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Review Article

# A Holistic Approach in Treating Heart Failure with Prosystole

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## I N F O

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## A B S T R A C T

Due to the rising interest in personal health, ageing population and promising solutions for individualised treatment, the market for nutritional supplements is anticipated to rise by more than 6% per year through 2018. Fish oil, vitamin D, multivitamins and coenzyme Q10 (CoQ10) are the most popular dietary supplements. Probiotics are also the supplement with the fastest rate of growth in this ranking. One of the largest global burdens of cardiovascular disease (CVD) is seen in India. According to projections, there would be 4.77 million CVD deaths in India annually by 2025, up from 2.26 million in 1990. Although the causes of increased CVD risk factor incidence rates are complicated, they probably involve urbanisation-related lifestyle changes as well as epidemiological and dietary changes brought on by economic development. This review brings in the significance of nutritional supplements as adjuvant therapy in the treatment of cardiovascular diseases.

**Keywords:** Cardiovascular Diseases, Nutritional Supplement, Medication, Prosystole

## Introduction

The Indian Council of Medical Research and Registrar General of India conducted a study in India which showed that approximately 60 per cent of the population was identified to be part of the world's heart disease burden. About 17.9 million people die every year due to Cardio Vascular Diseases (CVDs) across the globe. The cases of CVD were nearly 271 million in 1990 and doubled nearly to 523 million by the year 2019. The death rate due to CVD increased from 12.1 million in the year 1990 to 18.6 million in the year 2019. According to WHO, the age-adjusted CVD mortality in India is lower in women as compared to men (265 women and 349 men per 100,000 people). The reported rates are 2-3 times more than those in the United States (170 men and 108 women per 100,000 people). It has been observed that CVD in India has caused 20.3% and 16.9% mortality in men and women respectively. This high prevalence demands lifestyle modifications and appropriate medication.[1]

CVD is characterised by thick and narrow coronary arteries that bring blood to the heart, thereby disrupting the flow of oxygen and nutrients to the heart. Lifestyle modifications such as a healthy diet, regular exercise, low sodium intake, and quitting smoking and alcohol consumption are the primary steps in order to manage heart disease. When lifestyle modification is unable to bring in major changes,

medication is advised depending on the severity of the disease. Commonly used medications for the treatment of CVDs include the use of anticoagulants or blood thinners to decrease the clotting ability of the blood, and angiotensin-converting enzyme inhibitors to promote the expansion of blood vessels and also to regulate blood pressure. Beta-blockers aid in slowing the heart rate and calcium channel blockers interrupt the movement of calcium into the cells to lower the heart rate. Other medications help to relieve the heart's workload by getting rid of excess body fluids. Surgery may also be required if both lifestyle changes and medication do not support in improving the condition. Angioplasty, stent placement and bypass surgery are some of the medical procedures to treat heart diseases at various levels. Though drugs play a significant role in the prevention and cure of diseases, a wide range of drug regimens also contributes to adverse drug reactions. Drug therapy problems are encountered by the patients during prescribing, transcribing, dispensing and use of medication therapy.[2] This article elaborates on the significance of Prosystole – a nutritional supplement for the effective management of CVDs.

## Prosystole: A Nutritional Supplement

Prosystole symbolises the enhancement of ejection fraction in patients with systolic dysfunction. Each soft gelatin capsule contains 200 mg of omega 3 fatty acids + vitamin C 60 mg + magnesium 15 mg + l-methylfolate calcium 1 mg + benfotiamine 100 mg + adenosylcobalamin 500 mcg + CoQ10 15 mg + l-carnitine 60 mg + zinc sulphate monohydrate 10 mg + lycopene 6% 12 mg. Three components namely coenzyme Q10, l-carnitine and omega 3 PUFA contribute to the beneficiary action of this supplement in heart failure (Figure 1).

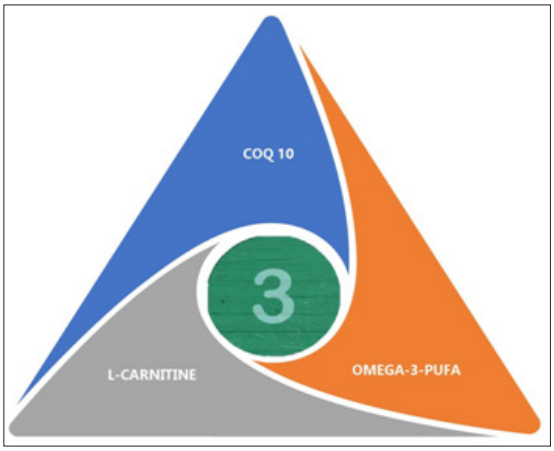


**Figure 1.Key Components of the Supplement**

## Physiological Role of Coenzyme Q10

10 stands for the quantity of isoprenyl chemical subunits in its tail, while Q stands for the quinone chemical groups. A 1,4-benzoquinone makes up the highly lipophilic molecule known as CoQ10. Coenzyme Q10 is a member of a class of substances distinguished by the presence of quinone moieties as well as the nature, size, and composition of their hydrophobic tails. It is a common component of most cellular membranes, although its main function is to promote ATP synthesis by taking part in redox processes in the mitochondria's electron transport chain (Figure 2). This coenzyme transfers electrons to complex III from complexes I and II within the electron transport chain. Besides providing antioxidant activity, this coenzyme also enhances endothelial function. A study on the in-vitro analyses of this enzyme on human umbilical vein endothelial cells has shown the reduction of the oxidised form of low-density lipoprotein-induced endothelin – 1, a potent vasoconstrictor. This supplement is also found to increase nitric oxide availability and decrease the cytochrome c secretion, which is required for the activation of proapoptotic proteins.[3-5]

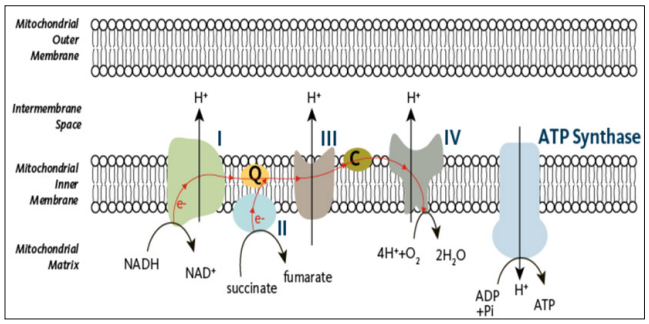


**Figure 2.Mechanism of Electron Transport Chain**

A study demonstrated by Lee et al. on 43 patients showed a significant improvement in antioxidant function with reduced levels of interleukin 6. Another study by Yuberro Serrano et al. revealed the synergic effect in reducing the expression of both stress and pro-inflammatory genes when CoQ10 was given along with a Mediterranean diet. CoQ10 may be an additional treatment option for patients with heart failure characterised by reduced ejection fraction, according to a recent trial. Small, heterogeneous research only provides a limited amount of evidence to support its broad use of CoQ10.[6-8]

## Physiological Role of L-carnitine

L-carnitine (L-C) makes it easier for long-chain fatty acids to enter the mitochondrial matrix, which results in the reduction of oxidative stress, necrosis of cardiac myocytes and inflammation, which all have cardioprotective effects. In order to maintain cellular homeostasis, l-carnitine also controls the influx of calcium, endothelium integrity, membrane phospholipid content and intracellular enzyme release. Carnitine depletion is an autosomal recessive metabolic illness that usually co-occurs with cardiovascular diseases (CVD). It is characterised by decreased expression

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of the "organic cation transporter-2" gene. Therefore, administering exogenous carnitine via dietary means acts as a good preventative measure against cardiac arrhythmia, ventricular dysfunction, toxic myocardial injury, and ischemia-reperfusion injury. A recent meta-analysis on the use of l-carnitine in the secondary prevention of cardiovascular disease was carried out by DiNicolantonio et al.[9] In individuals with acute myocardial infarction, l-carnitine was linked to a 40% reduction in angina (AMI), a 65% reduction in ventricular arrhythmias, and a 27% reduction in all-cause mortality. In addition to an increase in endothelial function, l-carnitine also displays cardioprotective effects by reducing oxidative stress, fibrosis, cardiac inflammation, nitric oxide, interstitial remodelling, and arterial hypertension.[10-12]

Preventing the buildup of long-chain acyl-CoA, which makes it easier for damaged mitochondria to produce free radicals, improves the repair mechanisms that cause oxidative damage to membrane phospholipids, thereby inhibiting malignant arrhythmias caused by long-chain acyl-CoA accumulation in the myocardium, reduction in ischemia-induced apoptosis, and the subsequent remodelling of the left ventricle. Levocarnitine may improve ischaemia and reperfusion. Propionyl-l-carnitine is a carnitine derivative which enhances the cellular carnitine content to enable the transport of free fatty acids into the mitochondria. It also has a high affinity for muscle carnitine transferase. Propionyl-l-carnitine increases the capacity to exercise in patients with heart failure and maintains cardiac function, according to a multicenter trial involving 537 participants.[13-15] Figure 3 shows the mechanism of action of L-carnitine.

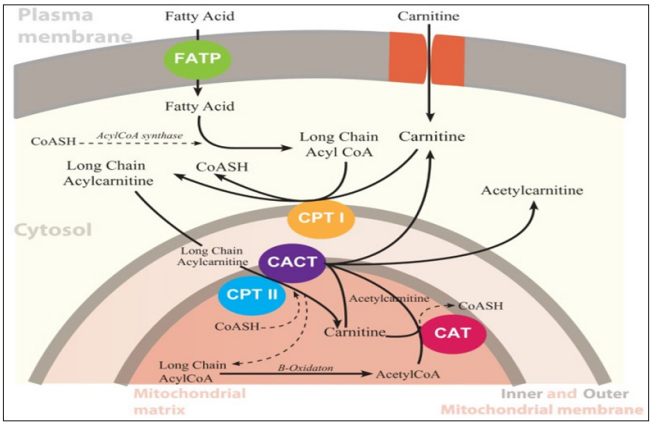


**Figure 3.Mechanism of Action of L-carnitine**

## Physiological Role of Omega-3 Fatty Acids

Important new discoveries were presented regarding the advantages of omega-3 fatty acids in case of cardiovascular disease since the first American Heart Association (AHA) Science Advisory was released in 1996. Few identified seafood, some nuts, and plant oils are dietary sources of omega-3 fatty acids. Flax seed oil, canola, soybean and walnut include the 18-carbon -linolenic acid (ALA) while fish and fish oils contain the 22-carbon docosahexaenoic acid (DHA) along with 20-carbon eicosapentaenoic acid (EPA).[16]

EPA and DHA seem to be more powerful than ALA. Population research and randomised, controlled trials provide strong evidence for the clinical advantages of omega-3 fatty acids, and more information is now available on ways in which these nutrients work. They have been described in a recent scientific statement titled "Fish".[17]

AHA suggests 1 g of EPA and DHA (combined) per day for people with a history of CHD. This can be acquired by eating oily fish or by taking supplements. Omega-3 fatty acid supplements, despite the choice to employ the decision, should be made after consulting a doctor. The quantity of EPA and DHA found in fish and fish oil is seen in the most recent omega-3 fatty acid scientific advisory from the AHA.[18]

Omega-3 fatty acids can considerably lower the occurrence of CVD events in people with coronary artery disease, according to conclusive evidence from randomised trials. The trials using fish or supplements containing omega-3 fatty acids sourced from marine sources provide the strongest support to date. To prove the cardioprotective advantages of ALA, more clinical research is required. Although supplements are a good alternative, it is best to increase omega-3 fatty acids through diet. To validate and further clarify the health advantages of omega-3 fatty acids for both primary and secondary prevention, additional clinical and mechanistic research is required.[19]

## Role of Magnesium in CVD

Magnesium is one of the vital minerals that exist in the body. It is also contained naturally in a variety of foods. It participates in over 300 enzymatic reactions as a cofactor. This dietary supplement is involved in reactions leading to the control of blood sugar and blood pressure, and hence it is important for the cardiovascular system. This mineral also plays a vital role in maintaining the cell membrane potential, functioning of the mitochondria, and regulation of antioxidative pathways. In a study, it was discovered that supplementing with magnesium at a median dose of 368 mg/day for a median time of 3 months significantly reduced systolic and diastolic blood pressure (DBP). Additionally, in comparison to placebo, these decreases were followed by an increase in serum magnesium of 0.05 mmol/L (95% CI 0.03 to 0.07). Due to a number of reasons, patients suffering from congestive heart failure frequently have magnesium deficiencies. Hypomagnesaemia also predisposes patients having heart failure to hypokalaemia, which raises the risk of ventricular arrhythmias and haemodynamic disturbances. Even people with congestive heart failure have been proven to have inferior clinical outcomes when magnesium levels are low. It has been discovered that

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taking an oral magnesium supplement reduces systolic vascular resistance, mean arterial pressure, non-sustained ventricular tachyarrhythmia, and frequency of couplets. Studies reveal that patients with specific heart problems can be cured by early detection and immediate magnesium administration. More prospective, randomised controlled trials, however, are required to understand the effectiveness of magnesium as a treatment method to prevent some of the aforementioned cardiovascular diseases.[9,20]

## Other Supplements for CVD

A recognised inhibitor of NADPH oxidase, benfotiamine (S-benzoylthiamine O-monophosphate), is an acyl derivative of thiamine that has been seen to prevent tissue damage in several animal types. It has been demonstrated that benfotiamine can prevent diabetes-related problems such as neuropathy, nephropathy, and retinopathy. Benfotiamine inhibits NADPH oxidase indirectly by activating the transketolase enzyme, which then prevents the synthesis of NADPH oxidase and stimulates the antioxidant defence mechanisms.[20,21] Lycopene is a popularly known unsaturated carotenoid found commonly in tomatoes, watermelon, papaya, red grapefruits, and guavas. The main and secondary prevention of cardiovascular illnesses is aided by lycopene, which may enhance vascular function also. Lycopene's major activity profile comprises the capacity to enhance the metabolic profile, decrease arterial stiffness, and have antiatherosclerotic, antihypertensive, anti-inflammatory, antiplatelet, antioxidant and protective endothelial actions.[22] It is important to acknowledge that folates may help to avoid cardiovascular disease. The synthetic version of folate is called folic acid. B-vitamin folate occurs naturally in several meals. Red blood cells, in particular, need it to develop into healthy cells. Folates play a significant role in the synthesis of nucleic acids and methionine regeneration and are crucial cofactors in the transfer and use of 1-carbon moieties. It is known that megaloblastic macrocytic anaemia results from florid folate shortage, which impairs DNA synthesis.[23] Supplemental cobalamin is helpful for treating a variety of inflammatory illnesses and also offers protection in pathologies linked to oxidative stress. Cyanocobalamin decreases the low-density lipid (LDL) oxidation in both healthy individuals and patients with coronary heart disease.[24,25]

## Conclusion

Current therapies in heart failure aim at antagonising the neurohormonal mechanisms thereby preventing ventricular remodelling for enhancing cardiac function. Prosystole addressed the need of the heart in terms of ATP production and energy in the heart muscle, especially in systolic dysfunction and reduced ejection fraction. The various nutrients of prosystole holistically aid in achieving this and constitute complete cardiac nutrition.

**Conflict of Interest:** None

## References

1. Huffman MD, Prabhakaran D, Osmond C, Fall CH, Tandon N, Lakshmy R, Ramji S, Khalil A, Gera T, Prabhakaran P, Biswas SK, Reddy KS, Bhargava SK, Sachdev HS; New Delhi Birth Cohort. Incidence of cardiovascular risk factors in an Indian urban cohort results from the New Delhi birth cohort. J Am Coll Cardiol. 2011 Apr 26;57(17):1765-74. [PubMed] [Google Scholar]
2. Bronzato S, Durante A. Dietary supplements and cardiovascular diseases. Int J Prev Med. 2018;9:80. [PubMed] [Google Scholar]
3. Witting PK, Pettersson K, Letters J, Stocker R. Anti-atherogenic effect of coenzyme Q10 in apolipoprotein E gene knockout mice. Free Radic Biol Med. 2000;29:295-305. [PubMed] [Google Scholar]
4. Tsai KL, Huang YH, Kao CL, Yang DM, Lee HC, Chou HY, Chen YC, Chiou GY, Chen LH, Yang YP, Chiu TH, Tsai CS, Ou HC, Chiou SH. A novel mechanism of coenzyme Q10 protects against human endothelial cells from oxidative stress-induced injury by modulating NO-related pathways. J Nutr Biochem. 2012;23:458-68. [PubMed] [Google Scholar]
5. Sharma A, Fonarow GC, Butler J, Ezekowitz JA, Felker GM. Coenzyme Q10 and heart failure: a state-of-the-art review. Circ Heart Fail. 2016;9(4):e002639. [PubMed] [Google Scholar]
6. Lee BJ, Huang YC, Chen SJ, Lin PT. Coenzyme Q10 supplementation reduces oxidative stress and increases antioxidant enzyme activity in patients with coronary artery disease. Nutrition. 2012;28(3):250-5. [PubMed] [Google Scholar]
7. González-Guardia L, Yubero-Serrano EM, Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Marin C, Camargo A, Delgado-Casado N, Roche HM, Perez-Jimenez F, Brennan L, Lopez-Miranda J. Effects of the Mediterranean diet supplemented with coenzyme q10 on metabolomic profiles in elderly men and women. J Gerontol A Biol Sci Med Sci. 2015;70(1):78-84. [PubMed] [Google Scholar]
8. Yubero-Serrano EM, Gonzalez-Guardia L, Rangel-Zuñiga O, Delgado-Lista J, Gutierrez-Mariscal FM, Perez-Martinez P, Delgado-Casado N, Cruz-Teno C, Tinahones FJ, Villalba JM, Perez-Jimenez F, Lopez-Miranda J. Mediterranean diet supplemented with coenzyme Q10 modifies the expression of proinflammatory and endoplasmic reticulum stress-related genes in elderly men and women. J Gerontol A Biol Sci Med Sci. 2012;67(1):3-10. [PubMed] [Google Scholar]
9. DiNicolantonio JJ, Liu J, O'Keefe JH. Magnesium for the prevention and treatment of cardiovascular disease. Open Heart. 2018;5(2):e000775. [PubMed] [Google Scholar]

**ISSN: 2278-2044**
**DOI: https://doi.org/10.24321/2278.2044.202311**

10. Wang ZY, Liu YY, Liu GH, Lu HB, Mao CY. L-carnitine and heart disease. Life Sci. 2018;194(1):88-97. [PubMed] [Google Scholar]
11. DiNicolantonio JJ, Lavie CJ, Fares H, Menezes AR, O'Keefe JH. L-carnitine in the secondary prevention of cardiovascular disease: systematic review and meta-analysis. Mayo Clin Proc. 2013;88(6):544-51. [PubMed] [Google Scholar]
12. Omori Y, Ohtani T, Sakata Y, Mano T, Takeda Y, Tamaki S, Tsukamoto Y, Kamimura D, Aizawa Y, Miwa T, Komuro I, Soga T, Yamamoto K. L-carnitine prevents the development of ventricular fibrosis and heart failure with preserved ejection fraction in hypertensive heart disease. J Hypertens. 2012;30(9):1834-44. [PubMed] [Google Scholar]
13. Orlandi A, Francesconi A, Ferlosio A, Lascio AD, Marcellini M, Pisano C, Spagnoli LG. Propionyl-L-carnitine prevents age-related myocardial remodeling in the rabbit. J Cardiovasc Pharmacol. 2007;50(2):168-75. [PubMed] [Google Scholar]
14. Dzugkoev SG, Mozhaeva IV, Otiev MA, Margieva OI, Dzugkoeva FS. [Effect of L-carnitine, afobazole and their combination with L-arginine on biochemical and histological indices of endothelial dysfunctions in cobalt intoxication in rats]. Patol Fiziol Eksp Ter. 2015;59(2):70-5. Russian. [PubMed] [Google Scholar]
15. Ferrari R, Merli E, Cicchitelli G, Mele D, Fucili A, Ceconi C. Therapeutic effects of L-carnitine and propionyl-L-carnitine on cardiovascular diseases: a review. Ann N Y Acad Sci. 2004 Nov;1033:79-91. [PubMed] [Google Scholar]
16. Kris-Etherton PM, Harris WS, Appel LJ; AHA Nutrition Committee; American Heart Association. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. Arterioscler Thromb Vasc Biol. 2003 Feb 1;23(2):151-2. [PubMed] [Google Scholar]
17. Stone NJ. Fish consumption, fish oil, lipids, and coronary heart disease. Circulation. 1996;94(9):2337-40. [PubMed] [Google Scholar]
18. Kris-Etherton PM, Harris WS, Appel LJ; American Heart Association. Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids and cardiovascular disease. Circulation. 2002;106(21):2747-57. [PubMed] [Google Scholar]
19. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman Jr JW, Kris-Etherton P, Goldberg IJ, Kotchen TA, Lichtenstein AH, Mitch WE, Mullis R, Robinson K, Wylie-Rosett J, Jeor SS, Suttie J, Tribble DL, Bazzarre TL. AHA dietary guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. Circulation. 2000;102(18):2284-99. [PubMed] [Google Scholar]
20. Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. Am J Cardiol. 1993;72(15):1156-62. [PubMed] [Google Scholar]
21. Raj V, Ojha S, Howarth FC, Belur PD, Subramanya SB. Therapeutic potential of benfotiamine and its molecular targets. Eur Rev Med Pharmacol Sci. 2018;22(10):3261-73. [PubMed] [Google Scholar]
22. Garson KL, Mapanga RF, Milne R, Essop MF. The effects of benfotiamine in attenuating hyperglycemia-induced cardiac pathology. J Afr Assoc Physiol Sci. 2010;2(1):5-13. [Google Scholar]
23. Mozos I, Stoian D, Caraba A, Malainer C, Horbańczuk JO, Atanasov AG. Lycopene and vascular health. Front Pharmacol. 2018;9:521. [PubMed] [Google Scholar]
24. Verhaar MC, Stroes E, Rabelink TJ. Folates and cardiovascular disease. Arterioscler Thromb Vasc Biol. 2002;22(1):6-13. [PubMed] [Google Scholar]
25. Earnest CP, Wood KA, Church TS. Complex multivitamin supplementation improves homocysteine and resistance to LDL-C oxidation. J Am Coll Nutr. 2003;22(5):400-7. [PubMed] [Google Scholar]

**ISSN: 2278-2044**
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