



# FOUR PILLARS CARDIO

Complete daily nutritional supplement\*

## Complete daily nutrition emphasizing cardiovascular health\*

- Includes the four major cornerstones of nutrition: vitamins and minerals, omega-3 fatty acids, phytonutrients, and human-sourced probiotics
- Supports cardiovascular health and muscle function\*
- Promotes healthy lipid and energy metabolism\*
- Provides Cardiophenol™ fruit blend for antioxidant support\*
- Supports eye, skin, immune, bone and gastrointestinal health\*



Four Pillars Cardio promotes optimal nutritional status with a unique combination of vitamins and minerals, omega-3 fatty acids, herbs, and probiotics.\* This blend of nutrients and standardized herbal extracts was specifically formulated to support cardiovascular health.\* Coenzyme Q<sub>10</sub> helps produce energy for cellular functions and muscle contractions, and promotes antioxidant defense in conjunction with Cardiophenol™ grape and organic cranberry extract.\* Hawthorn supports cardiovascular function, while garlic and the omega-3 fatty acids DHA and EPA promote healthy lipid metabolism and blood flow.\* Four Pillars Cardio also contains over 20 vitamins and minerals to support overall well-being, plus probiotics to help support gastrointestinal health.\*

\* 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.

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### SUPPLEMENT FACTS

Serving Size 1 Tablet

Amount per serving		%DV
Vitamin A (as vitamin A acetate)	1000 IU	20%
Vitamin C (ascorbic acid)	180 mg	300%
Vitamin D <sub>3</sub> (as cholecalciferol)	1000 IU	250%
Vitamin E (as <i>d</i> -alpha tocopheryl succinate)	30 IU	100%
Vitamin K <sub>2</sub> (as Menaquinone-7)	120 mcg	150%
Thiamin (as thiamin mononitrate)	12.5 mg	833%
Riboflavin	12.5 mg	735%
Niacin (as niacinamide)	25 mg	125%
Vitamin B <sub>6</sub> (as pyridoxal-5-phosphate)	12.5 mg	625%
Folate (as calcium L-5-methyltetrahydrofolate, Metafolin®▲)	400 mcg	100%
Vitamin B <sub>12</sub> (as methylcobalamin)	400 mcg	6667%
Biotin	100 mcg	33%
Pantothenic acid (as calcium <i>d</i> -pantothenate)	25 mg	250%
Calcium (as calcium citrate malate)	50 mg	5%
Iodine (as potassium iodide)	150 mcg	100%
Magnesium (as magnesium citrate)	25 mg	6%
Zinc (as zinc citrate)	11 mg	73%
Selenium (as selenomethionine)	100 mcg	143%
Copper (as copper gluconate)	1 mg	50%
Manganese (as manganese gluconate)	2.3 mg	115%
Chromium (as chromium polynicotinate)	60 mcg	50%
Molybdenum (as potassium molybdate)	45 mcg	60%
Potassium (as potassium citrate monohydrate)	50 mg	1%
Lutein (from Aztec marigold flower)	5 mg	†
Zeaxanthin (from Aztec marigold flower)	1 mg	†

† % Daily Value (DV) not established

Other ingredients: Cellulose, hypromellose, croscarmellose sodium, ascorbyl palmitate, silica, glycerin

▲ Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

### Recommended intake

**Adults:** Contents of one serrated blister pack strip: 1 tablet, 1 softgel, 1 capsule (light brown) and 1 capsule (off-white), all taken once daily with a meal, at least two to three hours before or after taking medications or as professionally directed.

### Pack Size

30 Day Supply  
(30 strips of 1 tablet, 2 capsules and 1 softgel)

### Product Code

FP03-30



### SUPPLEMENT FACTS

Serving Size 1 Softgel

Amount per serving		%DV
Calories	15	
Calories from Fat	10	
Total Fat	1 g	2%◆
Cholesterol	10 mg	4%◆
Eicosapentaenoic acid (EPA)	395 mg	†
Docosahexaenoic acid (DHA)	265 mg	†
Total omega-3 (EPA, DHA & other omega-3's provided as sardine & anchovy oil)	750 mg	†

◆ % Daily Values (DV) are based on a 2,000 calorie diet  
† % Daily Value not established

Other ingredients: Fish gelatin (tilapia, striped catfish, Nile perch, carp, shad, grunt, catfish), glycerin, orange oil, natural mixed tocopherols

### SUPPLEMENT FACTS

Serving Size 1 Capsule (light brown powder-filled)

Amount per serving		%DV
Magnesium (as magnesium citrate)	50 mg	13%
Cardiophenol™ Proprietary Blend	115 mg	†
Grape ( <i>Vitis vinifera</i> ) seed extract		
Organic cranberry ( <i>Vaccinium macrocarpon</i> ) fruit extract		
Garlic ( <i>Allium sativum</i> ) bulb std. extract (1% allicin)	100 mg	†
Hawthorn ( <i>Crataegus monogyna/laevigata</i> ) flower and leaf std. extract (3-6:1) (165-330 mg dried equivalent/1.5% flavonoids)	55 mg	†
Coenzyme Q <sub>10</sub> (from yeast fermentation)	40 mg	†

† % Daily Value (DV) not established

Other ingredients: Hypromellose, ascorbyl palmitate, silica

### SUPPLEMENT FACTS

Serving Size 1 Capsule (off-white powder-filled)

Amount per serving		%DV
<b>HLC Consortium</b>	10 billion CFU	†
<i>Lactobacillus acidophilus</i> (CUL-60)		
<i>Lactobacillus acidophilus</i> (CUL-21)		
<i>Bifidobacterium animalis</i> subsp. <i>lactis</i> (CUL-34)		
<i>Bifidobacterium bifidum</i> (CUL-20)		

† % Daily Value (DV) not established

Other ingredients: Cellulose, hypromellose

## Scientific Rationale:

### Pillar 1: Vitamins and Minerals

Multivitamin and mineral supplements help individuals to obtain recommended levels of essential nutrients.<sup>1</sup> Dietary supplementation may be especially important to specific populations, including pregnant or lactating women, individuals who avoid specific food groups or those who regularly consume processed and fast food.<sup>1</sup> Randomized, placebo-controlled trials have found that daily supplementation with multivitamin and mineral supplements raise nutrient levels in the plasma and promote general wellbeing, including cognitive support and the promotion of healthy homocysteine metabolism.<sup>2-7\*</sup> Pillar 1 provides a combination of more than 20 vitamins and minerals (plus lutein and zeaxanthin) to maintain overall health.<sup>8-23\*</sup> It has been reformulated to provide additional nutritional support when compared to the original Four Pillars product.

B vitamins are critical for supporting cellular energy metabolism and neurotransmitter synthesis.<sup>8\*</sup> Four Pillars Cardio provides Metafolin<sup>®</sup>, a patented, natural form of (6S) 5-methyltetrahydrofolate (5-MTHF). 5-MTHF is the naturally occurring, predominant form of folate commonly found in cells.<sup>9\*</sup> It can be used directly by the body and does not depend on the genotype of folate-dependent enzymes.<sup>9\*</sup> Metafolin<sup>®</sup> may be more appropriate for supplementation than folic acid as it does not mask the symptoms of vitamin B<sub>12</sub> deficiency.<sup>9\*</sup> Four Pillars Cardio also contains lutein and zeaxanthin, natural carotenoid pigments that are highly concentrated within the lens and macula of the retina.<sup>10\*</sup> As the primary carotenoids in these areas, they have a unique ability to protect the eye against oxidative damage produced by metabolic activity and light exposure.<sup>10\*</sup> Clinical trials have also shown that daily supplementation with lutein and zeaxanthin promotes healthy macular pigment optical density in older adults.<sup>11,12\*</sup> Vitamin K has an important role in maintaining bone health through the carboxylation of osteocalcin, a protein that regulates calcium uptake and bone mineral maturation.<sup>13\*</sup> Vitamin K<sub>2</sub> is provided as menaquinone-7, a highly bioavailable (compared to vitamin K<sub>1</sub> and menaquinone-4) and effective form of the vitamin, likely due to its long half-life time.<sup>14-16\*</sup> As free radical generation increases during exercise, Four Pillars Cardio contains selenium, plus the key antioxidant vitamins C and E for antioxidant defence.<sup>17\*</sup> This blend also supports healthy glucose metabolism, proper muscle and thyroid gland function, and the maintenance of eyesight, skin, membranes and immune function.<sup>18-23\*</sup>

### Pillar 2: Omega-3 Fatty Acids

Both omega-3 and omega-6 polyunsaturated fatty acids are critical to maintain overall health, yet omega-3 fatty acids are still under-consumed in the general population.<sup>24\*</sup> An increased use of high omega-6 fatty acid-vegetable oils over the past 100 years has accentuated the imbalance between levels of omega-6 and omega-3 consumption.<sup>24</sup> It has been estimated that approximately 200 years ago, the intake ratio of omega-6 to omega-3 fatty acids in North America was 1.5:1; today it is close to 16:1.<sup>24</sup> As omega-3 and omega-6 fatty acids compete for the same enzymes, increased intake of one will reduce the metabolism of the other.<sup>24</sup> Recent research has found that daily supplementation with DHA and EPA helps to promote cardiovascular health in adults, including support for healthy triglyceride metabolism and blood flow.<sup>25-30\*</sup>

### Pillar 3: Phytonutrients

#### Cardiophenol™

Oxidative stress can be generated by cellular respiration and certain enzyme systems.<sup>31\*</sup> The production of free radicals can result in the oxidative damage of lipids, proteins and nucleic acids, impairing the normal function of cells.<sup>31\*</sup> Free radical formation increases naturally with age and is amplified during exercise, as contracting muscles produce higher levels of oxidants.<sup>31,32\*</sup> In turn, oxidative stress during exercise can mediate the function of contractile proteins and result in muscular fatigue.<sup>32\*</sup> Antioxidants decrease oxidative stress by reacting with free radicals to prevent their propagation.<sup>31\*</sup>

Cardiophenol™ is a blend of grape and organic cranberry extracts. Clinical trials have found that cranberry and grape seed extracts contain polyphenols that support the antioxidant defense system, including decreased LDL oxidation.<sup>33-36\*</sup> These extracts may also promote healthy systolic function, likely due to the increased nitric oxide bioavailability associated with decreased oxidative stress.<sup>35,37,38\*</sup> Cranberry extract may also support cardiovascular function by promoting healthy lipid metabolism.<sup>34-35\*</sup>

#### Coenzyme Q<sub>10</sub>

Coenzyme Q<sub>10</sub> is required for electron transfer in the mitochondrial respiratory chain, which produces energy necessary for cellular functions and muscle contractions.<sup>39,40\*</sup> As a result, its highest levels are found in the most metabolically active tissues, including the heart.<sup>39</sup> Coenzyme Q<sub>10</sub> supplementation has been shown to promote cardiovascular health in adults, including support for endothelial function and contractility of the heart after exercise.<sup>41-44\*</sup> It also maintains antioxidant defense and promotes healthy expression of antioxidant enzymes, including catalase, superoxide dismutase and glutathione peroxidase.<sup>44-46\*</sup> Decreases in serum and tissue coenzyme Q<sub>10</sub> are associated with aging and statin drug use, and research demonstrates that it is difficult to increase coenzyme Q<sub>10</sub> levels from the diet alone.<sup>47\*</sup> Therefore, supplementation to increase coenzyme Q<sub>10</sub> levels may be especially beneficial in these populations.<sup>47\*</sup>

#### Hawthorn

Hawthorn is a red fruit-bearing plant with white flowers that is native to the temperate regions of Europe, Asia and eastern North America.<sup>48</sup> The most potent parts of the plant include its leaves and flowers, which contain a variety of flavonoid compounds.<sup>48</sup> These flavonoids possess antioxidant activity and may contribute to supporting cardiovascular health.<sup>48\*</sup> Research demonstrates that hawthorn promotes normal heart rhythms by mediating potassium channels in the heart, which stabilizes the length of the refractory period and action potential.<sup>48\*</sup> By regulating calcium levels in the cell, hawthorn may control the contractile force of heart muscles.<sup>48\*</sup> Hawthorn also promotes healthy blood flow by supporting nitric oxide production from endothelial cells.<sup>48\*</sup> In a meta-analysis that included 14 randomized, double-blind, placebo-controlled trials, hawthorn supplementation was found to significantly promote healthy cardiovascular function.<sup>49\*</sup>

## Garlic

The main bioactive compound in garlic is allicin.<sup>50</sup> When broken down, this sulfur-containing compound is responsible for garlic's characteristic odor.<sup>50</sup> Clinical trials have demonstrated that garlic supports cardiovascular health by promoting healthy artery, platelet and endothelial cell function.<sup>51-54\*</sup> Garlic also supports the antioxidant defense system and decreases oxidative stress in both lipids and DNA.<sup>52-54\*</sup> Studies have also extensively researched the ability of garlic to mediate lipid metabolism, and clinical trials have found that garlic supports healthy cholesterol metabolism.<sup>55-59\*</sup>

## Magnesium

Magnesium is a cofactor for over 600 enzymes that mediate, in part, amino acid synthesis and glycolysis.<sup>60\*</sup> It is also a natural calcium channel blocker that may promote cardiovascular health by regulating cardiac excitability, vascular-smooth muscle and endothelial cells.<sup>61-63\*</sup> A meta-analysis of 16 clinical trials found that dietary and circulating magnesium levels are associated with heart and cardiovascular health.<sup>64\*</sup> Specifically, meta-analyses have reported that magnesium supplementation promotes healthy heart rhythms, systolic and diastolic function, and glucose metabolism.<sup>65-67\*</sup> Magnesium is also a cofactor for the enzyme creatine kinase, which generates ATP from phosphocreatine stored in muscle tissues during intense exercise (known as lactic anaerobic metabolism).<sup>68\*</sup> Supplementation with magnesium has been found to support muscle function associated with intense exercise by improving lactic anaerobic metabolism.<sup>68\*</sup> Similarly, a clinical trial reported that magnesium intake supported exercise performance, as measured by VO<sub>2</sub> max, heart rate and left ventricular ejection fraction.<sup>65\*</sup>

## Pillar 4: Probiotics

The human intestinal tract contains more than 400 bacterial species, although its composition can be altered by diet, stress, medication and age.<sup>69\*</sup> Bacterial balance needs to be maintained for healthy intestines, which selectively allow absorbance and promote the excretion of dangerous substances.<sup>69,70\*</sup> Probiotics mediate microbial colonization of the gastrointestinal tract by reducing the pH and stimulating the production of antimicrobial peptides in the intestine.<sup>70\*</sup> In addition to controlling bacterial survival, probiotics strengthen the epithelial barrier.<sup>70\*</sup> They mediate the integrity of tight junctions and increase mucin release, which regulates permeability and reduces microbial adherence to cells.<sup>71\*</sup>

Additionally, approximately 80% of the body's immunologically active cells are located in gut-associated lymphoid tissue, demonstrating an important interaction between the intestines and the immune system.<sup>72\*</sup> Recent research has demonstrated a close relationship between the brain and gut, known as the "gut-brain axis."<sup>73\*</sup> Studies show that the gastrointestinal tract and brain communicate using four main information carriers (neurons, cytokines, gut hormones and microbial factors) to send neural, immune and endocrine messages.<sup>73\*</sup> This connection appears to be bi-directional, as the brain may influence microflora composition and gastrointestinal function, while gut health may impact cognition, mood, appetite and stress.<sup>73\*</sup>

The effect of probiotics on cardiovascular health is a rapidly emerging area of interest. A meta-analysis of randomized controlled trials reported that probiotic intake significantly promotes healthy total and LDL cholesterol metabolism.<sup>74\*</sup> An additional meta-analysis of randomized controlled trials found that probiotic supplementation promotes healthy systolic and diastolic function, likely through regulations of the rennin-angiotensin system, as well as lipid and glucose metabolism.<sup>75\*</sup>

Supplementation with a combination of microorganisms helps maximize intestinal colonization, promoting the growth of beneficial bacteria.<sup>70\*</sup> Four Pillars Cognitive is formulated using Seroyal's *Lactobacillus* and *Bifidobacterium* probiotic consortium. These microorganisms have been used in a wide body of clinical research, and have been found to promote gastrointestinal comfort and immune health (when combined with vitamin C).<sup>76-80\*</sup>

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