**Chromium:** A trace mineral involved in maintaining healthy blood sugar levels and proper carbohydrate and fat metabolism.<sup>38,39</sup> Research indicates that insufficient dietary chromium intake results in signs and symptoms similar to those of type 2 diabetes and cardiovascular disease. Individuals with impaired glucose tolerance or diabetes supplemented with chromium typically show improved lipid variables, blood glucose and insulin levels.<sup>38</sup>

**Iodine and Selenium:** Essential trace minerals for thyroid hormone synthesis and conversion, in synergy with adequate levels of vitamin A.<sup>40,41</sup> Compromised thyroid function may lead to impaired motor and intellectual development in infants, learning disability and lowered achievement motivation.<sup>42-46</sup> Maternal iodine sufficiency is critical for the neuropsychological development of offspring, and it is not uncommon for women in North America to have suboptimal iodine status.<sup>47</sup> Selenium is also a chelator of mercury and a component of glutathione activity and metabolism.

## **Medicinal Ingredients (per capsule):**

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Vitamin C (Ascorbic acid)	100 mg
Calcium (Dicalcium malate)	35 mg
Magnesium (Magnesium dimalate)	20 mg
Choline	12.5 mg
Mixed carotenoids	11 mg
Niacinamide (3-Pyridinecarboxamide)	4.5 mg NE
Tocotrienols (90% delta-tocotrienol, 10% gamma-tocotrienol)	
Iron (Iron (II) bisglycinate)	_
Pantothenic acid (Calcium D-pantothenate)	1.5 mg
Vitamin B6 (Pyridoxine hydrochloride)	0.47 mg
Vitamin B1 (Thiamine hydrochloride)	
Vitamin B2 (Riboflavin)	
Vitamin B12 (Methylcobalamin)	
Manganese (Manganese bisglycinate)	
Folate ([6S]-5-methyltetrahydrofolate, glucosamine salt)	
Copper (Cupric bisglycinate)	
Iodine (Potassium iodide)	_
Selenium (Selenium glycinate)	
Vitamin K1 (Phytonadione)	
Molybdenum (Molybdenum bisglycinate)	
Biotin	
Chromium (Chromic bisglycinate, Chromium nicotinate)	•
Vitamin D (Cholecalciferol)	
Zinc (Zinc bisglycinate)	
Non-Medicinal Ingredients: Microcrystalline cellulose hypromellose sunflower legithin magnesium	

**Non-Medicinal Ingredients:** Microcrystalline cellulose, hypromellose, sunflower lecithin, magnesium stearate (vegetable source), silicon dioxide. **Recommended Dose:** Adult Females: Take four capsules per day, two twice a day with meals, or as directed by your health care practitioner. Take a few hours before or after taking other medications.

#### **Complementary Formulas:**

Based on individual needs, consider adding these Designs for Health formulas:

- Sensitol™, if insulin resistance and risk of gestational diabetes is suspected
- OmegAvail™ Ultra DHA
- PaleoFiber® and a probiotic formula for digestive health, immune support and reduced risk of constipation

#### REFERENCE

For a list of references cited in this document, please visit: https://catalog.designsforhealth.com/assets/itemresources/Prenatal Pro References.pdf

Quatrefolic® is covered by U.S. Patent No. 7,947,662 and is a registered trademark of Gnosis S.p.A.

DeltaGold® is a registered trademark of American River Nutrition, LLC and protected by US Patent Numbers 6,350,453 and 8,586,109.

Ferrochel® is a registered trademark of Albion Laboratories, Inc.

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# PRENATAL PRO™

A SUPERIOR PRENATAL FORMULATION WITH HIGH BIOAVAILABILITY AND ANTIOXIDANT PROTECTION
120 VEGETARIAN CAPSULES | NPN80051531 | PRE120-CN

**Prenatal Pro™** is a four-a-day multivitamin/multimineral designed to provide a broad foundation of nutrients to augment and complement an average diet. Its formulation was guided by established Recommended Dietary Allowances (RDAs) and Adequate Intakes (Als), average nutrient consumptions and common insufficiencies in typical Western diets, and intensive support for a healthy pregnancy and optimal fetal development.

Prenatal  $\text{Pro}^{\text{TM}}$  is unique as it contains a blend of gamma and delta-tocotrienols, which are more potent antioxidants than alpha-tocopherol and have unique health benefits. (See the tech sheet for Annatto- $\text{E}^{\text{TM}}$  for details.) It also includes a bioidentical form of folate with superior bioavailability compared to folic acid, which may mitigate effects of common genetic polymorphisms on increased risk of birth defects.

The optimal intake of vitamins and minerals for pregnant women or women trying to conceive is a topic of ongoing research. This includes evaluation of the diet that humans evolved on for millions of years<sup>1-4</sup>, as well as research that proposes to redefine the minimum levels of nutrients that support healthy DNA replication (also referred to as genomic stability). This is relevant to pregnant women's health and to fetal development.<sup>5-8</sup> The newly proposed Australian RDA for folate (700 mcg) is higher than the US RDA (600 mcg dietary folate equivalents) but similar to the estimated average evolutionary intake of dietary folate of 736 mcg.<sup>4</sup>

In addition, beyond nutrient intakes recommended for broad swaths of general populations, it is sensible to take into account clinical status, age, and genetics when estimating required nutrient intakes. For example, as one study points out, polymorphisms related to the folate/homocysteine pathway may contribute to increased risk for a number of pregnancy-related pathologies.<sup>9</sup> The levels of vitamins B2, B6, B12 and folate found in Prenatal Pro™ are adequate for maintaining healthy homocysteine (Hcy) levels for a large section of the population but not for those with single nucleotide polymorphisms in particular Hcy metabolic pathways and/or folate receptor activity.<sup>10-12</sup>

### **HIGHLIGHTS**

**Folate:** provided as Quatrefolic®, a glucosamine salt 5-MTHF form of folate proven to dissociate reliably before absorption and raise plasma folate levels.¹⁴ This form of 5-MTHF is likely more bioavailable than naturally occurring folates because those are covalently bonded to polyglutamate chains.¹⁴ The Quatrefolic® form of folate was shown to be 1.12 times and 9.7 times more bioavailable than the calcium salt of 5-MTHF and folic acid, respectively.¹⁵ Research showed that plasma folate levels were brought above the desired level of 50 nM more quickly with 5-MTHF than with folic acid supplementation. This effect is critical because women with low folate status may first become aware of their pregnancy when fetal cell proliferation and differentiation develop at a fast pace and may already have been negatively impacted by folate deficiency.¹⁶

Folic acid is no longer considered an adequate source of folate for the following reasons: (a) genetic polymorphisms of folate metabolism are common and are responsible for a 35-70% reduced conversion of folic acid to the biological active form, 5-MTHF<sup>14,17</sup> (b) unmetabolized folic acid has been detected in umbilical cord blood at birth<sup>18</sup> (c) synthetic folic acid (derived from fortified foods and/or supplements) may increase the risk of various cancers, reduce natural killer (NK) cell activity, and may have other detrimental effects<sup>17,19</sup> (d) human physiology is adapted to natural folates; folic acid is not a naturally occurring molecule and has a distinct pathway of cell entry and different metabolic transformations compared to natural folates. These differences may be responsible for the detrimental effects associated with folic acid.<sup>17,20</sup>

Adequate folate status was also shown to be relevant to risk of pre-eclampsia, which was reduced by supplementation with 5-MTHF.<sup>21</sup> This may be due to improvement of nitric oxide levels, which would support healthy blood pressure. A study looked at the effect of supplementing pregnant women with 5-MTHF alone, folic acid alone, or 5-MTHF and folic acid combined, on their children's mental abilities at age 8.5 years. Results showed that progeny of mothers supplemented with 5-MTHF had "higher activation of the midcingulate cortex, indicating that early nutrition influences the functionality of specific brain areas involved in executive functions."<sup>22</sup>

**Tocotrienols:** provided as DeltaGold®, a tocopherol-free blend of gamma- and delta-tocotrienols sourced from annatto. Tocotrienols have higher antioxidant activity and unique benefits not observed with tocopherols. See the Annatto- $E^{\text{TM}}$  tech sheet for an extensive discussion of tocotrienol research and the shortcomings of tocopherols.

The safety of ingesting tocotrienols during pregnancy is underscored by the fact that DeltaGold® is "Generally Recognized as Safe," as defined by the US FDA, and by studies where very high doses of tocotrienols were administered to pregnant rats, which showed no adverse effects.<sup>23,24</sup>

Administration of tocotrienols to pregnant animals has shown protective effects against embryonic malformations by nicotine<sup>25</sup>, improvement in cognitive function in male offspring of rats<sup>26</sup> and prevention of fetal loss in female rats mated with corticosterone-treated males.<sup>27</sup> These results are confirmed by studies in which tocotrienols were added to mouse embryos in vitro and were shown to protect against adverse effects from nicotine or corticosterone treatment.<sup>28, 29</sup> Additionally, a rodent study showed that tocotrienol supplementation reduces corticosterone and noradrenaline levels in rats exposed to restraint stress.<sup>30</sup> Tocotrienols were shown in vitro to mitigate detrimental effects from methylmercury exposure.<sup>49</sup> This effect may be protective to the mother and to the fetal brain, where tocotrienols are deposited upon their supplementation.<sup>31</sup>

Tocotrienols are not easily found in common diets and their assimilation is impaired by concurrent consumption of tocopherols. Thus, tocopherols are not included in Prenatal  $Pro^{TM}$ , as the RDA for alpha-tocopherol can easily be obtained through the consumption of nuts, seeds, avocado, various vegetable oils and various animal foods.

**Vitamin D:** The amount included in this product is intended to be augmented by endogenously synthesized vitamin D from sun exposure and/or supplementation using one of Designs for Health's vitamin D formulas, as guided by blood levels. The majority of these formulas also provide significant amounts of vitamins K1 and K2, which work in synergy with vitamin D.

**Vitamin K:** Prenatal  $Pro^{TM}$  provides the RDA for vitamin K1, which was derived solely based on optimizing blood clotting. However, this level of intake may not ensure the support of optimal health for mother and child. New research shows that higher levels of vitamin K1 are required to support this nutrient's role in bone metabolism, arterial health and more (via conversion to vitamin K2). See the tech sheets for Vitamin D Supreme and  $Tri-K^{TM}$ , and the Vitamin K chapter in the Textbook of Natural Medicine for more information. Additional vitamin K may be derived from DFH formulas containing vitamins D and K.

**Vitamin B6:** provided in the naturally occurring phosphorylated form, pyridoxal-5-phosphate.

Vitamin B12: provided in the naturally occurring methylcobalamin form, which is safer and more

bioavailable than cyanocobalamin, commonly used in many prenatals. If higher doses of B12 are necessary, consider the DFH formula Tricobalamin™. See the Tricobalamin™ tech sheet for a detailed description of vitamin B12 metabolism, bioavailability issues and when to consider dosing vitamin B12 at levels above the RDA.

**Vitamin C:** provided as 400 mg ascorbic acid. This is higher than the RDA and higher than the amount provided by most prenatal formulas because average consumption of vitamin C from food in the US (94 mg<sup>35</sup>) is well below the estimated evolutionary intake (approx. 541 mg), owing to generally low intake of fresh fruits and vegetables. The important role of vitamin C in human physiology is especially relevant to the demands of a healthy pregnancy. It is an antioxidant and essential for optimal immune response, collagen biosynthesis, catecholamine metabolism, and dietary iron absorption.<sup>33</sup> In turn, poor collagen renewal results in impaired integrity of the skin, mucous membranes, blood vessels, and bone.<sup>34</sup> The RDA for vitamin C prevents only the extreme deficiency that results in scurvy; it does not provide for optimal health, so a higher intake is prudent.<sup>33</sup>

**Vitamin A:** The vitamin A in this product consists of a natural carotenoid mix from palm oil plus pre-formed vitamin A (as retinyl palmitate) for those that have impaired conversion of carotenoids to vitamin A. The majority of vitamin A sources in the Paleolithic diet were derived from plant-sourced carotenoids rather than pre-formed vitamin A.<sup>4</sup> Ideally, most vitamin A should be derived from a diet high in vegetables and fruits that provide carotenoids with vitamin A activity.

Mineral Chelates: The minerals chosen for Prenatal Pro™ offer superior absorption compared to minerals typically found in prenatal multivitamins. Zinc, manganese, molybdenum, and chromium are provided as highly bioavailable chelates. Mineral chelates do not depend on stomach acid for liberation and may be more effective for those with hypochlorhydria or other conditions that impair mineral absorption. Chelated minerals are designed to bypass obstacles to absorption and assimilation, such as food phytates, oxalates, fiber, ionic minerals or even medications that interfere with mineral absorption. Chelates are better tolerated and absorbed and are less likely to cause loose stools or other gastrointestinal discomfort.<sup>35</sup>

Magnesium, Calcium, Iron and Choline: Included at levels below the RDA because this formula is designed based on average intakes of the respective nutrients and to allow for more flexible and individualized regimens. The RDA for calcium is 1000 mg for pregnant women, while average calcium intake in women of reproductive age is 859 mg/day<sup>35</sup>, thus the difference of 140 mg is provided by Prenatal Pro™. The same rationale was applied to magnesium: the RDA is 360 mg but average dietary intake is estimated to be 281 mg.<sup>35</sup> The 80 mg of magnesium provided by Prenatal Pro™ makes up for this shortfall.

Calcium, magnesium, iron and choline may be derived from the diet and/or from DFH formulas such as OsteoForce™, OsteoForce™ Supreme, Osteoben®, various mineral formulas that provide standalone calcium or magnesium, Ferrochel® iron chelate, Phosphatidylcholine, GPC or XanthOmega™ Krill Oil.

Chelated Iron: (as Ferrochel® ferrous bisglycinate chelate) was chosen due to its high bioavailability and tolerability. The chelated form will not result in the constipation commonly induced by iron supplementation. Average intake of iron by women of reproductive age in the US is 14 mg/day with a range of 7.3–22.3 mg/day.³⁵ The value of 13 mg of iron chosen for this formula was derived as the difference between the RDA (27 mg) and this estimated average intake. It also ensures that the upper range of iron intake plus the amount in Prenatal Pro™ falls within a safe margin of 45 mg (the upper tolerable level of iron intake). Well-balanced diets, such as a Paleo-style diet, provide iron in the range of 17–22 mg/day. One study found that supplementation with iron bisglycinate chelate resulted in double the absorption compared to ferrous sulfate when taken with breakfast. This form of iron partially prevented the inhibitory effect of phytates, had low interactions with food, and showed high solubility in aqueous solutions even at a pH 6.³⁶

**Zinc:** This mineral is involved in a multitude of basic biochemical functions. Zinc deficiency is known to have adverse clinical impacts on the epidermal, gastrointestinal, immune, skeletal, reproductive and central nervous systems.<sup>37</sup>