Multi Vitamin Formulations

The gender-specific men's and women's multivitamins and the nerve tissue supplement contain ingredients in a form that the body can easily use, in the recommended daily amounts. These ingredients promote the health of the heart, brain, muscle, bone and other parts of the body by giving them the nutrients they need to function properly.

This document goes into what is in each supplement, why those ingredients are present (and in what amounts) and what that particular ingredient does in the body.

All ingredients in the supplements are natural and nontoxic, and help support good health.

Ingredient review for the Multi Vitamin Supplement

The broad-spectrum multivitamins were formulated for men and women according to the current knowledge of daily required amounts of nutrients, and the differences in need (as in iron) between men and women.

The polyphenolics, probiotics, and secondary nutrients like carnitine and ubiquinone (CoQ10) were added to help supplement the daily diet, and to help support the tissue-support supplement that it is meant to be taken along with. The focus of this section reviewing the multi-vitamin offering is to understand how these ingredients work in the body to improve overall health, and how the formula compares to the new recommended daily intake values for food and dietary supplements in the updated 21CFR section 101.9 [1].

The ingredient list and dosages for the men's and women's multivitamins are described in the table below.

| Ingredient | Men's Multi | Women's Multi |
|---------------------------------|-------------|---------------|
| Vitamin A- Palmitate | 900mcg | 900mcg |
| Vitamin C Ascorbic Acid | 90mg | 90mg |
| Vitamin D3 Cholecalciferol | 25mcg | 25mcg |
| Vitamin E- D-Alpha Mixed | 22.5mg | 22.5mg |
| Tocopherols | | |
| Vitamin K- K2 Menaquinone-7 | 45mcg | 45mcg |
| Vitamin B1- Benfotiamine | 25mg | 25mg |
| Vitamin B2- Riboflavin 5 | 60mg | 60mg |
| Phosphate | | |
| Vitamin B3- Niacinamide | 20mg | 20mg |
| Vitamin B6- Pyridoxine HCL | 100mg | 100mg |
| Vitamin B9- Methylfolate | 400mcg | 400mcg |
| Vitamin B12- Methylcobalamin | 1mg | 1mg |
| Pure 99% | | |
| Vitamin B7- Pure Biotin 100% | 300mcg | 300mcg |
| Vitamin B5- Calcium Pantothenic | 5mg | 5mg |
| Acid | | |
| Phosphorus | 150mcg | 150mcg |
| Iodine (Potassium Iodine) | 100mcg | 100mcg |
| Chromium Picolinate | 200mcg | 200mcg |
| Zinc Citrate 31% | 60mg | 60mg |

Table 1: Overview of the gender specific Multi-Vitamin

| TRAAC® Manganese Bisglycinate | 4mg | 4mg |
|-------------------------------|----------------|----------------|
| Chelate | | |
| Selenium (Sodium Selenate 50% | 200mcg | 200mcg |
| L-Selenomethionine 50%) | | |
| TRAAC® Molybdenum Glycinate | 120mcg | 120mcg |
| Chelate | | |
| Calcium Carbonate Powder | 400mg | 400mg |
| Magnesium (as oxide) | 400mg | 400mg |
| Iron (Ferrous Fumarate) | N/A | 18mg |
| Antioxidant Blend | | |
| Cranberry (fruit) | 100mg | 100mg |
| Garlic Powder | 75mg | 50mg |
| Ginger (Organic) | 50mg | 50mg |
| Grape Seed Extract 98% | 60mg | 60mg |
| Pine Bark 50% | 60mg | 60mg |
| Probiotic Blend | 10 billion CFU | 10 billion CFU |
| Enzyme Blend 6 Strains | 40mg | 40mg |
| Heart Blend | | |
| CoQ10 (Microactive) | 10mg | 10mg |
| L-Carnitine | 75mg | 75mg |
| D-Ribose | 120mg | 120mg |
| Resveratrol 50% | 60mg | 60mg |
| Lycopene | 1mg | 1mg |

Inactive ingredients: Stearates

Serving Size- 3

Benefits by Nutrient:

Vitamin K- K2 -- Menaquinone-7

Vitamin K2 was first described as a byproduct of fermented soybeans and is involved in bone health [2]. MK4 and MK7 are the most common versions of this vitamin. Their required daily doses are: MK4 at 45mg/day and MK7 at 45mcg/day.

While both are a normal part of the diet, MK7 is used in this supplement because it is converted to Vitamin K1 in the colon, is better able to be absorbed in the body, and results in increased benefits to health [3, 4].

Vitamin B1- Benfotiamine

When supplemented into the diet, benfotiamine is converted to its active form of vitamin B1 (thiamine diphosphate), and has been shown in studies to help promote weight loss, urinary health, improve mood, and support cognition. Studies show that supplementation with benfotiamine greatly increases the levels of B vitamins in the bloodstream, and the benefits received [5].

Activated B Vitamins - Riboflavin 5 Phosphate, Methylfolate, and Methylcobalamin

Other B vitamins are included in the multi are riboflavin 5 phosphate, methylfolate and methylcocabalamin. These are already activated, meaning they don't need to be converted by the body. These typically are compounds that are either phosphorylated or methylated.

Riboflavin 5 phosphate, the activated form of vitamin B2, also known simply as riboflavin, is a precursor to (the starting point for) flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN,) enzymes that are important to the energy cycle of cells [6].

Methylated folates (Vitamin B9), and methylcobolamin (Vitamin B12) are involved in the methylation cycle, which effects neurotransmitter metabolism (a vital part of the health of the nervous system,) homocysteine metabolism (which is involved in cardiovascular health and general wellness), and the body's production of glutathione (by regulating the metabolism of sulfur amino acids), a powerful antioxidant (Fig 1.)



Figure 1: Detailed methylation map

In studies in women on prenatal support, use of high doses of methylcobolamin (Vitamin B12) was more effective than other prenatal vitamin supplementation, reducing megoblastic anemia in these women [7, 8, 9].

When there is not enough Vitamin B12 in the body, the effect of methylfolate supplements is reduced because the body isn't able to convert them into usable forms fast enough. This is known as "methylfolate trapping." Taking active Vitamin B12 with other methylfolates (such as Vitamin B9) ensures that there is enough Vitamin B12 for the body to use, and makes the supplement more effective [10].

Chelated Minerals: TRAAC® Manganese Bisglycinate and TRAAC® Molybdenum Glycinate

TRAAC[®] minerals are amino acid chelates (compounds that trap, neutralize, and allow the body to remove certain minerals) that are produced by industry leader, Albion Minerals. The chelated material is reviewed with a special process called FT-IR, instead of the more common industry standard of NIR. This verifies that the complete chemical reaction for the mineral chelate has occurred [11]. These mineral chelates have been certified as a safe option that is easily absorbed and used by the body. The elements molybdenum and manganese are important parts of these chelation compounds.

Molybdenum is part of the important enzymes xanthine oxidase and sulfite oxidase, which break down and clear minerals and toxins. It is also an important co-factor in numerous other clearance pathways [12].

Manganese helps a mitochondrial antioxidant, superoxide dismutase, protect the mitochondria – the "power plants" of the cell. Because mitochondria produce free oxygen radicals, and are very susceptible to oxidative stress and damage, this antioxidant (and the manganese that works with it) are extremely important [13].

Chromium Picolinate

Chromium picolinate is a common source of chromium supplementation, providing the small amounts of chromium (trivalent chromium) that the body needs [14]. Chromium supplements help lower blood sugar and cholesterol levels, improving overall health. While there are many forms of chromium, most forms are absorbable. To date, only Chromium oxide has been shown to be less usable by the body than the others [15].

L-Selenomethionine

Organic forms of selenium have been shown in animals to improve selenium and antioxidant levels in the body [16]. However, certain individuals with hepatic burden (liver problems) may not be able to turn organic selenium into the more usable elemental selenium. This decreases the amount of selenoproteins, an important metabolic substance, in the body.

In a randomized trial of people with mild to moderate fibrosis of the liver, selenium levels in the supplemented cohort only rose with sodium selenite (inorganic selenium) and not the typical organic forms [17].

To ensure that selenium levels are at healthy amounts in the body regardless of liver function, both organic and inorganic selenium are included in the multi-vitamin supplements.

Ferrous Fumarate

This iron-containing chelated mineral has been in circulation as a dietary supplement ingredient as well as a global food fortification ingredient for quite some time. It works better as a constipation (compacted stool) aid than iron sulfate and may be better absorbed by the body when taken along with vitamin C (ascorbic acid) [18].

Microactive CoQ10

CoQ10, also known as ubiquinone or ubiquinol (depending on the redox state,) is a potent antioxidant, protecting cells from damage. It also is a part of the the electron transport chain, an important part of cell function.

CoQ10 is generally difficult to take in because of its crystalline structure. However, this form --Microactive CoQ10 -- has been processed in a way that helps increase its solubility and allows the body to absorb more of it. Studies have shown that this processing doubles the levels of CoQ10 in the bloodstream [19].

Ingredient Review for the Nerve/tissue Support Formula

The current formulation for the nerve/tissue support formula is a blend of nutrients and botanicals (chemicals from plants), as listed in the table below. These nutrients support the health and function of the nervous system, as well as the cartilage, ligaments, and tendons. These nutrients also support cardiometabolic (heart and lung) and reproductive health. This product has been formulated to be beneficial for both men and women.

| Ingredient | Amount per serving |
|--|--------------------|
| Revised Alpha Lipoic Acid (Sodium) | 300mg R-LA |
| Turmeric Extract (SE 95% Curcuminoids) | 150mg |
| Ashwagandha Powder | 200mg |
| Hyaluronic Acid | 50mg |
| Green Tea 50% ECGC | 300mg |
| Para-aminobenzoic acid (PABA) | 500mg |
| Inactiva ingradianta, Staarataa | Conving Size 2 |

Table 2: Supplement Formulation

Inactive ingredients: Stearates

Serving Size 3

Health Support of the Nerve/tissue Support Formula by System

Nervous tissue – Ingredients involved: RLA, CoQ10 (Microactive), L-Carnitine, D-Ribose, Resveratrol, Ashwagnadha

The ingredients listed above improve normal nerve function through neuroprotection (protecting neurons,) neuro-antioxidant activity (preventing damage to neurons by removing oxidizing/damaging chemicals,) and supporting normal cognitive (thought, learning, and problem solving) and memory health.

R-lipoic acid is the "poster child" for supporting the nervous system. It stimulates the nervous system to produce glutathione, an important antioxidant [20, 21]. Antioxidants prevent and help repair damage caused by oxidants, also known as free oxygen radicals, which are produced as waste products by cells. Left unchecked, oxidation can play a part in memory loss, cognitive declines, eyesight issues, and other problems that are often associated with aging. Therefore, antioxidants are important in supporting overall health.

Alpha-lipoic acid is a nutrient that is very important to the nervous system. When given as a supplement, alpha-lipoic acid improved sensory symptoms (sight, hearing, and so on) as well as cognition and memory [22-25]. There is also clinical data implying that it helps with carpal tunnel syndrome as well [26].

In conditions associated with cognitive and memory deficits, lipoic acid (a slightly different nutrient) has been shown to improve cognitive function [27]. The largest of the effects have been seen in individuals with mild dementia, where it slows the decline in function that is usually seen in these patients [28].

Coenzyme Q10 is another antioxidant that is known to have numerous roles within the body, including in the nervous system. In a study of diabetic neuropathy (pain), Coq10 supplementation was found to be effective in improving nerve conduction, and reducing pain and impairment [29]. In fibromyalgia, a

condition linked with central sensitization of pain pathways, CoQ10 was found to play a role in reducing pain levels and helped support physical fitness levels as well as overall health [30].

D- Ribose has also been shown to support neurological function in fibromyalgia, improving sleep and energy while decreasing pain [31]. In a related disorder, chronic fatigue syndrome, or myalgic encephalomyelitis, L-Carnitine supplementation shows some results as well [32].

Resveratrol, a substance best known for its presence in red wine and other fruits, was shown in one study to increase memory in healthy aging adults. In particular, it improved activity and connection in the hippocampus, the part of the brain responsible for memory [33].

Ashwagandha, an herb used in Ayurvedic medicine, has been associated with significant improvements in executive function, sustained attention, and information processing [34].

Working together, these nutrients improve cognition, memory, and neuron growth.

Musculoskeletal - Ingredients: Magnesium, Turmeric Extract, Hyaluronic Acid, Vitamin D, Ashwagandha

These ingredients improve muscle strength, recovery after injury, and bone and joint health.

For muscle health and strength in particular, the key players are magnesium and vitamin D. In women, magnesium has been shown to improve skeletal muscle power, and help reduce hs-CRP (a marker of inflammation) [35]. Magnesium in both aging men and women has been shown to protect bone and muscle mass, which can decline naturally with aging [36].

Vitamin D is associated with higher muscle strength in men and women [37]. Furthermore, vitamin D is crucial in maintaining muscle, bone, cartilage, and joint health as we age. It is recommended by groups like the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO), that postmenopausal women take in at least 20mcg of D3 a day [38]. This can be achieved through outdoor activity (vitamin D is produced in the skin when exposed to sunlight), but supplementation through diet helps ensure that enough of this vitamin is absorbed into the body.

The Ayurvedic herb ashwagandha has interesting data showing its support of the muscular and skeletal system. In an 8-week strength trial, ashwagandha was shown to promote both muscle strength and muscle recovery [39].

For joint support, turmeric and hyaluronic acid both have data to suggest that they help combat pain and joint mobility issues associated with osteoarthritis.

Extracts from the Turmeric plant (*Curcuma longa*), a relative of ginger, inhibits NF-kB, a protein that controls the transcription of DNA, the immune system, and how the body responds to stress. When NF-kB isn't regulated properly, it can be linked to cancer, inflammation, autoimmune disease, and infection – turmeric helps to keep this under control [40]. Tumeric has also been shown to help prevent the degradation of cartilage, promoting joint health [41].

Hyaluronic acid also helps to regulate the immune response by binding to the surface of cell membranes, particularly cartilage, and has been shown to help reduce inflammation in the joints [42]. Both ingredients have been shown to be effective in multiple clinical trials [43, 44].

Cardiometabolic - Ingredients: Green Tea Extract, Lycopene, Garlic, CoQ10 (Microactive), L-Carnitine, Probiotic Blend, B vitamins, Chromium, Ribose

These ingredients support normal heart, lung, and metabolism function, which includes blood glucose control, the natural breakdown of key substances, hepatic (liver) function, and vascular (breathing) and cardiac (heart and blood flow) support.

Cardiovascular health and the body's metabolism are linked. Over the years, there has been a steady increase in related diseases: Cardiovascular disease, Type 2 diabetes, non-alcoholic fatty liver disorder, and obesity. This increase is due to many causes – diet, pollutants in the environment, and changes in exercise. Oxidative stress is also part of the cause.

One generator of oxidative stress can be the bloodstream amino acid homocysteine [45]. High levels of this chemical increases the risk of cardiovascular disease. B vitamin supplementation helps the body break down homocysteine and naturally reduce its level in the bloodstream [46].

Lipid (fats) and blood sugar levels can also increase oxidative stress. Increased levels in the blood, especially low or very low-density lipoproteins, can increase the risks for heart disease. This is because these lipoproteins can become damaged through oxidization and form the building blocks for atherosclerosis – the hardening and clogging of arteries. Green tea extract has been shown to help balance lipid levels, reduce sugar levels in the bloodstream, and reduce the markers of inflammation (such as iron) in individuals that are overweight [51, 52].

Supplemental chromium use also supports blood-sugar control [53, 54] In addition, it may reduce stresseating by improving serotonin (a nervous system chemical) metabolism in the central nervous system [55]. Stress-eating contributes to high levels of lipids and sugars in the blood stream and is implicated in a wide range of health problems.

Probiotics – the ingestion of beneficial bacteria to support their presence in the gut – have been shown to reduce lipid levels in the blood stream and oxidative stress [56, 57]. Their mechanism of action is as yet unclear – and may be on multiple levels, including nutrient production and better digestion – but the metabolism of bile salts may be a part of it.

Antioxidants in the bloodstream reduce damage from oxidation and have been shown to help maintain normal blood pressure and circulatory system health. Lycopene and ubiquinone (CoQ10) are antioxidants that have been shown to reduce both systolic and diastolic blood pressure significantly, in clinical trials [47, 48, 49, 50].

Lastly, D-ribose and L-carnitine are nutrients that play a role in supporting blood vessel expansion. They help prevent blood vessels from collapsing and closing, which helps keep blood flowing to the heart even during ischemia (blood vessel blockage caused by atherosclerosis). In coronary heart disease, D-Ribose was shown to be significantly helpful in supporting the prevention of heart attacks [58]. Because

it improves blood flow, L-carnitine was shown to increase walking distance capabilities in some studies [59, 60].

Men's Health - Ingredients: Ashwagandha Powder, Para-aminobenzoic acid (PABA), Grape Seed Extract, Pine Bark, CoQ10 (Microactive), L-Carnitine, Lycopene.

These ingredients support prostate function, sexual function, and general genitourinary tract support in men.

Grape seed extract has been shown to help reduce the risk of prostate cancer in aging men by 41% by helping support proper hormone production and reducing oxidative stress and damage to the prostate [61]. Lycopene has also been shown in studies to help reduce the risk of prostate cancer through its action as an antioxidant [62, 63].

Pine bark extract has been shown to reduce prostate size (and the accompanying erectile dysfunction and lower urinary tract symptoms) in several studies [64].

PABA (para-aminobenzoic acid or vitamin B-x), a naturally occurring chemical found in green, leafy vegetables, and ubiquinone (CoQ10), an antioxidant, help support healthy penis structure. These ingredients have been studied for their ability to support a reduction in Peyronie's disease, an underreported, connective tissue disorder resulting in abnormal curvature of the penis, erectile dysfunction, and painful intercourse [65, 66, 67]

Ashwaganda and L-carnitine have been shown to improve semen quality in men through reducing oxidation, improving mitochondrial function (energy production), and supporting proper sex hormone function. This supplementation is very important, as semen quality is a growing issue in the US and other Westernized countries, with as much as a 50% measured reduction in sperm count [68, 69, 70, 71].

Men's health problems are often underreported due to social and psychological pressures, but are no less important. Supplementation with these nutrients can help.

Gender Specific Health (Women)-Ingredients: CoQ10, Lycopene, Ashwagandha

These ingredients help to support women's health, including ovary function, sexual function, and general genitourinary tract support.

Carotenoids, including lycopene, are broad-spectrum antioxidants that are highly beneficial in aging women. They prevent damage from free oxygen radicals [62, 63]. In post-menopausal women, carotenoid supplements have been shown to significantly reduce oxidative stress [72], help with healthy aging and promote a reduced risk of chronic disease.

Ashwagandha herb powder is not an aphrodisiac, but supplementation supports normal sexual arousal, lubrication, orgasm, and satisfaction in older women. It also reduced sexual distress and increased the number of successful sexual encounters [73].

Ubiquinone (CoQ10) combats oxidative stress in the ovaries, a main cause of ovarian aging and loss of hormone production and fertility (including menopause symptoms and related problems with cognition) [74]. CoQ10 use has been shown to restore oocyte function – the production and readying of new egg cells – and to increase fertility [75]. This antioxidant may also help maintain proper immune system function, preventing pregnancy loss [76, 77].

Review of Nutrient Amounts vs Current RDI Values

As of 2018, nutrient labels will be forced to change. This is part of an effort to decrease the practice of "fairy dusting" supplements with low amounts of nutrients so that they can be claimed on a label even if that ingredient is not in amounts large enough to produce an effect. Because "fairy dusting" is bad for consumers, changing the labelling practice helps to ensure better, more accurate labeling and better value for the consumer. A few of the requirements of this new labeling are:

- Column B2 ingredients now include Potassium, Vitamin D, Calcium, and Iron levels.
- If the supplementation has 2% or greater of the %DV (the percent daily value,) then it MUST be added to the label. Otherwise, it is excluded from the label completely [1].
- Other nutrients not in the vitamin B2 area should also follow suit.

In the Table below, the daily values (RDI) of each ingredient, and the amounts of each in the supplements, are compared. The nutrients in the multivitamins is equal to or greater than the values for adults and children over four years. MK7 is the exception, being lower than the RDI for Vitamin K, but does have significant health benefit data at the dose provided (45mcg/ day).

| | | RDI | |
|-----------|-------------------------|------------------------------------|-------------------|
| Nutrient | Unit of measure | Adults and children =4 years | Multivitamin Core |
| Vitamin A | Micrograms RAE (mcg) | 900 | 900 |
| Vitamin C | Milligrams (mg) | 90 | 90 |
| Iron | Milligrams (mg) | 18 | 18 |
| Vitamin D | Micrograms (mcg) | 20 | 25 |
| Vitamin E | Milligrams (mg) | 15 | 22.5 |

Table 3: Amount of nutrient in the Multi Core vs. the RDI for Adults and Children Four and Up.

| Vitamin K | Micrograms (mcg) | 120 | 45* |
|---------------------|-------------------------|-----|-------|
| Thiamin | Milligrams (mg) | 1.2 | 25 |
| Riboflavin | Milligrams (mg) | 1.3 | 60 |
| Niacin | Milligrams NE (mg) | 16 | 20 |
| Vitamin B6 | Milligrams (mg) | 1.7 | 100 |
| Folate | Micrograms DFE (mcg) | 400 | 400 |
| Vitamin B12 | Micrograms (mcg) | 2.4 | 1,000 |
| Biotin | Micrograms (mcg) | 30 | 300 |
| Pantothenic acid | Milligrams (mg) | 5 | 5 |
| lodine | Micrograms (mcg) | 150 | 100 |
| Magnesium | Milligrams (mg) | 420 | 400 |
| Zinc | Milligrams (mg) | 11 | 60 |
| Selenium | Micrograms (mcg) | 55 | 200 |
| Manganese | Milligrams (mg) | 2.3 | 4 |
| Chromium | Micrograms (mcg) | 35 | 200 |

| Molybdenum Micrograms (mcg) | 45 | 120 |
|--------------------------------|----|-----|
|--------------------------------|----|-----|

* = Clinical relevant dose. RDI does not represent accurately the use of MK7 as a Vitamin K source.

Conclusions

The multivitamin core has been formulated to meet or exceed the RDI for most nutrients listed in the new updates to nutrition labeling practices. The forms and amounts of each ingredient were carefully considered to ensure that the body would absorb each nutrient as well as possible. There is no evidence of fairy dusting practices within the formulation, so for both nutrient type and the nutrient amount there is a consistent quality to the formulation.

Together, the multivitamin and the nerve/tissue support product promote the health of men and women by giving the heart, brain, muscles, bones and other parts of the body the nutrients they need to function properly.

References:

- 1. 21CFR 101.9 Food Labeling. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=101.9
- Tsukamoto Y, Ichise H, Kakuda H, Yamaguchi M. Intake of fermented soybean (natto) increases circulating vitamin K2 (menaquinone-7) and gamma-carboxylated osteocalcin concentration in normal individuals. J Bone Miner Metab. 2000;18(4):216-22.
- 3. Vermeer C, Braam L. Role of K vitamins in the regulation of tissue calcification. J Bone Miner Metab. 2001;19(4):201-6.
- 4. Schurgers LJ, *et al.* Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. Blood. 2007 Apr 15;109(8):3279-83.
- 5. Xie F, Cheng Z, Li S, *et al*. Pharmacokinetic study of benfotiamine and the bioavailability assessment compared to thiamine hydrochloride. J Clin Pharmacol. 2014 Jun;54(6):688-95.
- 6. Powers HJ. Riboflavin (vitamin B-2) and health. Am J Clin Nutr. 2003 Jun;77(6):1352-60.
- Papoutsakis C, Yiannakouris N, Manios Y, *et al.* The effect of MTHFR(C677T) genotype on plasma homocysteine concentrations in healthy children is influenced by gender. Eur J Clin Nutr. 2006 Feb;60(2):155-62.
- Battistelli S, Vittoria A, Stefanoni M, *et al.* Total plasma homocysteine and methylenetetrahydrofolate reductase C677T polymorphism in patients with colorectal carcinoma. World J Gastroenterol. 2006 Oct 14;12(38):6128-32.
- 9. Bentley S, Hermes A, Phillips D, *et al.* Comparative effectiveness of a prenatal medical food to prenatal vitamins on hemoglobin levels and adverse outcomes: a retrospective analysis. Clin Ther. 2011 Feb;33(2):204-10.
- Smulders YM, Smith DE, Kok RM, *et al.* Cellular folate vitamer distribution during and after correction of vitamin B12 deficiency: a case for the methylfolate trap. Br J Haematol. 2006 Mar;132(5):623-9.
- 11. Albion chelates- http://www.albionminerals.com/human-nutrition/products-trade/traacs

- 12. Food and Nutrition Board, Institute of Medicine. Molybdenum. In: Dietary reference intakes for vitamin A, vitamin K, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington, D.C.: National Academy Press; 2001:420-441.
- 13. Leach RM, Harris ED. Manganese. In: O'Dell BL, Sunde RA, eds. Handbook of nutritionally essential minerals. New York: Marcel Dekker, Inc; 1997:335-355.
- Ashoush S, Abou-Gamrah A, Bayoumy H, Othman N. Chromium picolinate reduces insulin resistance in polycystic ovary syndrome: Randomized controlled trial. J Obstet Gynaecol Res. 2016 Mar;42(3):279-85.
- 15. ODS Monograph Chromium- https://ods.od.nih.gov/factsheets/Chromium-HealthProfessional/
- Jing CL, Dong XF, Wang ZM Comparative study of DL-selenomethionine vs sodium selenite and seleno-yeast on antioxidant activity and selenium status in laying hens. Poult Sci. 2015 May;94(5):965-75.
- 17. Burk RF, Hill KE, Motley AK, *et al.* Selenium deficiency occurs in some patients with moderate-tosevere cirrhosis and can be corrected by administration of selenate but not selenomethionine: a randomized controlled trial. Am J Clin Nutr. 2015 Nov;102(5):1126-33.
- Fidler MC, Davidsson L, Zeder C, Walczyk T, Hurrell RF. Iron absorption from ferrous fumarate in adult women is influenced by ascorbic acid but not by Na2EDTA. Br J Nutr. 2003 Dec;90(6):1081-5
- 19. Madhavi D, l Kagan D. A Study on the Bioavailability of a Novel Sustained Release Coenzyme Q10-β-Cyclodextrin Complex. Integrative Medicine 2010; 9(1).
- 20. Suh JH, Shenvi SV, Dixon BM, et al. Decline in transcriptional activity of Nrf2 causes age-related loss of glutathione synthesis, which is reversible with lipoic acid. Proc Natl Acad Sci U S A. 2004;101(10):3381-3386.
- 21. Suh JH, Wang H, Liu RM, Liu J, Hagen TM. (R)-alpha-lipoic acid reverses the age-related loss in GSH redox status in post-mitotic tissues: evidence for increased cysteine requirement for GSH synthesis. Arch Biochem Biophys. 2004;423(1):126-135.
- Ziegler D, Hanefeld M, Ruhnau K, et al. Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: A 7-month, multicenter, randomized, controlled trial (ALADIN III Study). Diabetes Care 1999;22:1296-301.
- Reljanovic M, Reichel G, Rett K, et al. Treatment of diabetic polyneuropathy with the antioxidant thioctic acid (alpha-lipoic acid): A 2-year, multicenter, randomized, double-blind, placebocontrolled trial (ALADIN II). Alpha Lipoic Acid in Diabetic Neuropathy [abstract]. Free Radic Res 1999;31:171-7.
- 24. Ziegler D, Hanefeld M, Ruhnau KJ, et al. Treatment of symptomatic diabetic peripheral neuropathy with the antioxidant alpha-lipoic acid: A 3-week, multicentre randomized controlled trial (ALADIN Study). Diabetologia 1995;38:1425-33.
- 25. Ruhnau KJ, Meissner HP, Finn JR, et al. Effects of 3-week oral treatment with the antioxidant thioctic acid (alpha-lipoic acid) in symptomatic diabetic polyneuropathy. Diabet Med 1999;16:1040-3.
- 26. Di Geronimo G., Caccese A. F., Caruso L., Soldati A., Passaretti U. Treatment of carpal tunnel syndrome with alpha-lipoic acid. Eur Rev Med Pharmacol Sci 2009;13(2):133-139.
- 27. Sauer J, Tabet N, Howard R. Alpha lipoic acid for dementia. Cochrane Database Syst Rev 2004;(1):CD004244.

- Hager K., Kenklies M., McAfoose J., Engel J., Münch G. Alpha-lipoic acid as a new treatment option for Alzheimer's disease--a 48 months follow-up analysis. J Neural Transm Suppl 2007;(72):189-193.
- Hernandez-Ojeda, J., Cardona-Munoz, E. G., Roman-Pintos, L. M., Troyo-Sanroman, R., Ortiz-Lazareno, P. C., Cardenas-Meza, M. A., Pascoe-Gonzalez, S., and Miranda-Diaz, A. G. The effect of ubiquinone in diabetic polyneuropathy: a randomized double-blind placebo-controlled study. J.Diabetes Complications 2012;26(4):352-358.
- 30. Lister RE. An open, pilot study to evaluate the potential benefits of coenzyme Q10 combined with Ginkgo biloba extract in fibromyalgia syndrome. J Int Med Res 2002;30:195-9.
- 31. Teitelbaum JE, Johnson C, St Cyr J. The use of D-ribose in chronic fatigue syndrome and fibromyalgia: a pilot study. J Altern Complement Med 2006;12:857-62
- 32. Plioplys AV, Plioplys S. Amantadine and L-carnitine treatment of Chronic Fatigue Syndrome. Neuropsychobiology 1997;35:16-23.
- 33. Witte AV, Kerti L, Margulies DS, Flöel A. Effects of resveratrol on memory performance, hippocampal functional connectivity, and glucose metabolism in healthy older adults. J Neurosci. 2014 Jun 4;34(23):7862-70.
- 34. Choudhary D, Bhattacharyya S, Bose S. Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions. J Diet Suppl. 2017 Nov 2;14(6):599-612
- 35. Welch AA, Kelaiditi E, Jennings A, et al. Dietary Magnesium Is Positively Associated With Skeletal Muscle Power and Indices of Muscle Mass and May Attenuate the Association Between Circulating C-Reactive Protein and Muscle Mass in Women. J Bone Miner Res. 2016 Feb;31(2):317-25
- 36. Welch AA, Skinner J, Hickson M. Dietary Magnesium May Be Protective for Aging of Bone and Skeletal Muscle in Middle and Younger Older Age Men and Women: Cross-Sectional Findings from the UK Biobank Cohort. Nutrients. 2017 Oct 30;9(11).
- 37. Beaudart C, Buckinx F, Rabenda V, *et al.* The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. Clin Endocrinol Metab. 2014 Nov;99(11):4336-45.
- Rizzoli R, Stevenson JC, Bauer JM, et al. The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Maturitas. 2014 Sep;79(1):122-32.
- 39. Wankhede S, Langade D, Joshi K, Sinha SR, Bhattacharyya S. Examining the effect of Withania somnifera supplementation on muscle strength and recovery: a randomized controlled trial. J Int Soc Sports Nutr. 2015 Nov 25;12:43.
- 40. Funk JL, Frye JB, Oyarzo JN, *et al.* Efficacy and mechanism of action of turmeric supplements in the treatment of experimental arthritis. Arthritis Rheum. 2006;54(11):3452-3464.
- 41. Li WQ, Dehnade F, Zafarullah M. Oncostatin M-induced matrix metalloproteinase and tissue inhibitor of metalloproteinase-3 genes expression in chondrocytes requires Janus kinase/STAT signaling pathway. J Immunol. 3-1-2001;166(5):3491-3498.
- 42. Dougados M. Sodium hyaluronate therapy in osteoarthritis: arguments for a potential beneficial structural effect. Semin Arthritis Rheum 2000;30(2 Suppl 1):19-25

- 43. Madhu K, Chanda K, Saji MJ. Safety and efficacy of Curcuma longa extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial. Inflammopharmacology 2013;21(2):129-36
- 44. Nieman DC, Shanely RA, Luo B, Dew D, Meaney MP, Sha W. A commercialized dietary supplement alleviates joint pain in community adults: a double-blind, placebo-controlled community trial. Nutr J 2013;12(1):154.
- 45. Moselhy SS, Demerdash SH. Plasma homocysteine and oxidative stress in cardiovascular disease. Dis Markers. 2003-2004;19(1):27-31.
- 46. Fratoni V, Brandi ML. B vitamins, homocysteine and bone health. Nutrients. 2015 Mar 30;7(4):2176-92.
- 47. Engelhard YN, Gazer B, Paran E. Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study. Am Heart J 2006;151:100.
- 48. Paran, E., Novack, V., Engelhard, Y. N., and Hazan-Halevy, I. The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients. Cardiovasc.Drugs Ther. 2009;23(2):145-151.
- 49. Langsjoen P, Willis R, Folkers K. Treatment of essential hypertension with coenzyme Q10. Mol Aspects Med 1994;S265-72.
- 50. Singh RB, Niaz MA, Rastogi SS, et al. Effect of hydrosoluble coenzyme Q10 on blood pressures and insulin resistance in hypertensive patients with coronary artery disease. J Hum Hypertens 1999;13:203-8
- 51. Suliburska J, Bogdanski P, Szulinska M, *et al.* Effects of green tea supplementation on elements, total antioxidants, lipids, and glucose values in the serum of obese patients. Biol Trace Elem Res. 2012 Dec;149(3):315-22.
- 52. Liu CY, Huang CJ, Huang LH, *et al.* Effects of green tea extract on insulin resistance and glucagonlike peptide 1 in patients with type 2 diabetes and lipid abnormalities: a randomized, doubleblinded, and placebo-controlled trial. PLoS One. 2014 Mar 10;9(3):e91163
- 53. Anderson RA, Cheng N, Bryden NA, et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. Diabetes 1997;46:1786-91.
- 54. Abraham AS, Brooks BA, Eylath U. The effects of chromium supplementation on serum glucose and lipids in patients with and without non-insulin dependent diabetes. Metabolism 1992;41:768-71.
- 55. Brownley KA, Von Holle A, Hamer RM, La Via M, Bulik CM. A double-blind, randomized pilot trial of chromium picolinate for binge eating disorder: results of the Binge Eating and Chromium (BEACh) study. J Psychosom Res. 2013 Jul;75(1):36-42
- 56. Rajkumar H, Mahmood N, Kumar M, *et al.* Effect of probiotic (VSL#3) and omega-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: a randomized, controlled trial. Mediators Inflamm. 2014;2014:348959
- 57. Wong VW, Won GL, Chim AM, *et al.* Treatment of nonalcoholic steatohepatitis with probiotics. A proof-of-concept study. Ann Hepatol. 2013 Mar-Apr;12(2):256-62
- 58. Pliml W, von Arnim T, Stalein A, et al. Effects of ribose on excercise-induced ischaemia in stable coronary artery disease. Lancet 1992;340:507-10.

- 59. Brevetti G, Chiariello M, Ferulano G, et al. Increases in walking distance in patients with peripheral vascular disease treated with L-carnitine: a double-blind, cross-over study. Circulation 1988;77:767-73.
- 60. Brevetti G, Chiariello M, Policicchio A, and et al. L-carnitine increases walking distance in patients with peripheral artery disease. Eur Heart J 1984;5(Abstr Suppl 1):138.
- 61. Brasky TM, Kristal AR, Navarro SL *et al*. Specialty supplements and prostate cancer risk in the VITamins and Lifestyle (VITAL) cohort. Nutr Cancer. 2011;63(4):573-82.
- 62. Rao AV, Agarwal S. Bioavailability and in vivo antioxidant properties of lycopene from tomato products and their possible role in the prevention of cancer. Nutr Cancer 1998;31:199-203.
- 63. Lu QY, Hung JC, Heber D, et al. Inverse associations between plasma lycopene and other carotenoids and prostate cancer. Cancer Epidemiol Biomarkers Prev 2001;10:749-56
- 64. Quarto G, Cola A, Perdonà S Efficacy of a formulation containing Serenoa repens, Crocus sativus and Pinus massoniana extracts in men with concomitant LUTS and erectile dysfunction. Minerva Urol Nefrol. 2017 Jun;69(3):300-306.
- 65. Sommer F, Schwarzer U, Wassmer G, *et al.* Epidemiology of Peyronie's disease International Journal of Impotence Research 2002; 14, 379–383
- 66. Safarinejad, M. R. Safety and efficacy of coenzyme Q10 supplementation in early chronic Peyronie's disease: a double-blind, placebo-controlled randomized study. Int J Impot.Res 2010;22(5):298-309.
- 67. Carson CC. Potassium para-aminobenzoate for the treatment of Peyronie's disease: is it effective? Tech Urol 1997;3:135-9.
- 68. Walsh B. MALE INFERTILITY CRISIS IN U.S. HAS EXPERTS BAFFLED http://www.newsweek.com/2017/09/22/male-infertility-crisis-experts-663074.html
- 69. Ambiye VR, Langade D, Dongre S, *et al.* Clinical Evaluation of the Spermatogenic Activity of the Root Extract of Ashwagandha (Withania somnifera) in Oligospermic Males: A Pilot Study. Evid Based Complement Alternat Med. 2013;2013:571420.
- 70. Zhou, X., Liu, F., and Zhai, S. Effect of L-carnitine and/or L-acetyl-carnitine in nutrition treatment for male infertility: a systematic review. Asia Pac.J Clin Nutr. 2007;16 Suppl 1:383-390.
- 71. Wang, Y. X., Yang, S. W., Qu, C. B, *et al.* [L-carnitine: safe and effective for asthenozoospermia]. Zhonghua Nan.Ke.Xue. 2010;16(5):420-422.
- 72. Zhao X, Aldini G, Johnson EJ, *et al.* Modification of lymphocyte DNA damage by carotenoid supplementation in postmenopausal women. Am J Clin Nutr. 2006 Jan;83(1):163-9.
- Dongre S, Langade D, Bhattacharyya S. Efficacy and Safety of Ashwagandha (Withania somnifera) Root Extract in Improving Sexual Function in Women: A Pilot Study. Biomed Res Int. 2015;2015:284154.
- 74. Özcan P, Fıçıcıoğlu C, Kizilkale O, *et al.* Can Coenzyme Q10 supplementation protect the ovarian reserve against oxidative damage? J Assist Reprod Genet. 2016 Sep;33(9):1223-30.
- 75. Ben-Meir A, Burstein E, Borrego-Alvarez A. Coenzyme Q10 restores oocyte mitochondrial function and fertility during reproductive aging. Aging Cell. 2015 Oct;14(5):887-95.
- 76. Talukdar A, Sharma KA, Rai R. Effect of Coenzyme Q10 on Th1/Th2 Paradigm in Females with Idiopathic Recurrent Pregnancy Loss. Am J Reprod Immunol. 2015 Aug;74(2):169-80.
- 77. Sandhir R, Sethi N, Aggarwal A, Khera A. Coenzyme Q10 treatment ameliorates cognitive deficits by modulating mitochondrial functions in surgically induced menopause. Neurochem Int. 2014 Jul;74:16-23.