Title: MULTIVITAMIN AND MINERAL NUTRITIONAL SUPPLEMENT

Abstract: This invention pertains to the field of nutritional supplementation, and in particular to a formation of vitamin and mineral supplements with highly advantageous health benefits. In a preferred embodiment, the supplement formulation comprises multiple dosage units, each providing different nutritional components of the supplement.
MULTIVITAMIN AND MINERAL NUTRITIONAL SUPPLEMENT

FIELD OF THE INVENTION

[0001] This invention pertains to the field of nutritional supplementation, and in particular to a formulation of vitamin and mineral supplements with highly advantageous health benefits. In a preferred embodiment, the supplement formulation comprises multiple dosage units, each providing different nutritional components of the supplement. The publications and other materials used herein to illuminate the background of the invention or provide additional details respecting the practice are incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] Micronutrients are elements or compounds which are present in foods in small or trace amounts and include vitamins, minerals or other elements. These micronutrients include compounds such as pantothenic acid, biotin and choline that are found in foods but for which a Recommended Dietary Allowance (RDA) has not yet been determined. Macronutrients consist of carbohydrates, fats (including essential fatty acids) and proteins (including essential amino acids) which supply both macronutrients and calories. Some elements such as calcium, sodium, potassium, chloride and phosphorus are consumed in relatively large amounts, while many such as iron, iodine, and zinc are consumed in small amounts (milligrams). Vitamins such as vitamin B12, and folic acid and the minerals copper, selenium and chromium are consumed in very small, or trace amounts (micrograms).

[0003] Inasmuch as the human body, does not synthesize many "essential compounds," these specific vitamins and minerals must be obtained from exogenous sources. The primary source of all nutrients is food. Ample evidence documents that a large number of persons of different ages, genders and socioeconomic status can not or do not obtain the Recommended Dietary Allowance of one or more essential macro- or micronutrients from their diet. Furthermore, substantial segments of the population do not demonstrate desirable eating patterns, that is, an adequate intake of the quantity or variety of food to fulfill the Recommended Dietary Allowances. In particular, large groups do not consume the recommended number of dietary servings of fruits and vegetables each day. Other factors such as smoking, physical inactivity, exposure to toxic environmental compounds and the avoidance of certain foods can also contribute to low or deficient intake or absorption of
nutrients.

[0004] In general, many women do not meet the RDA's for 6 out of 15 micronutrients (B6, vitamin E, calcium, iron, magnesium and zinc). Men often fail to meet the RDA's for 4 of 15 micronutrients (B6, vitamin E, magnesium and zinc). It also has been found that there is a significant prevalence and incidence in various population subgroups of deficiencies in specific vitamins and minerals, some of which are related to micronutrient deficiency diseases such as scurvy (vitamin C deficiency), pellagra (niacin deficiency), beri-beri (vitamin B1 deficiency), iron deficiency anemia and other vitamin and mineral deficiency states. Thus, vitamin and mineral supplementation has become a recognized method of meeting accepted medical and public health nutrition standards.

[0005] The effect of marginal nutrient deficiency states is only now being considered as a cause of suboptimal health status. Moreover, research conducted and published in the past three decades indicates that antioxidant micronutrients are involved in preventing molecular biological processes affecting health and disease at the subcellular and submolecular level. It is currently thought that free-radical effects on cells and tissues can be modified by antioxidant micronutrients, resulting in reduced cellular damage. Other specific micronutrients maintain immune system integrity, moderate the aging process and play a role in the prevention of atherogenesis and cancer.

[0006] In the last decade it has also been determined that "marginal" vitamin and mineral deficiency states occur, in which the blood or tissue levels are in the "low" range, without the presence of overt physical signs of deficiency disease, but which may cause symptoms of fatigue, lassitude, and a general sense of ill health. It is thus clear that nutrition science has progressed in defining the role of micro- and macronutrients in health and in disease prevention.

[0007] The effect of nutrients on coronary heart disease is thought mainly to be related to their effects on serum levels of lipids and lipoproteins. An emerging concept in nutritional health is that oxidized low density lipoprotein (LDL) is the key initiating agent in atherogenesis. Since, contrary to normal LDL, oxidized LDL is rapidly attacked by scavenging receptor macrophages. This induces the production of lipidladen foam cells. The end effect is cytotoxic to endothelial cells. Large epidemiological studies have shown a reduced incidence of cardiovascular disease in relation to dietary intake of micronutrients.
such as omega3-fatty acids, folic acid and vitamin E. The main beneficial effect of omega 3 fatty acids is to decrease triglyceride concentrations. Vitamins B6 and B12 are known to influence homocysteine plasma concentrations.

[0008] Vitamin E, an antioxidant, exerts its effects by blocking the effects of free radicals. The original concept that nutrients could affect biological and physiological systems began with the study of the aging process, in which intracellular oxidative reactions in brain cells were found to play a major role. Animal and human studies gave further impetus to these findings when it was shown that specific micronutrients, notably vitamin E, substantially blocked the induction of free radicals. Later, it was documented that lipid peroxidation formed free radicals with release of free-spinning electrons, which injured delicate subcellular organelle structures such as mitochondrial membranes. This, in turn, caused release of enzymes and other toxic compounds into the cytosol which induces further injury. As related to atherogenesis, both oxidized LDL and peroxidation of fatty acids are now considered to induce macrophages and other cells to transform into foam cells which comprise the fatty streak, the earliest histologically detectable origins of coronary atherosclerosis.

[0009] Nutritional formulations currently available which contain vitamin E generally are contained in softgel capsules which contain gelatin of animal origin. Traditionally, the primary sources of gelatin have been from bovine and porcine animals, although fish and birds have been indicated in the literature as alternative sources of gelatin. The source of gelatin is problematic since large groups around the world cannot ingest any pork or beef products (e.g., vegetarians and members of various religions). Furthermore, since there recently have been alleged instances of cross-species contamination from cattle to humans of bovine spongiform encephalopathy (BSE; "mad cow disease"), the use of uncontrolled by-products from animals has lost commercial acceptance.

[00010] The importance of the polyunsaturated omega 3-fatty acids, containing 18-22 carbon atoms, to proper nutrition is known in the art. The omega 3-fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential fatty acids in man. Besides their nutritional value, they are also known to possess beneficial pharmacological effects on the cardiovascular system and development of brain and retina functions, as well as on inflammatory and autoimmune diseases. These effects have led to
attempts to find nutritional compositions containing a high amount of omega3-fatty acids (particularly the omega3-fatty acids EPA and DHA) such as marine oils.

[00011] High levels of homocysteine confer a risk of vascular disease, increases the risk of atherosclerosis, and may be associated with Alzheimer's disease other forms of dementia and overall death risk. The physiological mechanism at this time is unclear. Risk ranges are provided below for cardiovascular diseases, as well as other homocysteine-related diseases:

<table>
<thead>
<tr>
<th>Homocysteine serum levels (μM)</th>
<th>Risk level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>very low</td>
</tr>
<tr>
<td>6-9</td>
<td>low</td>
</tr>
<tr>
<td>10-12</td>
<td>moderate</td>
</tr>
<tr>
<td>13-18</td>
<td>high</td>
</tr>
<tr>
<td>&gt;19</td>
<td>very high</td>
</tr>
</tbody>
</table>

It is generally well known that a preferable level of homocysteine is below 10 micromoles per liter. For genetic or nutritional reasons, some people have higher than the preferred level of homocysteine. Vitamin formulations generally do not contain enough vitamin B6 to aid in lowering homocysteine levels and in particular, omit one or several of the B vitamins, especially for example B6, B9 and B12.

[00012] Therefore, it would be of substantial benefit to provide a nutritional supplement formulation and system which overcomes these deficiencies and is able to provide correct nutritional support for both men and women.

**SUMMARY OF THE INVENTION**

[00013] Accordingly, the invention provides a nutritional supplement comprising about 400 IU alpha d-tocopherol, about 256 mg gamma d-tocopherol, about 89 mg delta d-tocopherol, about 20 mg beta d-tocopherol, about 1 g 30% EPA/20%HSA, about 50 mg Thiamin B1, about 50 mg Riboflavin B2, about 50 mg Niacin, about 50 mg Pyridoxine B5, about 400 mcg Folic Acid, about 50 mcg Vitamin B12, about 50 mcg Biotin, about 50 mcg
Pantothenic acid, about 50 mg Inositol, about 50 mg Choline Bitartate, about 15 mg PABA, about 500 mg vitamin C, about 50 mg Bioflavinoids, about 25 mg Rose Hips, about 1 g Calcium Citrate, about 400 mg of Magnesium, about 400 IU Vitamin D, about 75 mcg of Selenium, about 15 mg of Zinc, and optionally an additional 50 mcg Selenium.

[00014] In a further embodiment, the invention also provides a nutritional supplement which comprises a first dosage form comprising about 400 IU alpha d-tocopherol, about 256 mg gamma d-tocopherol, about 89 mg delta d-tocopherol and about 20 mg beta d-tocopherol; a second dosage form comprising about 1 g 30% EPA/20%DHA; a third dosage form comprising about 50 mg Thiamin B1, about 50 mg Riboflavin B2, about 50 mg Niacin, about 50 mg Pyridoxine B5, about 400 mcg Folic Acid, about 50 mcg Vitamin B12, about 50 mcg Biotin, about 50 mcg Pantothenic acid, about 50 mg Inositol, about 50 mg Choline Bitartate, and about 15 mg PABA; a fourth dosage form comprising about 500 mg vitamin C, about 50 mg Bioflavinoids, and about 25 mg Rose Hips; a fifth dosage form comprising about 500 mg Calcium Citrate, about 200 mg of Magnesium, about 400 IU vitamin D, and about 50 mcg of Selenium; and a sixth dosage form comprising about 500 mg Calcium Citrate, about 200 mg Magnesium, about 15 mg of zinc and optionally 50 mcg selenium.

[00015] In yet a further embodiment, the invention also provides a method of improving a physiological symptom in a human selected from the group consisting of plasma homocysteine levels, heart palpitations and astenia which comprises administering to the human the nutritional supplement as described above. The invention also provides a method for providing nutritional supplementation to a person comprising providing said person with a nutritional supplement as described above. For each method, the supplement is administered once per day.

[00016] In yet a further embodiment, the invention also provides a blister pack for dosage forms which comprises a substrate comprised of a first, a second, and a third section; said first section further comprising a first flap hingably connected to a first surface of said first section; said second section further comprising a second flap hingably connected to a second surface of said second section; said first section connected foldably to said second section; said third section connected foldably to said second section; a first matrix of blisters disposed on said first flap; and a second matrix of blisters disposed on said second flap.

[00017] In yet a further embodiment, the invention also provides a method of
contacting a person in need of a nutritional supplement regimen by a purveyor of nutritional supplement products, which comprises (a) informing a health care provider of the availability of nutritional supplement regimen products from said purveyor of nutritional supplement products; (b) providing contact information cards to said health care provider on which contact information for said persons can be provided, wherein said cards are provided with prepaid postage and a preprinted address of said purveyor of nutritional supplement products; (c) determining whether said person would benefit from a nutritional supplement regimen, wherein said determination is made by a health care provider; (d) recommending that said person begin a nutritional supplement regimen, wherein said recommendation is made by said health care provider; (e) providing said contact information card to said person by said health care provider; (f) filling out contact information on said information card by said person; (g) mailing said card to said purveyor of nutritional supplement products; and (h) contacting said person based on the contact information on said filled out information card.

[00018] In yet a further embodiment, the invention also provides a method of providing nutritional supplement products by a purveyor of nutritional supplement products to a person in need of a nutritional supplement regimen, which comprises (a) informing health care provider of the availability of nutritional supplement regimen products from said purveyor of nutritional supplement products; (b) providing contact information cards to said health care provider on which contact information for said persons can be provided, wherein said cards are provided with prepaid postage and a preprinted address of said purveyor of nutritional supplement products; (c) determining whether said person would benefit from a nutritional supplement regimen, wherein said determination is made by a health care provider; (d) recommending that said person begin a nutritional supplement regimen, wherein said recommendation is made by said health care provider; (e) providing said contact information card to said person by said health care provider; (f) filling out contact information on said information card by said person; (g) mailing said card to said purveyor of nutritional supplement products; (h) contacting said person based on the contact information on said filled out information card; (i) negotiating a sale of a nutritional supplement product to said person; and (j) providing said nutritional supplement product to said person.

[00019] In yet a further embodiment, the invention also provides a softgel capsule of vegetable origin comprising: potato starch, one or more polyalcohol, glycerol monostearate
and water. Optionally, flavoring and/or a coating, such as hydroxypropyl methylcellulose (HPMC) also is used. Preferably, no synthetic materials are used in the capsules and all ingredients are obtained from natural sources.

**DETAILED DESCRIPTION OF THE INVENTION**

[00020] The invention provides a multi-vitamin and mineral nutritional supplement or supplement regimen in the form of a daily program. This supplement and this program are designed to provide a synergistically effective combination of specific vitamins, minerals and other essential nutrients which can aid in reducing the risk of common debilitating conditions and diseases of adults and promote good health, in a cost effective and safe dosage for daily use, preferably as recommended by a physician. The inventive nutritional supplement and regimen may be used to prevent or reduce the risk of future health problems or to correct existing nutritional deficits. The conditions targeted by the inventive nutritional supplement include, for example, heart disease, some cancers, vision problems, osteoporosis and mental impairment.

[00021] The formulations of the invention are suitable for most adults independent of age or medical condition and are aimed towards reducing the risk of the most chronic debilitating diseases: cardiovascular diseases, some types of cancer, vision problems, osteoporosis and mental impairment. The inventors have found that a formulation has a synergistic effect when it includes omega3-fatty acids, added to a vitamin B complex, a balanced vitamin E complex, a slowly absorbed vitamin C complex and a complete calcium-magnesium-vitamin D-mineral complex, all as described in more detail below.

[00022] The invention also provides a dosage form of nutritional supplement in a purely vegetal softgel capsule of pharmaceutical quality which contains no ingredients of animal origin. The softgel capsule comprises potato starch and preferably is flavorless and odorless. Preferably, no synthetic materials are used in the manufacture of the capsules and all ingredients are obtained from natural sources. Most preferably, the softgel capsule is a VegaGels™ capsule.

[00023] The invention also provides a system for providing the nutritional supplement and the nutritional supplement regimen in a convenient package and package system.
[00024] The invention also provides a method for providing such a nutritional supplement or nutritional supplement program or regimen to persons in need thereof, preferably as judged by a licensed physician.

[00025] More specifically, the invention provides a nutritional supplement system comprising omega 3 fatty acids in a synergistically effective combination with Vitamin E which provides the benefit of antioxidant activity. The nutritional supplement and regimen also optionally provide a synergistic combination with other vitamins and minerals in optimal formulations for either male or female persons. Specific combinations of the components of the inventive formulations and systems provides a nutritional supplement which improves an individuals chances of achieving optimum health by ensuring adequate nutritional supplementation. In a particularly preferred embodiment, at least one of the formulations of the present invention is provided in a softgel capsule that is a gelatin free substitute gel cap containing no ingredients of animal origin.

[00026] In one embodiment, the invention provides a method of improving or maintaining a beneficial physiological condition in a human by administering the formulations of the invention. In a further embodiment, the invention provides a method of improving or stabilizing a physiological condition such as high serum homocysteine levels, heart palpitations and astenia in a human. Synergistic health benefits are provided by the methods and formulations of the invention, generally and for prevention of particular ailments, including changes in blood levels of homocysteine. The particular synergistic combination of vitamin E, omega3-fatty acids and proper amounts of particular B vitamins is important in that positive and/or prophylactic changes in plasma homocysteine, palpitation and astenia are associated with consumption of the nutritional supplements of the invention. Specifically, the vitamin B6, B9 and B12 of the inventive supplement work in synergy to lower the blood homocysteine levels. Therefore, persons having non-optimal homocysteine levels will particularly benefit from the inventive supplement.

[00027] The term contact as used herein includes, but is not limited to, communication via telephone, facsimile, telex, e-mail, regular postal service, courier and delivery services including those such as Federal Express or United Parcel Service, in person, and the like.

[00028] The term health care provider as used herein includes but is not limited to physicians, pharmacists, osteopaths, nurses, nurse practitioners, nurses aides, massage
therapists, acupuncturists and the like and their assistants and can include licensed or unlicensed practitioners, so long as there is an established form of contact or relationship between the health care provider or his/her offices and the purveyor of the nutritional supplement.

[00029] The term dosage form as used herein designates any means effective for administration of a dosage of part or all of the nutritional supplement, preferably for oral administration. Dosage forms may include, but are not limited to tablets, hard capsules, caplets, softgel capsules and the like, or any oral dosage form known to the nutritional and pharmaceutical arts. The nutritional supplement of the invention can be provided in solid or liquid form but in preferred embodiments, at least one dosage unit comprises a vegetable soft gel capsule such as VegaGels™ caplets.

[00030] As used in the present invention, a physiological symptom is “improved” in a person if it is changed from a level that is less associated with optimal health to a level that is more associated with optimal level of health. For example, improved serum homocysteine levels, palpitations and astenia will be reduced with the methods of the invention. Optimal levels of these signs or symptoms are well known with in the art. See, e.g., Klor et al. Eur. J. Med. Res. 2(6):243-257 (1997), the disclosures of which are incorporated by reference.

[00031] The nutritional supplement is preferably provided as plural oral dosage forms such as soft or hard capsules, tablets, caplets, and the like. In a preferred embodiment, the nutritional supplement and the supplements of the system do not contain any components of animal origin. Advantageously, one or more of the dosage forms of the formulation are contained within a soft gelatin-like capsule of vegetable origin, such as a VegaGels™ capsule. Preferred dosage forms are free of genetically modified organisms, are of pharmaceutical grade and are tamper proof.

[00032] The nutritional supplements of the present invention are advantageously provided in any suitable dosage form known in the art, for example, tablets, powders, granules, beads, chewable lozenges, capsules, liquids, liposomes, dragees, transdermal patches, implants or any conventional dosage forms, using conventional equipment and techniques known in the art. Oral dosage forms are preferred, and cost efficient dosage forms such as tablets, capsules, caplets and softgel capsules are highly preferred. In a particularly preferred embodiment, at least one of the dosage forms which provide the nutritional
supplement components of the invention are provided in softgel capsules of vegetable origin and most preferably in VegaGels™ caplets. The solid and liquid forms may contain, in addition to the active nutritional supplements any nutritionally or pharmaceutically acceptable excipients or fillers suitable to the active ingredient and the dosage form. Such acceptable inactive or inert ingredients or fillers may include diluents, flavorants, colorants, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like. Non-limiting examples may include oils such as soybean oil, corn oil, sesame oil, fish oil or any edible oil.

[00033] When preparing dosages forms incorporating the compositions of the present invention, the nutritional components are advantageously blended with lubricants such as hydrogenated vegetable oil, stearic acid and the like; diluents such as starch, lactose, mannose, and sucrose; disintegrants such as carboxymethyl cellulose and sodium starch glycolate and the like; suspending agents such as povidone, polyvinyl alcohol, and the like; absorbents such as silicon dioxide and the like; preservatives and antioxidants such as methylparaben, propylparaben, tocopherols and sodium benzoate; surfactants such as sodium lauryl sulfate, polysorbate 80, and the like; and colorants such as dyes and the like.

[00034] For preparing the composition from the compounds described by this invention, inert, pharmaceutically acceptable carriers may be used which are either solid or liquid form. A solid carrier advantageously contains one or more substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders or tablet disintegrating agents. The solid carrier material also may includes encapsulating material. Suitable solid carriers include, but are not limited, to magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like.

[00035] Liquid form preparations include solutions, oils, suspensions, and emulsions. Aqueous solutions suitable for oral use are prepared by dissolving the active component in water or other suitable liquid and adding suitable colorants, flavors, stabilizing agents, and thickening agents as desired, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other suspending agents known in the art. Other liquid formulations may comprise nutritionally or pharmaceutically acceptable edible oils such as corn, soybean, sesame, fish and the like.
The nutritional supplement and supplement regimen is advantageously provided with plural separate dosage units, preferably 2-10 separate dosage units, most preferably 3-8 dosage units or 4-7 dosage units, and most preferably 6 separate dosage units. The most preferred embodiment of the inventive nutritional supplement comprises

1. a dosage form comprising vitamin E complex (alpha, beta, delta and gamma d-tocopherols, preferably from natural sources),
2. a dosage form comprising omega3-fatty acids,
3. a dosage form comprising vitamin C complex (a slow release vitamin C combination including bioflavinoids (preferably from citrus extracts or another natural source) and rose hips extract),
4. a dosage form comprising vitamin B complex (thiamin, riboflavin, niacin, pyridoxine, folic acid, vitamin B12, biotin, pantothenic acid, inositol, choline bitartrate and para-aminobenzoic acid (PABA, a vitamin B complex factor)),
5. a dosage form comprising calcium, vitamin D and minerals (calcium citrate, magnesium, vitamin D and selenium), and
6. a dosage form comprising either
   a. additional calcium and minerals provided in a formulation designed for women (calcium citrate, magnesium and zinc), or
   b. additional calcium, selenium and other minerals provided in a formulation designed for men (calcium citrate, magnesium, selenium and zinc).

Preferably, at least one of dosage form 1 and dosage form 2 is a softgel capsule such as VegaGels™.

The vitamin E complex of the invention advantageously includes about 100 to about 1000 IU alpha d-tocopherol or preferably about 200 to about 600 IU alpha d-tocopherol and most preferably about 400 IU alpha d-tocopherol and can comprise, for example, 250, 300, 450, 500, 600, 750 or 1,000 IU alpha d-tocopherol. The vitamin E complex also advantageously contains about 100 to about 500 mg gamma d-tocopherol or preferably about 200 to about 300 mg gamma d-tocopherol or most preferably 256 mg gamma d-tocopherol. The vitamin E complex also advantageously contains about 50 to about 120 mg delta d-
tocopherol or preferably about 75 to about 100 mg delta d-tocopherol or most preferably about 89 mg delta d-tocopherol. The vitamin E complex also advantageously contains about 5 to about 40 mg beta d-tocopherol or preferably about 10 to about 30 mg beta d-tocopherol or most preferably about 20 mg beta d-tocopherol.

[00038] The omega3-fatty acid composition contained in the dosage form comprising omega3-fatty acids advantageously includes at least about 10% to about 50% EPA and at least about 5% to about 40% DHA or preferably about 20% to about 40% EPA and about 10% to about 30% DHA or most preferably about 30% EPA and about 20% DHA, and suitably may contain any amount of EPA and DHA within these ranges. The total amount of the omega3-fatty acid composition advantageously is at least about 0.5 g, and preferably is at least about 0.5 to about 3 g, or more preferably about 1 g to about 2 g and most preferably about 1 g, for example 0.75 g, 1.5 g or 2 g. In a preferred embodiment, the omega3-fatty acid composition is EPAX5500TG (ProNova).

[00039] The vitamin C complex of the invention advantageously includes about 200 to about 800 mg vitamin C or more. More preferably the complex includes about 400 to about 600 mg vitamin C or most preferably 500 mg vitamin C, for example 500, 600, 800 or 1000 mg. In addition, the vitamin C complex advantageously includes about 30 to about 75 mg bioflavinoids or preferably about 40 to about 60 mg bioflavinoids or most preferably about 50 mg bioflavinoids, for example 30, 50, 70 mg bioflavinoids and about 10 to about 35 mg rose hips or preferably about 20 to about 30 mg rose hips or most preferably about 25 mg rose hips, for example about 15, 20, 25 or 30 mg rose hips. Bioflavinoids (also known as flavinoids) are made up of a group of hundreds or thousands of related chemicals found in many plant foods and herbs. These substances are powerful antioxidants and may play a role in fighting cancer and heart disease. Some bioflavinoids enhance the actions of vitamin C and other antioxidants. The more common groups of bioflavinoids include, but are not limited to, flavones, flavonols, flavonones and isoflavones. Quercetin is a major flavonol in the Western diet. Rose hips are a very rich source of vitamin C and also contain pectin, a soluble fiber, and various acidic compounds which have laxative effects.

[00040] The vitamin B complex of the invention advantageously includes the ranges of compounds as shown in Table 1, below:
Table 1. Vitamin B Complex

<table>
<thead>
<tr>
<th>Compound</th>
<th>Advantageous amounts (mg)</th>
<th>Preferred amounts (mg)</th>
<th>Most preferred amounts (mg)</th>
<th>Exemplary amounts (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>thiamine (B1)</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>riboflavin (B2)</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>niacin</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>pyridoxine (B5)</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>folic acid</td>
<td>0.1-0.7</td>
<td>0.3-0.5</td>
<td>0.4</td>
<td>0.2, 0.4, 0.6</td>
</tr>
<tr>
<td>B12</td>
<td>0.01-0.08</td>
<td>0.03-0.06</td>
<td>0.05</td>
<td>0.02, 0.04, 0.07</td>
</tr>
<tr>
<td>biotin</td>
<td>0.01-0.08</td>
<td>0.03-0.06</td>
<td>0.05</td>
<td>0.02, 0.04, 0.07</td>
</tr>
<tr>
<td>pantothenic acid</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>inositol</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>choline bitartrate</td>
<td>10-80</td>
<td>30-60</td>
<td>50</td>
<td>25, 55</td>
</tr>
<tr>
<td>PABA</td>
<td>5-25</td>
<td>10-20</td>
<td>15</td>
<td>5, 20, 25</td>
</tr>
</tbody>
</table>

[00041] The dosage unit comprising calcium, vitamin D and minerals advantageously includes about 100 to about 800 mg calcium citrate or preferably about 200 to about 700 mg calcium citrate or most preferably about 500 mg calcium citrate. The dosage unit also advantageously includes about 100-300 mg magnesium or preferably about 150 to about 250 mg magnesium or most preferably about 200 mg magnesium. The dosage unit also advantageously includes about 200 to about 600 IU vitamin D or preferably about 300 to about 500 IU vitamin D or most preferably about 400 IU vitamin D. The dosage unit also advantageously includes about 50 to about 100 mcg selenium or preferably about 60 to about 90 mcg selenium or most preferably about 75 mcg.

[00042] The dosage unit comprising additional calcium and minerals provided in a
formulation designed for women advantageously includes about 100 to about 800 mg calcium citrate or preferably about 200 to about 700 mg calcium citrate or most preferably about 500 mg calcium citrate. The dosage unit also advantageously includes about 100-300 mg magnesium or preferably about 150 to about 250 mg magnesium or most preferably about 200 mg magnesium. The dosage unit also advantageously includes about 5 to about 25 mg zinc or preferably about 10 to about 20 mg zinc or most preferably about 15 mg zinc.

[00043] The dosage unit comprising additional calcium, selenium and other minerals provided in a formulation designed for men advantageously includes about 100 to about 800 mg calcium citrate or preferably about 200 to about 700 mg calcium citrate or most preferably about 500 mg calcium citrate. The dosage unit also advantageously includes about 100-300 mg magnesium or preferably about 150 to about 250 mg magnesium or most preferably about 200 mg magnesium. The dosage unit also advantageously includes about 5 to about 25 mg zinc or preferably about 10 to about 20 mg zinc or most preferably about 15 mg zinc. The dosage unit also advantageously includes about 30 to about 70 mcg selenium or preferably about 40 to about 60 mcg selenium or most preferably about 50 mcg selenium.

[00044] Although the nutritional supplement is preferably formulated in separate dosage units as described above, the nutritional supplement may be formulated in less than or more than 6 separate dosage units, including 1 dosage unit, but contain the same nutritional supplements in the ranges described. The preferred formulation of the nutritional supplement product is also shown in Figure 1.

[00045] Most individualized nutritional supplement programs are conducted without either direct or indirect supervision by a physician or other health care provider. The present invention provides a method for contacting a consumer in need of a nutritional supplement regimen by a purveyor of nutritional supplement products through a health care provider or with the supervision of a health care provider. In another embodiment, the invention comprises a method of providing nutritional supplement products by a purveyor of nutritional supplement products to a person in need of a nutritional supplement regimen through a health care provider or with the supervision of a health care provider.

[00046] The invention further provides a dosage package for convenient and accurate dispensing of the nutritional supplement of the invention. In a preferred embodiment, the dosage containers of the invention comprise a folding paper matchbook style card about 6.25
x 9 inches with a depth of .54 inches when folded. See Figure 2. In a preferred embodiment, the dosage container comprises a match box style container having three sections of equal or approximately equal size, with the two outer sections easily folded over to meet and enclose the inner section, thus providing an inner and outer portion the container. The individual blisters for holding the individual modules of the nutritional supplement can be attached to the inside of the folded over container.

[00047] A preferred dosage container of the invention comprises a matchbook style folding card about 6.25 x 9 inches with a depth of about .54 inches, when folded. The package preferably contains 42 individual blisters. The package may be color coded, with the male formulation package preferably being blue and the female formulation package preferably being pink. The individual blisters can further be divided on more than one blister card attached to the interior of the folded package containing a week's supply of the nutritional supplement. In a particularly preferred embodiment, the 42 individual blisters of the dosage container are arranged in seven rows across the card, each row comprising 6 columns, wherein each row is separated by a perforation extending lengthwise down the card.

[00048] A blister pack for dosage forms may include a substrate with a first, second, and third sections. The substrate may be composed of e.g., card stock, fiber board or plastic. The sections are connected to each other with, for example, fold lines or hinges, so that the blister pack can be folded like, for example, a match book. The first section has a first flap hingably connected to a first surface of the first section that contains a first matrix of blisters. The matrix may have, for example, six rows and seven columns of blisters, each blister holding one dosage form. Blisters are well-known in the art of packaging and may compose a transparent plastic bubble attached to the first section that can be torn or perforated to release the dosage form contained therein. Each row may be labeled with, for example, the name of the dosage forms contained in the blister packs of that row. Each column may be labeled with, for example, the name of a weekday.

[00049] The dosage container can contain for example between 1 and 30 days supply of the nutritional supplement, and for example can contain 1, 7, 15, or 30 days supply of the nutritional supplement or any convenient amount of the dosage units of the supplement. A person of ordinary skill in the art can readily contemplate variations on the number of modules contained within the dosage container and such variations are contemplated by the
present invention.

Various methods are known in the art for retaining individual dosages in a card containing blister packs and non-limiting examples are provided in U.S. Patent No. 5,833,072 and 6,024,222. In general, a blister part of a blister package comprises one blister part, which consists of a set of interconnected foils covering each other. One relatively rigid foil is in most cases referred to as the base and comprises cavities or "blisters", which accommodate a single tablet or capsule. The other foil, which is flat, is in most cases referred to as the lid and seals the opening of the blisters. A group of such blisters can be provided as a "blister assembly" and in a preferred embodiment, are provided as a matchbox style assembly as described above.

The name of each dosage form of the vitamin supplement may be provided on the left side of the matchbox and the day of the week printed across the top of the inside of the package as depicted in Figure 3. The package preferably is perforated into sections, for example 7 sections in a preferred embodiment, with each section containing a daily supply of the supplement encased in six individual blisters, so that a supply of dosage units sufficient for one day may be conveniently detached.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry and vitamin and pharmaceutical manufacture which are known to one of ordinary skill in the related art. The invention is further illustrated by the following example, which is not intended to be limiting.

Example

Twenty three individuals were maintained on a nutritional supplement according to the invention (vitamin E complex (including 400 IU alpha tocopherol), vitamin C (slow release with 50 mg bioflavonoids), vitamin B 50 complex (as shown in Table 1 above, most preferred amounts), 500 mg calcium citrate, and 1g EPAX5500TG (ProNova) for 8 weeks. Subjects 3, 22 and 23 were administered an additional 1mg vitamin B12 once per week. The results of the study are shown in Table 2, which provides serum homocysteine levels (µM) in each individual before and after administration of the nutritional supplement regimen. Before administration of the nutritional supplement according to the invention,
average serum homocysteine in the subjects was 12.9 μM, while after 8 weeks administration of the inventive nutritional supplement this level had been reduced to 9.06 μM, a reduction of 29.8%. This confers a p<0.001 statistical significance. Every subject enjoyed a drop in homocysteine levels.
Table 2. Serum Homocysteine Level Changes After Nutritional Supplementation.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.3</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>11.1</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>19.3</td>
<td>9.5</td>
</tr>
<tr>
<td>4</td>
<td>8.6</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>7.5</td>
</tr>
<tr>
<td>8</td>
<td>7.6</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>10.7</td>
<td>7.7</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>11</td>
<td>22.2</td>
<td>17.7</td>
</tr>
<tr>
<td>12</td>
<td>10.7</td>
<td>7</td>
</tr>
<tr>
<td>13</td>
<td>11.6</td>
<td>7</td>
</tr>
<tr>
<td>14</td>
<td>6</td>
<td>5.9</td>
</tr>
<tr>
<td>15</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>16</td>
<td>12.3</td>
<td>9</td>
</tr>
<tr>
<td>17</td>
<td>9.9</td>
<td>8</td>
</tr>
<tr>
<td>18</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>19</td>
<td>10.9</td>
<td>8</td>
</tr>
<tr>
<td>20</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>21</td>
<td>14.2</td>
<td>9</td>
</tr>
<tr>
<td>22</td>
<td>22.5</td>
<td>8</td>
</tr>
<tr>
<td>23</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Average</td>
<td>12.9</td>
<td>9.06</td>
</tr>
</tbody>
</table>
Claims

1. A nutritional supplement comprising:
   about 400 IU alpha d-tocopherol,
   about 256 mg gamma d-tocopherol,
   about 89 mg delta d-tocopherol,
   about 20 mg beta d-tocopherol,
   about 1 g 30% EPA/20%DHA,
   about 50 mg Thiamin B1,
   about 50 mg Riboflavin B2,
   about 50 mg Niacin,
   about 50 mg Pyridoxine B5,
   about 400 mcg Folic Acid,
   about 50 mcg Vitamin B12,
   about 50 mcg Biotin,
   about 50 mcg Pantothenic acid,
   about 50 mcg Inositol,
   about 50 mg Choline Bitartrate,
   about 15 mg PABA,
   about 500 mg vitamin C,
   about 50 mg Bioflavonoids,
   about 25 mg Rose Hips,
   about 1 g Calcium Citrate,
   about 400 mg of Magnesium,
   about 400 IU Vitamin D,
   about 75 mcg of Selenium,
   about 15 mg of Zinc, and
   optionally an additional 50 mcg Selenium.

2. A nutritional supplement of claim 1, said supplement comprising a total of 125 mcg Selenium.
3. A nutritional supplement which comprises:
   (a) a first dosage form comprising about 400 IU alpha d-tocopherol, about 256 mg
       gamma d-tocopherol, about 89 mg delta d-tocopherol and about 20 mg beta d-tocopherol;
   (b) a second dosage form comprising about 1 g 30% EPA/20%DHA;
   (c) a third dosage form comprising about 50 mg Thiamin B1, about 50 mg
       Riboflavin B2, about 50 mg Niacin, about 50 mg Pyridoxine B5, about 400 mcg Folic Acid,
       about 50 mcg Vitamin B12, about 50 mcg Biotin, about 50 mcg Pantothenic acid, about 50
       mg Inositol, about 50 mg Choline Bitartate, and about 15 mg PABA;
   (d) a fourth dosage form comprising about 500 mg vitamin C, about 50 mg
       Bioflavinoids, and about 25 mg Rose Hips;
   (e) a fifth dosage form comprising about 500 mg Calcium Citrate, about 200 mg of
       Magnesium, about 400 IU vitamin D, and about 75 mcg of Selenium; and
   (f) a sixth dosage form comprising about 500 mg Calcium Citrate, about 200 mg of
       Magnesium, about 15 mg of zinc and optionally 50 mcg selenium.

4. A nutritional supplement of claim 3 wherein the sixth dosage form comprises 50 mcg
   of selenium.

5. A method of improving a physiological symptom in a human selected from the group
   consisting of plasma homocysteine levels, heart palpitations and astenia which comprises
   administering to the human the nutritional supplement of claim 1 or claim 3.

6. A method for providing nutritional supplementation to a person comprising providing
   said person with a nutritional supplement of claim 1 or claim 3.

7. A blister pack for dosage forms which comprises:
   a substrate comprised of a first, a second, and a third section;
   said first section further comprising a first flap hingably connected to a second surface
   of said second section;
   said second section further comprising a second flap hingably connected to a second
   surface of said second section;
said first section connected foldably to said second section;
said third section connected foldably to said second section;

a first matrix of blisters disposed on said first flap; and

a second matrix of blisters disposed on said second flap.

8. A method of contacting a person in need of a nutritional supplement regimen by a purveyor of nutritional supplement products, which comprises:

(a) informing health care provider of the availability of nutritional supplement regimen products from said purveyor of nutritional supplement products;

(b) providing contact information cards to said health care provider on which contact information for said persons can be provided, wherein said cards are provided with prepaid postage and a preprinted address of said purveyor of nutritional supplement products;

(c) determining whether said person would benefit from a nutritional supplement regimen, wherein said determination is made by a health care provider;

(d) recommending that said person begin a nutritional supplement regimen, wherein said recommendation is made by said health care provider;

(e) providing said contact information card to said person by said licensed physician;

(f) filling out contact information on said information card by said person;

(g) mailing said card to said purveyor of nutritional supplement products; and

(h) contacting said person based on the contact information on said filled out information card.

9. A method of providing nutritional supplement products by a purveyor of nutritional supplement products to a person in need of a nutritional supplement regimen, which comprises:

(a) informing health care provider of the availability of nutritional supplement regimen products from said purveyor of nutritional supplement products;

(b) providing contact information cards to said health care provider on which contact information for said persons can be provided, wherein said cards are provided with prepaid postage and a preprinted address of said purveyor of nutritional supplement products;
(c) determining whether said person would benefit from a nutritional supplement regimen, wherein said determination is made by a health care provider;
(d) recommending that said person begin a nutritional supplement regimen, wherein said recommendation is made by said health care provider;
(e) providing said contact information card to said person by said health care provider;
(f) filling out contact information on said information card by said person;
(g) mailing said card to said purveyor of nutritional supplement products;
(h) contacting said person based on the contact information on said filled out information card;
(i) negotiating a sale of a nutritional supplement product to said person; and
(j) providing said nutritional supplement product to said person.

10. A softgel capsule of vegetable origin comprising: potato starch, one or more polyalcohol, glycol monostearate, and water.

11. A softgel capsule of claim 10 further comprising a flavoring and a hydroxypropyl methyl cellulose coating.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 47/00
US CL. : 424/400, 439, 464, 489

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/400, 439, 464, 489

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPatents, USPG-Pub, Derwent, JPO, EPO

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>US 5,514,382 A (SULTENFUSS) 7 May 1996 (07.05.1996), columns 9-12.</td>
<td>1-11</td>
</tr>
</tbody>
</table>

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "E" earlier application or patent published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed
  "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
  "&" document member of the same patent family

Date of the actual completion of the international search
10 June 2003 (10.06.2003)

Date of mailing of the international search report
24 JUN 2003

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703)305-3230

Telephone No. 703-308-1235

Authorized officer:

Telephone No. 703-308-1235

Form PCT/ISA/210 (second sheet) (July 1998)