PROTOCOL FOR LIFE BALANCE®

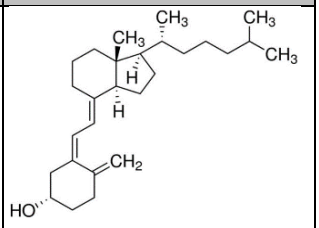
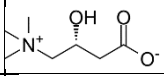
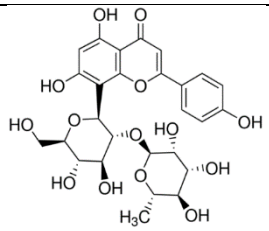
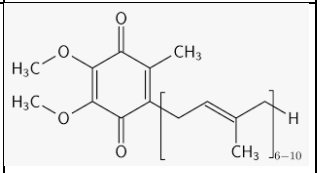
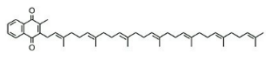
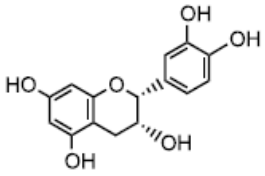
Dietary Supplement Information
for Physicians with Naturokinetics®
PRODUCT CODE: P3383
CATEGORY: CARDIOVASCULAR SUPPORT*

Clinical Cardio-6

TECHNICAL SUMMARY

Clinical Cardio-6 is a powerful combination of targeted nutrients and botanicals that are known to promote optimal cardiovascular health.* With L-carnitine and CoQ_{10} to support energy production in the heart, hawthorn and MegaNatural®-BP™ grape seed extract to support blood pressure already within the normal range, and MK-7 to help maintain arterial flexibility, Clinical Cardio-6 offers a comprehensive formula for healthy cardiovascular structures and functions.*

Chemical Name & Structure Formula:

Ingredient	Chemical Name or Molecular Formula	Structural Formula
Vitamin D_3	Cholecalciferol (activated 7-dehydrocholesterol; (3β,5Z,7E)-9,10-secocholesta-5,7,10(19)-trien-3-ol).	
L-Carnitine	3-hydroxy-4-(trimethylammonio)butanoate	
Vitexin-2″-O-rhamnoside	Vitexin-2″-O-rhamnoside	
Coenzyme Q10	2,3-dimethoxy-5-methyl-6-decaprenylbenzoquinone	
Vitamin K_2	2-methyl-3-farnesylgeranylgeranyl-1,4-naphthoquinone (menaquinone-7; MK-7)	
MegaNatural®-BP™ is standardized to a minimum 90% polyphenols including epicatechin	(2R,3S)-2-(3,4-Dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol	

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, soy, milk, egg, fish, or shellfish ingredients. Produced in a GMP facility that processes other ingredients containing these allergens. Cholecalciferol is from lanolin (sheep origin). MK-7 is produced using a soy-free substrate (chickpeas).

Delivery Form: Vegetable Capsules

Supplement Facts

Serving Size 1 Capsule

	Amount Per Serving	% Daily Value
Vitamin D (as D_3 Cholecalciferol) (from Lanolin)	25 mcg (1,000 IU)	125%
L-Carnitine (Carnipure®) (from 373 mg L-Carnitine Tartrate)	250 mg	†
Hawthorn Extract (*Crataegus laevigata* and/or *monogyna*) (Leaf & Flower) (Standardized to min. 1.8% Vitexin-2″-O-rhamnoside)	150 mg	†
Grape Seed Extract (MegaNatural®-BP™) (*Vitis vinifera*) (Standardized to min. 90% Polyphenols)	75 mg	†
Coenzyme Q10 (CoQ10) (Ubiquinone)	50 mg	†
Vitamin K_2 (as Menaquinone-7) (MK-7) (MenaQ7®) (from chickpea)	90 mcg	†

† Daily Value not established.

Other ingredients: Hypromellose (cellulose capsule), Microcrystalline Cellulose, Stearic Acid (vegetable source) and Silicon Dioxide.

- **Helps Maintain Blood Pressure Already Within the Healthy Range***
- **Clinically Validated Ingredients**

SUGGESTED USAGE: Take 1 capsule twice daily with food, or as directed by your healthcare practitioner.

ROLE AS NUTRIENT/FUNCTION

Vitamin D_3's function in the body is well established, allowing for the tight regulation of calcium levels in the blood, as well as phosphate homeostasis.* In addition, more recent discoveries have shown that vitamin D is also involved in many other bodily functions such as regulation of cell proliferation, cell differentiation, immunomodulation, and cardiovascular health.*

Vitamin K_2 is a generic term for a group of molecules of different sizes. This product has menaquinone-7, a purified form of vitamin K_2 with unique biological properties. Vitamin K is essential for the proper function (gamma-carboxylation of glutamyl amino acid residues) of GLA-proteins in the body, including proteins involved in extracellular matrix mineralization such as osteocalcin in bones and other matrix GLA-proteins (MGP) found in cartilage and artery walls.* Clinical data suggest that MK-7 supplementation is able to induce prolonged carboxylation of osteocalcin and MGP in the blood.*

Preliminary data suggest that synergy exists between vitamin D_3 and vitamin K_2.* It appears that this synergy is the result of several combined biological functions. For example, they are both involved in osteocalcin regulation in the body; vitamin D_3 regulates its production and vitamin K_2 is necessary for its activation.*

L-carnitine is required for energy production.* It facilitates the transport of fatty acids across the inner mitochondrial membrane for subsequent β-oxidation, a process also known as the carnitine shuttle.* Fatty acids are the predominant substrate for energy production in skeletal and cardiac muscle at rest.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Hawthorn extract has free radical scavenging and cardio protective properties.* It regulates coronary blood flow and enhances oxygen flow and utilization by the heart.* Hawthorn exerts simultaneous inotropic and vasodilatory action.*

CoQ_{10} has multiple cellular and extracellular functions, primarily based on its ability to undergo redox cycling.* CoQ_{10} is involved in ATP synthesis (as part of the electron transport chain of the inner membrane of mitochondria) and has the ability to act as a free radical scavenger.* CoQ_{10} is especially important for heart muscle function where its concentration is higher than in any other tissue in the body.*

MegaNatural®-BP™ is a grapeseed extract standardized to minimum 90% polyphenols. This proprietary grapeseed extract has been extensively investigated in laboratory settings and in randomized clinical studies. Results from these investigations show that MegaNatural®-BP™ has powerful free radical scavenging properties as well as has demonstrated its ability to contribute to endothelial relaxation in laboratory settings.* It may also affect platelet aggregation.*

NATUROKINETICS®

Liberation: Vegetable capsules disintegrate within 60 minutes in a USP water disintegration test.

Absorption: Absorption information for this formula has not been clinically evaluated; however, absorption data for each ingredient are available below.

Both vitamin D_3 and K_2 are fat soluble vitamins. Following oral ingestion, MK-7 is rapidly and well absorbed in the intestine and enters blood circulation via the lymphatic system as part of the chylomicron fraction of plasma.

Like vitamin K_2, vitamin D_3 is absorbed with other dietary fats in the small intestine, enters the blood circulation via the lymphatic system, and is transported in the chylomicron fraction of plasma.

CoQ_{10} is also a fat-soluble substance and its absorption follows the same process as that of lipids in the gastrointestinal tract. After oral ingestion, peak blood levels is reached after approximately 6 h.

Vitamin K_2, D_3, and CoQ_{10} are most efficiently absorbed when consumed with foods containing fat.

L-Carnitine is absorbed in the intestine using an active specific transporter. After oral ingestion peak blood levels are reached after 3 hours.

Vitexin-2-O-rhamnoside (VOR), the compound to which our hawthorn extract is standardized, is absorbed via passive diffusion. After a single oral administration of hawthorn extract, VOR peak blood level is reached after 45 minutes.

After oral ingestion of 200 mg and 300 mg MegaNatural®-BP™, an increase of epicatechin levels in the blood is detectable with a maximum concentrations of 3 nM and 21 nM, respectively. Peak plasma concentration of epicatechin were obtained respectively, 2 hours and 1 hour after oral ingestion. Epicatechin is known to be poorly absorbed intact because of its extensive metabolism in the GI tract. Some epicatechin metabolites formed in the GI tract are rapidly absorbed in the small intestine and reach the bloodstream. Other metabolites are absorbed in the colon before reaching the bloodstream.

Distribution: MK-7 has a long half-life; indeed after oral ingestion, it can be detected in the plasma for more than 48 hours and up to 92 hours.

MK-7's distribution in tissues has not been yet fully elucidated; however, it is known to be present in the liver, pancreas, heart, and bone lipids.

Once vitamin D enters the circulation, it is cleared by the liver or stored in fat tissues within a few hours. However, the vitamin D deposited in fat is not readily available to exert its bodily functions.

Approximately 98% of the body's carnitine is located within cardiac and skeletal muscle tissues. Carnitine crosses the blood-brain barrier where it selectively accumulates in the hypothalamus.

Tissue distribution of VOR is dependent on the blood flow or perfusion rate of the organ. Considerable amounts are detected in liver and kidneys, followed by lung, heart and spleen. VOR does not cross blood-brain barrier.

Tissue distribution of CoQ_{10} is related to its metabolic activity and the tissue/organ lipid content. Inside cells, 40-50% of CoQ_{10} is located inside mitochondria.

Tissue distribution of MegaNatural®-BP™ has not been evaluated. However, it is known that epicatechin, one of its constituents, is mainly distributed in the plasma after oral ingestion, and is metabolized and eliminated from the body before being able to be deposited in tissues.

Metabolism: In the bloodstream, chylomicrons carrying vitamin K are metabolized into chylomicron remnants which are cleared by the liver. MK-7 metabolism in the liver is only partially known, it is most likely degraded through omega- and beta-oxidation and the obtained metabolites are then conjugated with glucuronic acid.

Vitamin D is an inactive prohormone and must first be metabolized to its active form before it can exert its biological functions. This metabolism is complex with a first phase occurring in the liver and a second phase in the kidney. It is tightly regulated by the parathyroid gland, which is sensitive to changes in blood calcium and phosphate levels.

Orally ingested L-carnitine enters the total body carnitine pool, which is comprised of exogenous (approx. 75%) and endogenous carnitine. It is transported into cardiac and skeletal muscle tissue via carnitine transporters, and then intracellularly, into mitochondria. Besides acylation, there are no known metabolic pathways of carnitine degradation in humans.

The exact metabolic pathway of VOR is currently unknown.

CoQ_{10}cycles between its reduced form (ubiquinol) and oxidized form (ubiquinone) as it participates in metabolic reactions.

Epicatechin metabolism is very complex, it is extensively metabolized in the proximal GI tract, which partially explains why, after oral ingestion, only a small fraction of intact epicatechin can be detected in the bloodstream. In addition to being metabolized in enterocytes, epicatechin is also metabolized in the liver.

Elimination: The products of MK-7, vitamin D, VOR, CoQ_{10} metabolism are mainly excreted via hepatobiliary route.

Urinary elimination is a minor route for MK-7, vitamin D.

Carnitine is eliminated from the body primarily via renal excretion of non-esterified carnitine and acylcarnitine esters. However, under normal

conditions, only a very small fraction (usually < 5%) of filtered carnitine is excreted.

Epicatechin and its metabolites are mainly excreted in urine with a minor route of elimination in feces.

CLINICAL VALIDATION

- **Helps Maintain Blood Pressure Already Within the Healthy Range*.** In a randomized, placebo controlled clinical trial with 24 adult volunteers receiving 150 mg or 300 mg grape seed extract daily for four weeks, normal blood pressure was significantly lowered in the grape seed group after four weeks vs. baseline.*
- **Energy Production and Muscle Function Support.*** In a double-blind randomized clinical trial with 14 healthy adult volunteers, 24 weeks of supplementation with L-Carnitine Tartrate (Carnipure™, 2 g twice a day with 80 g of simple carbohydrates per intake) resulted in a significant increase in the total muscle carnitine content (21% as compared to baseline confirmed by biopsy), while it remained unchanged in the control group (80 g of carbohydrates twice a day). When subjected to a standardized cycling exercise challenge, the carnitine group increased work output by 11% while the control showed no change.* Additionally, the carnitine group utilized 55% less muscle glycogen ($P < 0.05$) during the challenge, which is consistent with an increase in lipid utilization for energy production.*

SAFETY INFORMATION

Tolerability: Vitamin D_3 is typically well tolerated.

Minor GI manifestations (nausea, abdominal discomfort) have been sometimes described with vitamin K_2, carnitine, CoQ_{10}, grape seed extract, and hawthorn supplementation.

Dizziness, headaches, heart palpitations have been sometimes described with L-carnitine L-tartrate, hawthorn, and grape seed extracts supplementation.

While L-carnitine L-tartrate is generally well tolerated, agitation, restlessness and motor over-activity have been reported.

Contraindications: Individuals receiving vitamin K antagonists (VKA), hypercalcemia, hypothyroidism, seizure, and allergy to hawthorn should consult a healthcare professional prior to use of the product.

INTERACTIONS

Drug Interactions: May interact with cardiac glycosides, statin medications, thiazide diuretics, anti-hypertensive medication, and anti-coagulant medication.

Supplement Interactions: Vitamin D increases calcium and magnesium absorption and may therefore interact with calcium and magnesium supplementation.

CoQ_{10} and vitamin K_2 have similar chemical structures, concomitant use may theoretically have an additive effect.

Supplementation with grape seed extract may interfere with iron absorption.

Interaction with Lab Tests: Theoretically, blood calcium and urinary calcium may be modified by a combined supplementation with vitamin K_2 and vitamin D_3. However, this has not been clinically evaluated.

Osteocalcin blood levels can be increased by vitamin K_2 supplementation.

Hawthorn may interfere with serum digoxin immunoassay.

STORAGE

Store in cool, dry environment in a tightly sealed container. Store at ambient temperature. Protect from excessive heat, light and moisture.