetable oils was necessary for reproduction in rats. The unidentified compound was named vitamin E, or the "antisterility" vitamin. Incidentally, the chemical name tocopherol comes from the Greek words "tokos" meaning "offspring" and "Phero" meaning "to bring forth." Unfortunately, human studies did not support this notion when an isolated tocopherol (d-alpha tocopherol) from wheat germ oil was researched by Evans and Bishop, because it did not contain the entire vitamin E complex necessary to support fertility (Kotarski, 1979).

Summary

Lipophilic Factors in Chlorophyll:

- Supply blood-clotting factors to prevent hemorrhaging
- Prevent toxicity reactions associated with miscarriage by functioning as antagonists to guanidine
- Maintain vascular integrity

Lipophilic Factors in Wheat Germ:

- Improve oxygen transport to maternal tissues
- Treat sub-clinical/clinical respiratory alkalosis associated with habitual spontaneous abortion
- Replace antioxidant-loss due to excess lipid peroxidation/free fatty acid production caused by stress-induced catecholamine response associated with uterine vasoconstriction

Drug/Nutrient Interactions, Nutrient/Nutrient Interactions, and Drug/Nutrient Depletions

- Lipase-inhibiting drugs such as orlistat, used to manage obesity, act by inhibiting fat absorption. Thus, they may inhibit the absorption of key nutrient factors found in chlorophyll and wheat germ and supplementation of these essential nutrients may be required (Heck et al., 2000; Finer et al., 2000; Melia et al., 1996).
- Mineral oil can inhibit the absorption of the fat-soluble fractions of chlorophyll and wheat germ (Becker, 1952).
- Warfarin is a coumarin anticoagulant drug that acts by inhibiting the synthesis of vitamin K dependant clotting factors. Hence, supplementation with vitamin K, or a diet high in vitamin K will impact the effects of this and related medications and may affect the required dosage range for treatment. Monitor a client's PT/INR closely if introducing the fat-soluble fraction of chlorophyll into the protocol (Bell, 1978; Dupont Pharma, 2001).
- Antibiotics alter intestinal microflora that produce vitamin K2. Hence, antibiotic use may reduce the body's supply of the vitamin K complex. Supplementation with chlorophyll may be necessary (Cummings et al., 1997).
- Anticonvulsant medications such as phenytoin, fosphenytoin, and barbiturates have been shown to increase the degradation of vitamin K through oxidation, resulting in potential bleeding complications. Supplementation with chlorophyll may prove beneficial by increasing the availability of clotting factors in the blood (Keith et al., 1983; Keith and Gallop, 1979).

- Cholestyramine and colestipol are examples of bile acid sequestrants that have been shown to inhibit the absorption of the fat-soluble fractions of chlorophyll and wheat germ (Knodel et al., 1987).
- Fenofibrate and clofibrate may result in a significant decrease in the amount of vitamin E available in the liver due to their ability to increase the production of hydrogen peroxide in the body (Lores Arnaiz et al., 1997).
- Gemfibrozil can result in a 40% decline in serum vitamin E levels in hypercholesterolemic men (Aberg et al., 1998).
- Chitosan may reduce the absorption of key lipophilic compounds found in chlorophyll and wheat germ (Deuchi et al., 1995).
- High intake of polyunsaturated fatty acids (PUFAs), including omega-3 and omega-6 fatty acids, can result in excess lipid peroxidation, which may be prevented with supplementation of wheat germ oil (Weber et al., 1997).

* Haloperidol may cause a depletion of vitamin E factors due to its effect on monoamine metabolism (VonVoigtlander et al., 1990).

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