



(86) 1993/09/21

(87) 1994/03/31

(45) 2001/05/01

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(51) Int.Cl.⁶ A61K 33/24, A61K 33/18, A61K 33/06

(30) 1992/09/23 (07/949,213) US

(54) **SUPPLEMENT DE MULTI-VITAMINES ET DE MINERAUX
POUR LES FEMMES ENCEINTES**

(54) **MULTI-VITAMIN AND MINERAL SUPPLEMENT FOR
PREGNANT WOMEN**

(57) Complément multivitaminé et minéral destiné à être administré à une femme enceinte pendant le premier trimestre, le second trimestre et le troisième trimestre de sa grossesse, comprenant des dosages spécifiques d'un composé de calcium pharmaceutiquement acceptable, de la vitamine D, de l'acide folique, la vitamine B₁₂, la vitamine B₆ et la vitamine B₁. Le complément pré-natal est spécifique pour maximaliser le développement du fœtus et assurer la bonne santé de la mère pendant chaque trimestre de la grossesse.

(57) Multi-vitamin and mineral supplements for administration to a pregnant woman during her first, second, and third trimesters of pregnancy are provided herein. These supplements include specific regimens of a pharmaceutically-acceptable calcium compound, vitamin D, folic acid, vitamin B₁₂, vitamin B₆, and vitamin B₁. The prenatal supplements are specifically tailored to maximize fetal development and maternal health during each trimester of pregnancy.

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Abstract

Multi-vitamin and mineral supplements for administration to a pregnant woman during her first, second, and third trimesters of pregnancy are provided herein. These supplements include specific regimens of a pharmaceutically-acceptable calcium compound, vitamin D, folic acid, vitamin B₁₂, vitamin B₆, and vitamin B₁. The prenatal supplements are specifically tailored to maximize fetal development and maternal health during each trimester of pregnancy.

(a) TITLE OF THE INVENTION

MULTI-VITAMIN AND MINERAL SUPPLEMENT FOR PREGNANT WOMEN

(b) TECHNICAL FIELD TO WHICH THE INVENTION RELATES

The present invention relates to multi-vitamin and mineral supplements, and particularly to novel multi-vitamin and mineral supplements for administration during pregnancy.

(c) BACKGROUND ART

Vitamin and mineral preparations are commonly administered to treat specific medical conditions or as general nutritional supplements. Recent studies have elucidated the important physiological roles played by vitamins and minerals, and established a correlation between deficiencies or excesses of these nutrients and the etiologies of certain disease states in humans. See, e.g., Diplock, "Antioxidant Nutrients and disease Prevention: An Overview, " Am. J. Clin. Nutr., 53:189-193 (1991); Documenta Geigy Scientific Tables, 457-497 (Diem and Cemtuer eds., 7th ed., 1975).

It has further become recognized that various groups of the human population require different quantities and types of vitamins and minerals to prevent or alleviate diseases, as well as to other essential nutrients during the third trimester of fetal development when such nutrients are most needed, and may provide excessive levels of other nutrients during the first and second trimesters when such dosage levels are unneeded and perhaps even harmful. For example, the excessive presence of iron in conventional prenatal supplements often produces stomach upset in the mother during the first trimester of fetal growth, when morning sickness is most pronounced.

(d) DESCRIPTION OF THE INVENTION

It would therefore be desirable to provide a prenatal multi-vitamin and mineral supplement which overcomes the aforementioned deficiencies of the prior art.

The present invention provides multi-vitamin and mineral supplements which are specifically tailored for administration during the first, second, and third trimesters of pregnancy. The formulations of aspects of the invention have been found to maximize the

benefit of vitamin and mineral supplementation both for the developing fetus and the mother, while concurrently minimizing the undesirable side effects characteristic of known prenatal nutritional supplements.

The compositions of various aspects of the invention include certain essential nutritional components in dosage levels which have been found to optimize fetal development and maintain the mother's health during each of the trimesters of pregnancy.

The invention is based on the discovery that prenatal multi-vitamin and mineral supplements can be provided which are specifically tailored for administration during each of the trimesters of pregnancy. The products of aspects of the invention provide optimum nutritional components and amounts which have been found to benefit fetal growth and the mother's health throughout pregnancy, while concurrently minimizing the undesired side effects of conventional unitary formulations.

By a first broad aspect of this invention, a multi-vitamin and mineral supplement is provided for administration to a pregnant woman during her first trimester of pregnancy, which comprises from 200 mg to 300 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 350 I.U. to 450 I.U. of vitamin D, from 0.5 mg to 1.5 mg of folic acid; from 5 mcg to 10 mcg of vitamin B₁₂, from 12 mg to 20 mg of vitamin B₆, and from 1.0 mg to 2.0 mg of vitamin B₁.

By a first variant of this first broad aspect of this invention, the pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.

By a second variant of this first broad aspect of this invention, and/or the above variant thereof, the multi-vitamin and mineral supplement further comprises from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 375 I.U. to 425 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 7 mcg to 9 mcg of vitamin B₁₂, from 14 mg to 18 mg of vitamin B₆, and from 1.3 mg to 1.7 mg of vitamin B₁.

By a third variant of this first broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement further comprises from 10 mg to 40 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable

magnesium compound. By a first variation thereof, the pharmaceutically-acceptable magnesium compound comprises magnesium stearate.

By a fourth variant of this first broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement comprises from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 375 I.U. to 425 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 7 mcg to 9 mcg of vitamin B₁₂, from 14 mg to 18 mg of vitamin B₆; and from 1.3 mg to 1.7 mg of vitamin B₁, and the supplement further comprises up to 4500 I.U. of beta carotene, up to 30 mg of vitamin E, up to 3.7 mg of vitamin B₂, up to 20 mg of vitamin B₃, up to 100 mg of vitamin C, up to 80 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound, up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and up to 40 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

By a fifth variant of this first broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement of claim 1 or claim 2, which comprises from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 375 I.U. to 425 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 7 mcg to 9 mcg of vitamin B₁₂, from 14 mg to 18 mg of vitamin B₆, from 1.3 mg to 1.7 mg of vitamin B₁, and the supplement further comprises from 3500 I.U. to 4500 I.U. of beta carotene, from 20 mg to 30 mg of vitamin E, from 3 mg to 3.7 mg of vitamin B₂, from 10 mg to 20 mg of vitamin B₃, from 60 mg to 100 mg of vitamin C, from 50 mg to 80 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound, from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, from 0.5 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and from 20 mg to 30 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound. By

a first variation thereof, the pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film-forming material which permits release of the ferrous sulphate in the intestine of a woman administered the supplement. By a second variation thereof, the pharmaceutically-acceptable copper compound comprises cupric oxide. By a third variation thereof, the pharmaceutically-acceptable iodine compound comprises potassium iodide. By a fourth variation thereof, the pharmaceutically-acceptable zinc compound comprises zinc sulphate.

By a second aspect of this invention, a multi-vitamin and mineral supplement is provided for administration to a pregnant woman during her second trimester of pregnancy, which comprises from 275 mg to 375 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 400 I.U. to 500 I.U. of vitamin D; from 0.5 mg to 1.5 mg of folic acid, from 7 mcg to 12 mcg of vitamin B₁₂, from 14 mg to 22 mg of vitamin B₆, and from 1.1 mg to 2.1 mg of vitamin B₁.

By a first variant of this second aspect of the invention, the pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.

By a second variant of this second aspect of the invention, and/or the above variant thereof, the multi-vitamin and mineral supplement comprises from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 425 I.U. to 475 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 9 mcg to 11 mcg of vitamin B₁₂, from 16 mg to 20 mg of vitamin B₆, and from 1.4 mg to 1.8 mg of vitamin B₁.

By a third variant of this second aspect of the invention, and/or the above variants thereof, the multi-vitamin and mineral supplement further comprises from 35 mg to 65 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound. By a first variation thereof, the pharmaceutically-acceptable magnesium compound comprises magnesium stearate.

By a fourth variant of this second aspect of the invention, and/or the above variants thereof, the multi-vitamin and mineral supplement comprises from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound,

from 425 I.U. to 475 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 9 mcg to 11 mcg of vitamin B₁₂, from 16 mg to 20 mg of vitamin B₆, from 1.4 mg to 1.8 mg of vitamin B₁, and the supplement further comprises up to 5500 I.U. of beta carotene, up to 35 mg of vitamin E, up to 4 mg of vitamin B₂, up to 20 mg of vitamin B₃, up to 120 mg of vitamin C, up to 100 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound, up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and up to 65 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

By a fifth variant of this second aspect of the invention, and/or the above variants thereof, the multi-vitamin and mineral supplement comprises from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 425 I.U. to 475 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 9 mcg to 11 mcg of vitamin B₁₂, from 16 mg to 20 mg of vitamin B₆, from 1.4 mg to 1.8 mg of vitamin B₁, and the supplement further comprises from 4500 I.U. to 5500 I.U. of beta carotene, from 25 mg to 35 mg of vitamin E, from 3.3 mg to 4 mg of vitamin B₂, from 14 mg to 22 mg of vitamin B₃, from 80 mg to 120 mg of vitamin C, from 65 mg to 95 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound, from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, from 0.5 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and from 45g to 55 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

By a sixth variant of this second aspect of the invention, and/or the above variants thereof, the pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film-forming material which permits release of the ferrous sulphate in the intestine of a woman administered the supplement.

By a seventh variant of this second aspect of the invention, and/or the above variants thereof, the pharmaceutically-acceptable copper compound comprises cupric oxide.

By an eighth variant of this second aspect of the invention, and/or the above variants thereof, the pharmaceutically-acceptable iodine compound comprises potassium iodide.

By a ninth variant of this second aspect of the invention, and/or the above variants thereof, the pharmaceutically-acceptable zinc compound comprises zinc sulphate.

By a third broad aspect of this invention, a multi-vitamin and mineral supplement is provided for administration to a pregnant woman during her third trimester of pregnancy, which comprises from 450 mg to 550 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 450 I.U. to 550 I.U. of vitamin D, from 0.5 mg to 1.5 mg of folic acid, from 9 mcg to 14 mcg of vitamin B₁₂, from 16 mg to 24 mg of vitamin B₆; and from 1.2 mg to 2.2 mg of vitamin B₁.

By a first variant of this third broad aspect of this invention, the pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.

By a second variant of this third broad aspect of this invention, and/or the above variant thereof, the multi-vitamin and mineral supplement comprises from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 475 I.U. to 525 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 11 mcg to 13 mcg of vitamin B₁₂, from 18 mg to 22 mg of vitamin B₆, and from 1.5 mg to 1.9 mg of vitamin B₁.

By a third variant of this third broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement further comprises from 85 mg to 115 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound. By a first variation thereof the pharmaceutically-acceptable magnesium compound comprises magnesium stearate.

By a fourth variant of this third broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement comprises from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 475 I.U. to 525 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 11 mcg to 13 mcg of vitamin B₁₂, from 18 mg to 22 mg of vitamin B₆, from 1.5

mg to 1.9 mg of vitamin B₁, and the supplement further comprises up to 6500 I.U. of beta carotene, up to 40 mg of vitamin E, up to 4.3 mg of vitamin B₂, up to 22 mg of vitamin B₃, up to 140 mg of vitamin C, up to 120 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound, up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and up to 115 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

By a fifth variant of this third broad aspect of this invention, and/or the above variants thereof, the multi-vitamin and mineral supplement comprises from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 475 I.U. to 525 I.U. of vitamin D, from 0.75 mg to 1.25 mg of folic acid, from 11 mcg to 13 mcg of vitamin B₁₂, from 18 mg to 22 mg of vitamin B₆, from 1.5 mg to 1.9 mg of vitamin B₁, and the supplement further comprises from 5500 I.U. to 6500 I.U. of beta carotene, from 30 mg to 40 mg of vitamin E, from 3.6 mg to 4.3 mg of vitamin B₂, from 16 mg to 24 mg of vitamin B₃, from 100 mg to 140 mg of vitamin C, from 85 mg to 115 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound; from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound, from 0.05 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound, from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound, and from 95 mg to 105 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

By a sixth variant of this third broad aspect of this invention, and/or the above variants thereof, the pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film forming material which permits release of the ferrous sulphate in the intestine of a woman administered the supplement.

By a seventh variant of this third broad aspect of this invention, and/or the above variants thereof, the pharmaceutically-acceptable copper compound comprises cupric oxide.

By an eighth variant of this third broad aspect of this invention, and/or the above variants thereof, the pharmaceutically-acceptable iodine compound comprises potassium iodide.

By a ninth variant of this third broad aspect of this invention, and/or the above variants thereof, the pharmaceutically-acceptable zinc compound comprises zinc sulphate.

By a fourth broad aspect of this invention, a multi-vitamin and mineral system is provided for administration to a pregnant woman, which comprises (A) a multi-vitamin and mineral supplement for administration to a pregnant woman during her first trimester of pregnancy, that supplement comprising from 200 mg to 300 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 350 I.U. to 450 I.U. of vitamin D, from 0.5 mg to 1.5 mg of folic acid, from 5 mcg to 10 mcg of vitamin B₁₂, from 12 mg to 20 mg of vitamin B₆, and from 1.0 mg to 2.0 mg of vitamin B₁; (B) a multi-vitamin and mineral supplement for administration to a pregnant woman during her second trimester of pregnancy, that supplement comprising from 275 mg to 375 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 400 I.U. to 500 I.U. of vitamin D, from 0.5 mg to 1.5 mg of folic acid, from 7 mcg to 12 mcg of vitamin B₁₂, from 14 mg to 22 mg of vitamin B₆,; and from 1.1 mg to 2.1 mg of vitamin B₁; and (C) a multi-vitamin and mineral supplement for administration to a pregnant woman during her third trimester of pregnancy, that supplement comprising from 450 mg to 550 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound, from 450 I.U. to 550 I.U. of vitamin D, from 0.5 mg to 1.5 mg of folic acid, from 9 mcg to 14 mcg of vitamin B₁₂, from 16 mg to 24 mg of vitamin B₆, and from 1.2 mg to 2.2 mg of vitamin B₁.

By a fifth broad aspect of this invention, a product is provided for providing a vitamin and nutrient supplement regimen to pregnant women comprising a first formulation comprising a first mixture of vitamins and minerals wherein the amounts of vitamins and minerals in the first mixture optimize fetal development and maintain the mother's health during the first trimester of pregnancy, a second formulation comprising a second mixture of vitamins and minerals wherein the amounts of vitamins and minerals in the second mixture optimize fetal development and maintain the mother's health during the second trimester of pregnancy, and a third formulation comprising a third mixture of vitamins and

minerals wherein the amounts of vitamins and minerals in the third mixture optimize fetal development and maintain the mother's health during the third trimester of pregnancy.

By a first variant of this fifth broad aspect of the invention, the second formulation contains more calcium, iron, magnesium, vitamin C and vitamin D than the first formulation, and wherein the third formulation contains more calcium, iron, magnesium, vitamin C and vitamin D than the second formulation.

Each of the above prenatal nutritional formulations of aspects of the invention may be administered in any conventional pharmaceutical delivery system, with or without additional nutritional components as described in further detail below.

If desired, the products of aspects of the invention may be conveniently marketed as a prenatal multi-vitamin and mineral system which comprises the three distinct multi-vitamin and mineral supplements described above. The prenatal multi-vitamin and mineral system contemplated by broad aspects of the invention includes means for permitting the pregnant woman to differentiate between the formulations for administration during the first, second, and third trimesters.

Useful pharmaceutically-acceptable calcium compounds include any of the well-known calcium supplements, e.g., calcium carbonate, calcium sulphate, calcium oxide, calcium hydroxide, calcium apatite, calcium citrate-malate, bone meal, oyster shell, calcium gluconate, calcium lactate, calcium phosphate, calcium levulinate, and the like. Preferably, calcium compounds selected from the group consisting of calcium carbonate, calcium sulfate, and mixtures thereof are employed.

The first trimester multi-vitamin and mineral supplement of aspects of the invention may include additional nutritional components well-known in the art. For example, the supplement may include from 10 mg to 40 mg of elemental magnesium, in the form of one or more pharmaceutically-acceptable magnesium compounds, e.g., magnesium stearate, magnesium carbonate, magnesium oxide, magnesium hydroxide, and magnesium sulphate. Magnesium stearate is preferred.

When a prenatal supplement having additional nutritional components is provided as described above, the pharmaceutically-acceptable iron compound may be selected from any of the well-known iron II (ferrous) or iron III (ferric) supplements, e.g., ferrous sulphate, ferric chloride, ferrous gluconate, ferrous lactate, ferrous tartrate, iron-sugar-carboxylate

complexes, ferrous fumarate, ferrous succinate, ferrous glutamate, ferrous citrate, ferrous pyrophosphate, ferrous cholinisocitrate, and ferrous carbonate.

Preferably, the iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which has been coated with a pharmaceutically-acceptable, film-forming material which permits release of the ferrous sulphate in the intestine of a woman administered the supplement. Suitable coatings include any material known in the art for forming enteric, controlled-release, or sustained-release coatings, e.g., cellulose ethers including hydroxypropyl methylcellulose, methylcellulose, ethylcellulose, and carboxymethylcellulose; cellulose esters, e.g., cellulose acetate, cellulose acetate phthalate, and cellulose nitrate; and acrylate and methacrylate copolymers. The coated iron compound has been found to provide increased iron bioavailability by minimizing interaction between the iron compound and divalent cations, e.g., calcium, in the prenatal supplement. As iron is believed to be a cause of morning sickness, release of the iron in the intestine also minimizes stomach upset.

In a preferred embodiment of the first trimester formulation, the vitamin C and folic acid nutritional components are also coated to provide controlled release.

The first trimester multi-vitamin and mineral supplement may contain a pharmaceutically-acceptable copper compound in the form of cupric oxide, cupric sulphate, or cupric gluconate, with cupric oxide being preferred. Preferred pharmaceutically-acceptable iodine compounds include sodium iodide or potassium iodide, with potassium iodide being most preferred. Useful pharmaceutically-acceptable zinc compounds include zinc sulphate, zinc chloride, and zinc oxide, with zinc sulphate being preferred.

Useful pharmaceutically-acceptable calcium compounds for this second trimester formulation include the calcium salts listed above, again preferably selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.

The second trimester formulation may similarly include other nutritional agents known in the art. For example, this aspect of the invention contemplates the optional addition to the second trimester formulation of from 35 mg to 65 mg of elemental magnesium, in the form of a pharmaceutically-acceptable magnesium compound as listed above, preferably magnesium stearate.

Preferred pharmaceutically-acceptable compounds for the second trimester formulation are the same as described above with respect to the first trimester formulation. Also, the iron, vitamin C, and folic acid components are again preferably provided with a controlled-release coating.

Pharmaceutically-acceptable calcium compounds for this second trimester formulation include those salts enumerated above, again preferably selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.

Preferred pharmaceutically-acceptable compounds for this third trimester formulation are the same as described above with respect to the first trimester composition. Again, the iron, vitamin C, and folic acid components are preferably coated with a suitable controlled-release film forming material.

The third trimester formulation may optionally be provided in multiple dosage units, to facilitate administration of the increased levels of nutrients.

The nutritional supplements provided by aspects of the invention may therefore be marketed together as a single product, which will facilitate compliance with the administration of the proper formulation, thereby enhancing the benefits achieved by the products of aspects of the invention. The formulations for trimesters one, two, and three may be differentiated by any conventional means known in the pharmaceutical art. For example, different coloured tablets may be provided; tablets may be scored with appropriate markings; and/or distinct packaging may be used to distinguish each formulation.

The nutritional supplements of aspects of the invention may be provided in any suitable dosage form known in the art. For example, the compositions may be incorporated into tablets, powders, granules, beads, chewable lozenges, capsules, liquids, or similar conventional dosage forms, using conventional equipment and techniques known in the art. Tablet dosage forms are preferred.

When preparing dosage forms incorporating the compositions of aspects of the invention, the nutritional components are normally blended with conventional excipients, e.g., binders, including gelatin, and pregelatinized starch, lubricants, e.g., hydrogenated vegetable oil, and stearic acid; diluents, e.g., lactose, mannose, and sucrose; disintegrants, e.g., carboxymethyl cellulose and sodium starch glycolate; suspending agents, e.g.,

povidone, and polyvinyl alcohol; absorbents, e.g., silicon dioxide; preservatives, e.g., methylparaben, propylparaben, and sodium benzoate; surfactants, e.g., sodium lauryl sulphate and , POLYSORBATE_{TM} 80; and colourants, e.g., F. D. & C dyes.

All of the products of aspects of the invention have been found to provide optimal nutritional supplementation for a developing fetus and mother during the first, second, and third trimesters of fetal development. For example, the third trimester composition includes increased amounts of calcium, which is crucial for bone development in the fetus during the third trimester. The reduced iron content of the first trimester formulation has been found to avoid stomach upset in the mother during the first trimester, unlike conventional prenatal supplements. Levels of beta carotene and vitamin D and certain of the other components are gradually increased in the first, second, and third trimester formulations, in correlation with the increasing need for these nutritional components as the pregnancy progresses. The compositions of aspects of this invention are also formulated to optimize fetal nerve tissue growth and development during the latter half of the second trimester and the third trimester.

All of the aforementioned benefits are achieved without wasting vitamin and mineral materials, as characteristic of unitary prenatal supplements of the prior art. This makes the products of aspects of the invention more cost effective than conventional prenatal supplements.

Although the products of aspects of this invention are preferably intended for administration to humans, it will be understood that the formulations may also be utilized in veterinary therapies for other animals.

(e) AT LEAST ONE MODE FOR CARRYING OUT THE INVENTION

The following example is given to illustrate an embodiment of this invention but is not deemed to be limiting thereof. All amounts specified in the application are based on milligrams unless otherwise indicated. The term "I.U." represents International Units.

Example

Preparation of Prenatal Multi-Vitamin and Mineral Supplements

The following compositions were used to prepare multi-vitamin and mineral supplements for administration during the first, second, and third trimesters of pregnancy:

<u>Component</u>	<u>Trimester I</u>	<u>Trimester II</u>	<u>Trimester III</u>
Beta Carotene, I.U.	4000	5000	6000
Vitamin D, I.U.	400	450	500
Vitamin E, mg	25	30	35
Vitamin B ₁ , mg	1.5	1.6	1.7
Vitamin B ₂ , mg	3.4	3.7	4.0
Vitamin B ₃ , mg	16	18	20
Vitamin B ₅ , mg	16	18	20
Vitamin B ₁₂ , mcg	8	10	12
Vitamin C, mg	80	100	120
Folic Acid, mg	1	1	1
Calcium, mg	250	325	500
Iron, mg	65	80	100
Copper, mg	2	2	2
Iodine, mg	0.15	0.15	0.15
Zinc, mg	20	20	20
Magnesium, mg	25	50	100

Tablets incorporating the above formulations were prepared using conventional procedures and materials known in the pharmaceutical art. The resulting prenatal supplement tablets were recovered and stored for future use.

Claims

1. A multi-vitamin and mineral supplement for administration to a pregnant woman during her first trimester of pregnancy, which comprises:
 - (a) from 200 mg to 300 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 350 I.U. to 450 I.U. of vitamin D;
 - (c) from 0.5 mg to 1.5 mg of folic acid;
 - (d) from 5 mcg to 10 mcg of vitamin B₁₂;
 - (e) from 12 mg to 20 mg of vitamin B₆; and
 - (f) from 1.0 mg to 2.0 mg of vitamin B₁.
2. The multi-vitamin and mineral supplement of claim 1, wherein the pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.
3. The multi-vitamin and mineral supplement of claim 1 or claim 2, which further comprises:
 - (a) from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 375 I.U. to 425 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 7 mcg to 9 mcg of vitamin B₁₂;
 - (e) from 14 mg to 18 mg of vitamin B₆; and
 - (f) from 1.3 mg to 1.7 mg of vitamin B₁.
4. The multi-vitamin and mineral supplement of claim 1, claim 2 or claim 3, which further comprises from 10 mg to 40 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.
5. The multi-vitamin and mineral supplement of claim 4, wherein the pharmaceutically-acceptable magnesium compound comprises magnesium stearate.

6. The multi-vitamin and mineral supplement of claim 1 or claim 2, which comprises:
- (a) from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 375 I.U. to 425 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 7 mcg to 9 mcg of vitamin B₁₂;
 - (e) from 14 mg to 18 mg of vitamin B₆; and
 - (f) from 1.3 mg to 1.7 mg of vitamin B₁;
- and said supplement further comprises
- (g) up to 4500 I.U. of beta carotene;
 - (h) up to 30 mg of vitamin E;
 - (i) up to 3.7 mg of vitamin B₂;
 - (j) up to 20 mg of vitamin B₃;
 - (k) up to 100 mg of vitamin C;
 - (l) up to 80 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;
 - (m) up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;
 - (n) up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;
 - (o) up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and
 - (p) up to 40 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.
7. The multi-vitamin and mineral supplement of claim 1 or claim 2, which comprises:
- (a) from 225 mg to 275 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 375 I.U. to 425 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;

- (d) from 7 mcg to 9 mcg of vitamin B₁₂;
 - (e) from 14 mg to 18 mg of vitamin B₆;
 - (f) from 1.3 mg to 1.7 mg of vitamin B₁;
- and said supplement further comprises
- (g) from 3500 I.U. to 4500 I.U. of beta carotene;
 - (h) from 20 mg to 30 mg of vitamin E;
 - (i) from 3 mg to 3.7 mg of vitamin B₂;
 - (j) from 10 mg to 20 mg of vitamin B₃;
 - (k) from 60 mg to 100 mg of vitamin C;
 - (l) from 50 mg to 80 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;
 - (m) from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;
 - (n) from 0.5 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;
 - (o) from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and
 - (p) from 20 mg to 30 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

8. The multi-vitamin and mineral supplement of claim 7, wherein said pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film-forming material which permits release of said ferrous sulphate in the intestine of a woman administered the supplement.

9. The multi-vitamin and mineral supplement of claim 7 or claim 8, wherein said pharmaceutically-acceptable copper compound comprises cupric oxide.

10. The multi-vitamin and mineral supplement of claim 7, claim 8 or claim 9, wherein said pharmaceutically-acceptable iodine compound comprises potassium iodide.

11. A multi-vitamin and mineral supplement of any one of claims 7 to 10, wherein said pharmaceutically-acceptable zinc compound comprises zinc sulphate.
12. A multi-vitamin and mineral supplement for administration to a pregnant woman during her second trimester of pregnancy, which comprises:
 - (a) from 275 mg to 375 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 400 I.U. to 500 I.U. of vitamin D;
 - (c) from 0.5 mg to 1.5 mg of folic acid;
 - (d) from 7 mcg to 12 mcg of vitamin B₁₂;
 - (e) from 14 mg to 22 mg of vitamin B₆; and
 - (f) from 1.1 mg to 2.1 mg of vitamin B₁.
13. The multi-vitamin and mineral supplement of claim 12, wherein said pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.
14. The multi-vitamin and mineral supplement of claim 12 or claim 13, which comprises:
 - (a) from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 425 I.U. to 475 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 9 mcg to 11 mcg of vitamin B₁₂;
 - (e) from 16 mg to 20 mg of vitamin B₆; and
 - (f) from 1.4 mg to 1.8 mg of vitamin B₁.
15. The multi-vitamin and mineral supplement of claim 12, claim 13 or claim 14, which further comprises from 35 mg to 65 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

16. The multi-vitamin and mineral supplement of claim 15, wherein said pharmaceutically-acceptable magnesium compound comprises magnesium stearate.
17. The multi-vitamin and mineral supplement of any one of claims 12 to 16, which comprises:
- (a) from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 425 I.U. to 475 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 9 mcg to 11 mcg of vitamin B₁₂;
 - (e) from 16 mg to 20 mg of vitamin B₆;
 - (f) from 1.4 mg to 1.8 mg of vitamin B₁;
- and said supplement further comprises
- (g) up to 5500 I.U. of beta carotene;
 - (h) up to 35 mg of vitamin E;
 - (i) up to 4 mg of vitamin B₂;
 - (j) up to 20 mg of vitamin B₃;
 - (k) up to 120 mg of vitamin C;
 - (l) up to 100 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;
 - (m) up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;
 - (n) up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;
 - (o) up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and
 - (p) up to 65 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.
18. The multi-vitamin and mineral supplement of any one of claims 12 to 16, which comprises:

- (a) from 300 mg to 350 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 425 I.U. to 475 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 9 mcg to 11 mcg of vitamin B₁₂;
 - (e) from 16 mg to 20 mg of vitamin B₆;
 - (f) from 1.4 mg to 1.8 mg of vitamin B₁;
- and said supplement further comprises
- (g) from 4500 I.U. to 5500 I.U. of beta carotene;
 - (h) from 25 mg to 35 mg of vitamin E;
 - (i) from 3.3 mg to 4 mg of vitamin B₂;
 - (j) from 14 mg to 22 mg of vitamin B₃;
 - (k) from 80 mg to 120 mg of vitamin C;
 - (l) from 65 mg to 95 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;
 - (m) from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;
 - (n) from 0.05 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;
 - (o) from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and
 - (p) from 45g to 55 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

19. The multi-vitamin and mineral supplement of any one of claims 12 to 18, wherein said pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film-forming material which permits release of said ferrous sulphate in the intestine of a woman administered the supplement.

20. The multi-vitamin and mineral supplement of any one of claims 12 to 19, wherein said pharmaceutically-acceptable copper compound comprises cupric oxide.
21. The multi-vitamin and mineral supplement of any one of claims 12 to 20, wherein said pharmaceutically-acceptable iodine compound comprises potassium iodide.
22. The multi-vitamin and mineral supplement of any one of claims 12 to 21, wherein said pharmaceutically-acceptable zinc compound comprises zinc sulphate.
23. A multi-vitamin and mineral supplement for administration to a pregnant woman during her third trimester of pregnancy, which comprises:
 - (a) from 450 mg to 550 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 450 I.U. to 550 I.U. of vitamin D;
 - (c) from 0.5 mg to 1.5 mg of folic acid;
 - (d) from 9 mcg to 14 mcg of vitamin B₁₂;
 - (e) from 16 mg to 24 mg of vitamin B₆; and
 - (f) from 1.2 mg to 2.2 mg of vitamin B₁.
24. The multi-vitamin and mineral supplement of claim 23, wherein said pharmaceutically-acceptable calcium compound is selected from the group consisting of calcium carbonate, calcium sulphate, and mixtures thereof.
25. The multi-vitamin and mineral supplement of claim 23 or claim 24, which comprises:
 - (a) from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (b) from 475 I.U. to 525 I.U. of vitamin D;
 - (c) from 0.75 mg to 1.25 mg of folic acid;
 - (d) from 11 mcg to 13 mcg of vitamin B₁₂;
 - (e) from 18 mg to 22 mg of vitamin B₆; and

- (f) from 1.5 mg to 1.9 mg of vitamin B₁.

26. The multi-vitamin and mineral supplement of claim 23, claim 24 or claim 25, which further comprises from 85 mg to 115 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

27. The multi-vitamin and mineral supplement of claim 26, wherein said pharmaceutically-acceptable magnesium compound comprises magnesium stearate.

28. The multi-vitamin and mineral supplement of any one of claims 23 to 27, which comprises:

(a) from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;

(b) from 475 I.U. to 525 I.U. of vitamin D;

(c) from 0.75 mg to 1.25 mg of folic acid;

(d) from 11 mcg to 13 mcg of vitamin B₁₂;

(e) from 18 mg to 22 mg of vitamin B₆;

(f) from 1.5 mg to 1.9 mg of vitamin B₁;

and said supplement further comprises

(g) up to 6500 I.U. of beta carotene;

(h) up to 40 mg of vitamin E;

(i) up to 4.3 mg of vitamin B₂;

(j) up to 22 mg of vitamin B₃;

(k) up to 140 mg of vitamin C;

(l) up to 120 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;

(m) up to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;

(n) up to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;

(o) up to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and

(p) up to 115 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound.

29. The multi-vitamin and mineral supplement of any one of claims 23 to 27, which comprises:

(a) from 475 mg to 525 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;

(b) from 475 I.U. to 525 I.U. of vitamin D;

(c) from 0.75 mg to 1.25 mg of folic acid;

(d) from 11 mcg to 13 mcg of vitamin B₁₂;

(e) from 18 mg to 22 mg of vitamin B₆;

(f) from 1.5 mg to 1.9 mg of vitamin B₁;

and said supplement further comprises

(g) from 5500 I.U. to 6500 I.U. of beta carotene;

(h) from 30 mg to 40 mg of vitamin E;

(i) from 3.6 mg to 4.3 mg of vitamin B₂;

(j) from 16 mg to 24 mg of vitamin B₃;

(k) from 100 mg to 140 mg of vitamin C;

(l) from 85 mg to 115 mg of elemental iron, dosed in the form of a pharmaceutically-acceptable iron compound;

(m) from 1 mg to 3 mg of elemental copper, dosed in the form of a pharmaceutically-acceptable copper compound;

(n) from 0.05 mg to 0.2 mg of elemental iodine, dosed in the form of a pharmaceutically-acceptable iodine compound;

(o) from 15 mg to 25 mg of elemental zinc, dosed in the form of a pharmaceutically-acceptable zinc compound; and

(p) from 95 mg to 105 mg of elemental magnesium, dosed in the form of a pharmaceutically-acceptable magnesium compound;

30. The multi-vitamin and mineral supplement of claim 28 or claim 29, wherein said pharmaceutically-acceptable iron compound comprises a pharmaceutically-acceptable ferrous sulphate compound which is coated with a pharmaceutically-acceptable, film forming material which permits release of said ferrous sulphate in the intestine of a woman administered the supplement.

31. The multi-vitamin and mineral supplement of claim 28, claim 29 or claim 30, wherein said pharmaceutically-acceptable copper compound comprises cupric oxide.

32. The multi-vitamin and mineral supplement of any one of claims 28 to 31, wherein said pharmaceutically-acceptable iodine compound comprises potassium iodide.

33. The multi-vitamin and mineral supplement of any one of claims 28 to 32, wherein said pharmaceutically-acceptable zinc compound comprises zinc sulphate.

34. A multi-vitamin and mineral system for administration to a pregnant woman, which comprises:

(a) a multi-vitamin and mineral supplement for administration to a pregnant woman during her first trimester of pregnancy, said supplement comprising:

- (i) from 200 mg to 300 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
- (ii) from 350 I.U. to 450 I.U. of vitamin D;
- (iii) from 0.5 mg to 1.5 mg of folic acid;
- (iv) from 5 mcg to 10 mcg of vitamin B₁₂;
- (v) from 12 mg to 20 mg of vitamin B₆; and
- (vi) from 1.0 mg to 2.0 mg of vitamin B₁;

(b) a multi-vitamin and mineral supplement for administration to a pregnant woman during her second trimester of pregnancy, said supplement comprising:

- (i) from 275 mg to 375 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
- (ii) from 400 I.U. to 500 I.U. of vitamin D;

- (iii) from 0.5 mg to 1.5 mg of folic acid;
 - (iv) from 7 mcg to 12 mcg of vitamin B₁₂;
 - (v) from 14 mg to 22 mg of vitamin B₆; and
 - (vi) from 1.1 mg to 2.1 mg of vitamin B₁; and
- (c) a multi-vitamin and mineral supplement for administration to a pregnant woman during her third trimester of pregnancy, said supplement comprising:
- (i) from 450 mg to 550 mg of elemental calcium, dosed in the form of a pharmaceutically-acceptable calcium compound;
 - (ii) from 450 I.U. to 550 I.U. of vitamin D;
 - (iii) from 0.5 mg to 1.5 mg of folic acid;
 - (iv) from 9 mcg to 14 mcg of vitamin B₁₂;
 - (v) from 16 mg to 24 mg of vitamin B₆; and
 - (vi) from 1.2 mg to 2.2 mg of vitamin B₁.

35. A product for providing a vitamin and nutrient supplement regimen to pregnant women comprising:

a first formulation comprising a first mixture of vitamins and minerals wherein the amounts of vitamins and minerals in said first mixture optimize fetal development and maintain the mother's health during the first trimester of pregnancy;

a second formulation comprising a second mixture of vitamins and minerals wherein the amounts of vitamins and minerals in said second mixture optimize fetal development and maintain the mother's health during the second trimester of pregnancy; and

a third formulation comprising a third mixture of vitamins and minerals wherein the amounts of vitamins and minerals in said third mixture optimize fetal development and maintain the mother's health during the third trimester of pregnancy.

36. The product of claim 35, wherein said second formulation contains more calcium, iron, magnesium, vitamin C and vitamin D than said first formulation, and wherein said third formulation contains more calcium, iron, magnesium, vitamin C and vitamin D than the said second formulation.