

---

**Research Article**


---



ISSN    Print    2231 – 3648  
              Online    2231 – 3656

---

Available Online at: [www.ijpir.com](http://www.ijpir.com)

---

**International Journal of  
Pharmacy and Industrial  
Research**


---

## **Trio Q Softgels–An Advanced Unique CoQ10 formulation specially designed as Liquid solubilisate provides vital nutrient support for cellular energy metabolism & oxidative injury**

**GovindShukla, AnushaPalkamshetti, ShirishaK, NavyaVancha, C.J.Sampath Kumar**

Lactonova Nutripharm (P) Ltd, Makers of **TrioQ Softgels**  
 81/3, IDA Mallapur, Hyderabad, Telangana, India-500 076.

---

### **ABSTRACT**

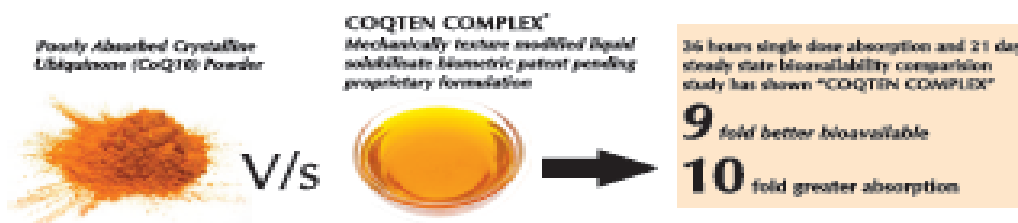
Mitochondria of the cells play a vital role in the production of energy at cellular level which is essential for the survival of a cell. CoQ10 is one of the coenzyme in the electron transport chain in the inner mitochondrial membrane where oxidative phosphorylation occurs for the production of ATP from the reducing equivalents such as NADPH<sub>2</sub>, FADH<sub>2</sub>, etc. Besides, CoQ10 works as an antioxidant, protecting lipids and other cell components from oxidation. Thus, it is a particularly promising cardio protective agent. Apart from this there are so many functions of CoQ10 which are vital for the sustenance of life. When cells age, mitochondrial CoQ10 levels decrease. But dietary supplementation has been shown to help, maintain energy production and aid persons against disorders of CoQ10 deficiency disorders. This review gives an overview of functions of the CoQ10, reports related to consumption versus alleviation of diseases and its importance of dietary supplement in nowadays life.

**Keywords:** TrioQ Softgels, CoQ10, Energy production, Nutrient.

---

### **INTRODUCTION**

**TrioQ is an advanced unique CoQ10 formulation specially designed as liquid solubilisate which imparts enhanced absorption over a broader temperature range.**



### **Author for Correspondence:**

GovindShukla

Lactonova Nutripharm (P) Ltd, Makers of TrioQ Softgels  
 81/3, IDA Mallapur, Hyderabad, Telangana, India-500 076.

CoQ10 is an enzyme which is naturally found in many cells of the body. In fact, it is found in every single mitochondrial cell and about 95% of our body's energy is produced by this way, which converts sugars and fats into energy. It is a component of electron transport chain of inner mitochondrial matrix and participates in The respiration ultimately generating the energy in the form of ATP. Some of the organs such as heart, liver and kidneys have the highest concentrations of CoQ10 as these organs need a lot of energy for their functioning.

### CoQ10

CoQ10 structure consists of a benzoquinone with an isoprenoid side chain attached at sixth carbon. CoQ10 can give up electrons easily thus acting as a powerful antioxidant against free radical<sup>8</sup>. CoQ10 along with vitamin E increases the resistance of LDL to oxidation and prevents coronary heart disease<sup>9</sup>. Ageing also occur due to decline in levels of CoQ10. HMG-CoA reductase inhibitors like lovastatin, simvastatin can cause CoQ10 deficiency<sup>11</sup>.

Researchers revealed that 2.5ug/ml or preferably 3.5ug/ml is required to have a good impact on severely diseased heart<sup>12</sup>. A study was

done on 109 patients suffering from hypertensive heart diseases and isolated dys function. On replacement of CoQ10 there occurred lowering of elevated blood pressure, improvement in diastolic function and a decrease in myocardial thickness in 53 percent of patients<sup>13</sup>. Diastolic dysfunction is more common in women than in men. So, CoQ10 may offer a 'gender advantage' for aging women<sup>14</sup>. An early research suggested that mitral valve prolapse might be associated with CoQ10 deficiency<sup>15</sup>. CoQ10 was first isolated by Frederick Crane in 1957 from beef heart. Q-indicates its membership in quinone group and Fig. 1 indicates the no. of isoprenoid units and its side chain<sup>1</sup>. It was named as ubiquinone by Dr, R.A. Mortan because of its wide spread availability in living organisms<sup>2</sup>. Dr. Y. Yamamura was the person who organized clinical trial of CoQ10 in human subjects for the first time. A year later, they demonstrated CoQ10 deficiency in case of human heart diseases<sup>3</sup>. In 1978 Peter Mitchell was awarded nobel prize for CoQ10 and energy transfer<sup>4</sup>. In 1985 Per Langsjoen tested CoQ10 in double-blind fashion and reported it as a valuable nutrient for cardiomyopathy<sup>5</sup>. Larsernster found that CoQ10 acts as a free radical scavenger<sup>6</sup>.

### Composition

Supplement Facts		
Serving size : 1 Softgel		Servings per pack : 30
Each softgel contains:		
Coenzyme Q10 (CoQ10 Complex <sup>**</sup> )	100mg	**
* FDA (Recommended Dietary Allowance) **Not established.		
Other Ingredients : Gelatin & Vegetable oils.		

### Coq10 and its implication in disease states

#### Cardiovascular diseases

##### Arrhythmia

An experimental study was conducted on rabbits. In this, rabbits were given CoQ10 before ligation procedure. On isolation of cellular mitochondria 40 minutes after tying a major blood vessel to heart muscle, higher levels of free radicals and lower levels of CoQ10 were identified. Degree of oxidative damage reduced proportionately due to retreatment with CoQ10 dosage<sup>16</sup>. A study was

conducted on 27 patients with premature ventricular ectopic beats; the reduction in premature ventricular contractions (pvc) activity was significantly greater after 4-5 weeks of coq10 administration. Although CoQ10 antiarrhythmic effect was primarily seen in diabetics. Also a significant reduction of palpitations was noted for hypertensive otherwise healthy patient<sup>17</sup>.

### **Myocardial Protection in Cardiac Surgery**

CoQ10 supplementation in pre-operative cardiac patients improved right and left ventricular myocardial ultrastructure, which was measured by light microscopy both pre and postoperative<sup>18</sup>. Researches even revealed that pretreatment with CoQ10 is effective in preserving heart function following coronary artery bypass surgery (CABG) and valvular surgery<sup>19</sup>. Naylar worked with rabbit heart model of coronary insufficiency and reperfusion, presented with CoQ10 role in preserving an oxygen deficient myocardium<sup>20</sup>.

### **Atherosclerosis and Lipid Peroxidation**

CoQ10 has a unique ability to recycle vitamin E which has tremendous treatment implications, especially when it showed to block lipid peroxidation<sup>21</sup>. CoQ10 can decrease lipid peroxidation in healthy well nourished adults and in those with arteriosclerotic plaque<sup>22</sup>.

### **Thyroid, Adriamycin and CoQ10**

Research by Suzuki indicated a direct relationship between cardiac performance and CoQ10 supplementation in patients with thyroid disorders<sup>23</sup>. Kishi and colleagues performed an animal study which revealed that the administration of CoQ10 was more protective against the damage induced by Adriamycin when compared to vitamin E alone<sup>24</sup>. A rat model is treated with Adriamycin, the administration of CoQ10 restored blood levels to normal range and prevented ADRIAMYCIN-induced structural changes in the heart<sup>25</sup>.

### **Optimum Aging**

The free radical theory of aging (1956) stated that free radical reaction, modified by genetic and environmental factors were responsible for the aging and death of all living organisms<sup>26</sup>. Age-related decline in CoQ10 levels is observed both in animals and humans<sup>27</sup>. CoQ10 can prevent oxidative stress induced apoptosis (cell death) by inhibiting lipid peroxidation in plasma membrane<sup>28</sup>.

### **Immunity and Defense**

A study was conducted on 6 patients with AIDS or AIDS-related complex who were treated with 200mg of CoQ10 daily. T-cell immunity increased

in 3 patients and 5 reported symptomatic improvement<sup>29</sup>.

### **Cancer**

In a study, 83 patients in the United States who had cancer of the breast, lung, prostate, pancreas, colon, stomach, rectum and other sites were found to have deficiency of CoQ10 in blood<sup>30</sup>.

### **Periodontal Diseases**

Several studies revealed that oral administration of CoQ10 to patients with periodontal diseases was effective in suppressing inflammatory changes in gingival which was assessed by gingival index, pocket depth and tooth mobility scores<sup>31</sup>.

### **Neurodegenerative Disorders**

In a study reported in the New England Journal of Medicine, Alzheimer's patients with nutritional support of vitamin E along with CoQ10 showed a reduction in the progression of their disease<sup>32</sup>. Human brains experience a progressive reduction in levels of CoQ10 along with neurotransmitters during ageing process<sup>33</sup>. Fallon and colleagues conducted a study on rats and confirmed that administration of CoQ10 along with nicotinamide blocks toxin-induced damage to substantia nigra<sup>34</sup>. Supplemental CoQ10 increased NADH oxidation at mitochondrial level which acts as an electron acceptor for plasma membrane – associated NADH dehydrogenase<sup>35</sup>.

### **Diabetes**

Research revealed that diabetic patients with very low levels of CoQ10 are highly prone to death from congestive heart failure within an arrow time period<sup>36</sup>.

### **Chronic Obstructive Pulmonary Disease (COPD)**

Fujimato's data revealed that CoQ10 supplementation has favorable results on chronic obstructive pulmonary disease patients, who have low oxygen levels at rest and during exercise<sup>37</sup>. A study conducted in Stockholm, Sweden revealed that patients with COPD and coronary heart disease had deficiencies in the levels of vitamin E and CoQ10 in plasma and lower leg muscles tissues which might be the result of

malnutrition but also suggested depressed resistance to cell trauma<sup>38</sup>.

### Damaged Skin

At the ninth International Symposium on Biomedical and Clinical Aspects of CoQ10, Poda and Parker proposed that CoQ10 was the first antioxidant to be affected by oxidative stress in the skin. They hypothesized that CoQ10 could be a sensitive marker to evaluate the antioxidant capacity of topically applied sunscreens and even to measure the effect of exposure to UV in our day to day life<sup>39</sup>. A presentation at International Coenzyme Q10 Association Conference in Boston (May 1998) suggested that “fountain of youth” effect maybe due to hydration of the skin in combination with the improvement of hyaluronic acid synthesis by CoQ10<sup>40</sup>.

### Infertility

Research demonstrated that sperms rely on additional energy for motility which may be actually dependent on bioenergetics function of CoQ10<sup>41</sup>.

### Athlete

Researchers speculated that high metabolic stress and elevated levels of radical formation in marathon runners along with lower CoQ10 and vitamin E levels were indication of a continuing drain on their antioxidant scavenging potential<sup>42</sup>. Marathon runners who were pretreated with CoQ10 had lower plasma levels of tissue breakdown products compared to their controlled counterparts<sup>43</sup>.

### Muscular Dystrophy

Folker suggested that any patient suffering from muscular dystrophy should be treated with CoQ10 indefinitely<sup>44</sup>.

### Mitochondrial Encephalopathy

In a study, 6 patients suffering with mitochondrial cytopathies were treated with 150mg of CoQ10 over 6 month period showed improvement in brain variables and muscle mitochondrial function<sup>45</sup>.

#### SUPPORTING STUDIES:

➤ A study on 12 patients with stable Angina Pectoris were given 150mg/day of CoQ10 has resulted in increased exercise tolerance on tread mill and is proved to be safe and effective in Angina Pectoris.

- Kamikawa T, Kobayashi A, Yamashita T, Hayashi H, Yamazaki N. Effects of coenzyme Q10 on exercise tolerance in chronic stable angina pectoris. *Am J Cardiol* 1985;56:247-251.

➤ A study on 27 patients with ventricular premature beats (Arrhythmias). They were given 60mg/day CoQ10 enzyme for 4 to 5 weeks which has shown significant reduction in ventricular premature beats.

- Fujioka T, Sakamoto Y, Mimura G. Clinical study of cardiac arrhythmias using a 24-hour continuous electrocardiographic recorder (5th report) antiarrhythmic action of coenzyme Q10 in diabetics. *Tobok J Exp Med* 1983;141 (Suppl):453-463.

➤ A study on 126 patients with dilated cardiomyopathy were given 100mg of CoQ10 for a period of 24 months showed significant improvement in the cardiac parameters. Hence, helps in treatment of cardiomyopathy.

- Langsjoen PH, Folkers K, Lyson K, Muratsu K, Lyson T, et al. Effective and safe therapy with coenzyme Q10 for cardiomyopathy. *Klin Wochenschr* 1988;66:583-590.

➤ The studies have shown that pre-operative administration of CoQ10 increases the tolerance of the heart to ischemia during aortic cross clamping.

- Tanaka J, Tominaga R, Yoshitoshi M, Matsui K, Komori M, Sese A, et al. Coenzyme Q10: the prophylactic effect on low cardiac output following cardiac valve replacement. *Ann Thorac Surg* 1982;33:145-151.

### CoQ10 in dietary substances

CoQ10 richest food is sardine and mackerel followed by reindeer muscle meat, pork and beef heart, liver etc. and its quantity varies in other meat substances. Even though plants does not have reasonable amount of CoQ10, some of the plant materials such as broccoli, spinach, soy products, peanuts can improve the CoQ10 levels in the body. CoQ10 levels may be lost by frying or firing. While boiling, food should not be overcooked to spare CoQ10 levels. Canned foods have very low

level of CoQ10 when compared to fresh and unprocessed food items. As CoQ10 is a fat soluble substance, it should be taken along with olive or soy bean oil or any other fat substance for a maximum benefit. Dose of the CoQ10 varies according to the health conditions of the person.

- A normal person should have 30 to 60mg.
- Cancer patients - 200 to 600 mg per day.
- Cardiac related problems - 360 mg per day.
- Diabetic patients- 200 mg per day

## Limitations of coQ10

- As the biosynthetic pathway for cholesterol and CoQ10 are same, the statin drugs (cholesterol lowering drugs) which are aiming at HMG CoA reductase also reduce the CoQ10 levels in the body.

- CoQ10 may reduce the body's response to blood thinners such as warfarin and therefore should be taken according to the directions of physicians.
- Blood pressure lowering drugs such as beta blockers also has lowering effect on CoQ10. So, these drugs are supplemented with dietary substitutes.

## ADVANCED TRIOQ TECHNOLOGY WITHIN

In scientific world it is well known that CoQ10 is not easily absorbed by the body. Dry powder formulation of CoQ10 is not well absorbed because CoQ10 crystals do not fully dissolve in the GI tract.

Advanced TrioQ utilizes revolutionary lipid solubilise technique that keeps CoQ10 fully dissolved over a broader range of temperature resulting in 10 times greater absorption than the dry powder.

TrioQ is a special blend of CoQ10 in its liquid solubilise form and certain lipid molecules which helps the transportation of the CoQ10 through different membranes of the body. TrioQ formulation keeps the CoQ10 completely dissolved without forming crystals till absorption in all bodily temperatures.

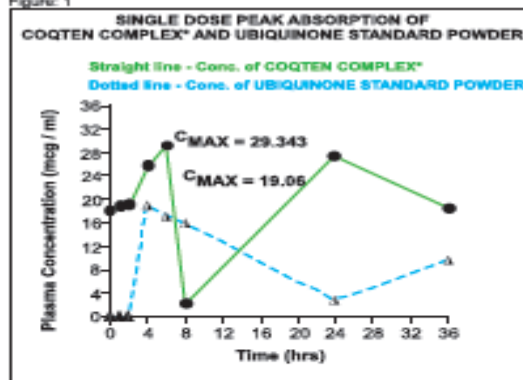


Transmission reflection microscopic image (TRM) with zero crystals in sample of COQTEN COMPLEX\* in TrioQ taken in (IICT) Indian Institute of Chemical Technology Hyderabad Dt. 19.05.2014 Sample Ref.No. 23899

## ADVANCED TRIO-Q ABSORPTION IS BACKED UP WITH STRONG PRECLINICAL EVIDENCE:

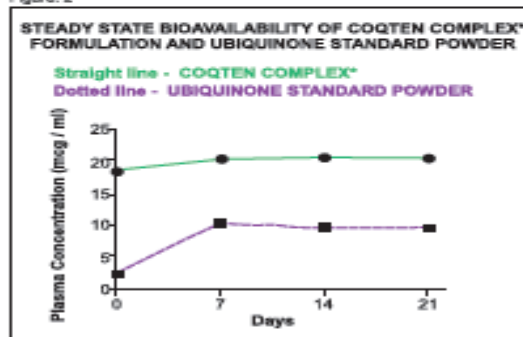
21 days pre-clinical study for the determination of study state bioavailability and % absorption of "COQTEN COMPLEX" formulation and powder at different time intervals in rodents has resulted in: 54% greater absorption with 20% of the dosage of Ubiquinone standard powder and nine folds more bioavailable than Ubiquinone standard powder with equivalent dose.

Figure: 1



A single dose oral administration of COQTEN COMPLEX\* and UBIQUINONE STANDARD POWDER has resulted in higher absorption of COQTEN COMPLEX\* with a  $C_{max}$  of 29.343 mcg/ml whereas the  $C_{max}$  for standard powder was found to be 19.06 mcg/ml.

Figure: 2



"COQTEN COMPLEX\*" has shown 54% greater absorption with 20% of the dosage of Ubiquinone standard powder and nine folds more steady state bioavailable than Ubiquinone standard powder with equivalent dose.

Ref:  
Pharmacokinetic comparison studies of ubiquinone and coqten complex in rodents by HPLC method.  
Study conducted in KLE university's college of pharmacy, Bangalore.



<p><b>Ubiquinone V/s COQTEN COMPLEX* in TrioQ</b></p> <p>There was nine fold increase in the bioavailability of the "COQTEN COMPLEX" compared to that with the standard powder because the given percentage concentration of ubiquinone in powder was 100% whereas the given percentage concentration of ubiquinone in "COQTEN COMPLEX" was 21%. Hence, for 100% concentration of ubiquinone in "COQTEN COMPLEX", the increase in bioavailability was found to be NINE FOLD.</p> <p><math>C_{max}</math> of the "COQTEN COMPLEX" and standard powder as shown in Figure 1 was found to be 29.343 mcg/ml and 19.06 mcg/ml respectively.</p> <p><math>T_{max}</math> of the "COQTEN COMPLEX" and standard powder 6<sup>th</sup> hour and 4<sup>th</sup> hour.</p> <p><math>AUC_{0-24}</math> "COQTEN COMPLEX" 689.385mcg/ml*hr</p> <p><math>AUC_{0-24}</math> Standard powder 312.21mcg/ml*hr</p> <p>Maximum % absorption of the "COQTEN COMPLEX" and standard powder was found to be 48.9 and 31.76 respectively.</p> <p>The efficacy of absorption of orally administered CoQ10 powder (Ubiquinone standard) is poor because it is insoluble in water, limited solubility in lipids, and relatively large molecular weight and crystal size, due to this the standard powder absorption and bioavailability was lesser compared with that of the "COQTEN COMPLEX".</p> <p>The <math>T_{max}</math> value of about 6 hour or longer indicates that the "COQTEN COMPLEX" is absorbed slowly from the gastrointestinal tract and this is attributable to both its crystalline form, hydrophobicity and high molecular weight.</p> <p>A second plasma "COQTEN COMPLEX" peak observed at 24 hour may be due to both enterohepatic recycling and redistribution from the liver to circulation.</p>	<p><b>Ubiquinol V/s COQTEN COMPLEX* in TrioQ</b></p> <p>Human body requires both the forms of Coenzyme Q10 i.e. ubiquinone and ubiquinol.</p> <p>Recently, ubiquinol is considered as the preferred form of Coenzyme Q10 but the studies have shown that ubiquinol is unstable in the stomach, lacks superior absorption and when ubiquinol is exposed to air, it gets converted to ubiquinone-defeating the purpose of using ubiquinol.</p> <p>In contrast, <b>TrioQ</b> is formulated with Ubiquinone (CoQten complex) as a liquid solubilisate form which is very much stable (does not form crystals) at different temperature and shown to have better absorption &amp; bioavailability.</p> <p><b>TiroQ over other coenzyme Q10 formulations:</b></p> <p>It can therefore be concluded that the COQTEN COMPLEX* in TrioQ is proved to be better than the ubiquinone standard powder in terms of both absorption and bioavailability as observed in the results. COQTEN COMPLEX* has shown nine fold more bioavailability than the standard powder. Further COQTEN COMPLEX* also maintained a steady state bioavailability throughout the study period of 21 days which is proved to be again better than the standard powder.</p> <p><b>COQTEN COMPLEX* in TrioQ The gold standard coenzyme q10 from COQTEN COMPLEX* for unmatched superior absorption and bioavailability</b></p>
--	--

## CONCLUSION

CoQ10 is vital compound that keeps the body's metabolism going on. Unfortunately, many doctors will not prescribe it as the dietary supplement for cardiac patients. Though the rationale for CoQ10 in the treatment of wide variety of diseases has been published in a number of studies, it is not use dup to its potential. Without a doctors support, the versatility of the CoQ10 in its functions cannot be capitalized for its therapeutic benefits. Though CoQ10 may not guarantee a cure, it has shown its

vast lifesaving potential in selected patients. Related reports of inefficiency of CoQ10 are due to deficiency of other nutrients, enzymes, B vitamins, minerals and cofactors which are necessary for its biosynthesis and utilization by the body.

## ACKNOWLEDGEMENTS

Authors are thankful to the Staff & Management of Lactonova Nutripharm pvt. Ltd HYDERABAD Telangana for their cooperation and support.

## REFERENCES

- [1]. Crane FL. et al., Isolation of a quinine from beaf heart mitochondria. Biochimica et Biophys Acta. 25, 1957, 220-221.
- [2]. Littaru GP. Energy and Defence. Rome. 1955, 14-24.

- [3]. Littarru GP, Ho L and Folkers K. Deficiency of CoQ10 in human heart disease. Part I and II. *Int J Vit Nutr Res.* 42(2), 1972, 291.
- [4]. Mitchell P. Possible molecular mechanisms of the proton motive function of cytochrome systems. *J Theoret Biol.* 62, 1976, 327 – 367.
- [5]. Langsjoen PH, Vadhanavikit S and Folkers K. Response of patients in classes III and IV of cardiomyopathy to therapy in a blind and crossover trial with coenzyme Q10. *Proc Natl Acad of Sci.* 82, 1985, 4240 – 4244.
- [6]. Ernster L and Forsmark P. Ubiquinol: an endogenous antioxidant in aerobic organisms. Seventh International Symposium on Biomedical and Clinical Aspects of Coenzyme Q. Folkers K. et al. (eds.) *The Clin Invest.* 71(8), 1993, 60 – 65.
- [7]. Kidd PM. et al. Coenzyme Q10: Essential Energy Carrier and Antioxidant. HK Biomedical consultants. 1988, 1-8.
- [8]. McGuire JJ. et al. Succinate ubiquinone reductase linked recycling of  $\alpha$ -tocopherol in reconstituted systems and mitochondria: requirement for reduced ubiquinol. *Arch Biochem Biophys.* 292, 1992, 47-53.
- [9]. Kalen A, Appelkvist EL, Dallner G. Age-related changes in the lipid compositions of rat and human tissues. 24, 1989, 579-581.
- [10]. Ghirlanda G. et al. Evidence of plasma CoQ10 –lowering effect by HMG Co A reductase inhibitors: A double blind, placebo-controlled study. *J Clin Pharm.* 33(3), 1993, 226-9.
- [11]. Langsjoen PH. et al. Long –term efficacy and safety of Coenzyme Q10 therapy for idiopathic dilated cardiomyopathy. *Am J Cardiol.* 65, 1990, 512-23.
- [12]. Langsjoen PH, Langsjoen P and Folkers K. Isolated diagnostic dysfunction of the myocardium and 24 hr response to CoQ10 treatment. *Clin Invest.* 71(8), 1993, S140-4.
- [13]. Proceedings from American College of Cardiology: Women and Heart Disease. 15, 1997.
- [14]. Oda T. Coenzyme Q10 therapy on the cardiac dysfunction in patients with mitral valve prolapse. Dose vs. effect and dose vs. serum level of Coenzyme Q10. In: Folkers, K, Yamamura Y, (eds.). *Biomedical and Clinical Aspects of Coenzyme Q10*, Elsevier Sci Publ B.V., Amsterdam, 5(17), 1986, 873-878.
- [15]. Otani T, Tanaka H, Onoue T. et al. In Vitro study on contribution of oxidative metabolism of isolated rabbit heart mitochondria to myocardial reperfusion injury. *Circ Res.* 55, 1984, 168-175.
- [16]. Fujioka T, Sakamoto Y and Mimura G. Clinical study of cardiac arrhythmias using a 24 hour continuous electrocardiographic recorder (5<sup>th</sup> report)- Antiarrhythmic action of Coenzyme Q10 in diabetes. *Tohoku J Exp Med.* 141, 1983, 453-463.
- [17]. Chen YF, Y T, WU SC. Effectiveness of Coenzyme Q10 on myocardial preservation during hypothermic cardioplegic arrest. *J Thorac Cardiovasc Surg.* 107, 1994, 242-7.
- [18]. Sunamori M, Tanaka H, Maruyama T. et al. Clinical experience of CoQ10 to enhance interoperate myocardial protection in coronary artery revascularization. *Cardiovasc Drug Therapy.* 5, 1991, 297-300.
- [19]. Nallar WG. The use of Coenzyme Q10 in ischemic heart muscle. In: of Coenzyme Q Elsevier, North Holland, Biomedical press, Amsterdam. 2, 1980, 409-425.
- [20]. Frei B, Kim MC and Ames BN. Ubiquinol-10 is an effective lipid soluble antioxidant at physiological concentrations. *Proc Natl Acad Sci.* 87, 1990, 48-79-48883.
- [21]. Thomas SR, Neuzil J and Stocker R. Inhibition of LDL oxidation by Ubiquinol-10. A protective Mechanism for Coenzyme Q in atherogenesis? In: Littarru GP, Alleva R, Battino M, Folkers K. (eds) *Mol Aspects of Med.* 18, 1997, 1 –309.
- [22]. Suzuki H. et al. Cardiac performance and Coenzyme Q10 in thyroid disorders. *Endocrinol Japan.* 31, 1984, 755.
- [23]. Kishi Y. et al. Protective effect of Coenzyme Q on Adriamycin toxicity in beating heart cells, In: *Biomedical and Clinical Aspects of Coenzyme Q* Folkers K, Yamamura Y. (eds.) Elsevier. 4, 1984, 181-188.
- [24]. Ogura R. et al. The role of ubiquinone (Coenzyme Q10) in preventing Adriamycin-induced mitochondrial disorders in rat heart. *J Appl Biochem.* 1, 1979, 325-335.
- [25]. Harman D. Aging: A theory based on free radical and radiation chemistry. *J Gerontol.* 11, 1956, 298-300.
- [26]. Beyer RE, Emster. The antioxidant role of Coenzyme Q. In: Lenaz, G. et al. (eds): *Highlights in Ubiquinone Research*. Taylor and Francis, London. 1990, 191-213.

- [28]. Villaba JM. et al. Role of cytochrome b5 reductase on the antioxidant function of Coenzyme Q in the plasmamembrane. *Molec Aspects Med.* 8, 1997, 7-13.
- [29]. Folkers K, Langsjoen P, Nra T. et al. Biochemical deficiencies of Coenzyme Q10 in HIV- infection and exploratory treatment. *Biochem Biophys Res Commun.* 153, 1988, 888-896.
- [30]. Folkers K. et al. Unpublished manuscript.
- [31]. Hanioka T. et al. Therapy with Coenzyme Q10 for patients with perital disease. Effect of Coenzyme Q10 on the immune system, *J of Dental Health.* 43, 1993, 667-672.
- [32]. Sano M. et al. A Controlled trial of selegiline, alpha-tocopherol or both as treatment for Alzheimer's disease. *NEng J of Med.* 336, 1997, 1216-22.
- [33]. Edulnd C, Soderberg M and Kristensson K. Isoprenoids in aging and neurodegeneration. *Neurochemisrty Int.* 25, 1994, 35-38.
- [34]. Fallon J. et al. MPP<sup>+</sup> produces progressive neuronal degeneration which is mediated by oxidative stress. *Exp Neurol.* 144(1), 1997, 193-8.
- [35]. Linnane AW. et al. Mitochondrial DNA mutation and the aging process: bioenergy and pharmacological intervention. *Mutation Research.* 275, 1992, 195-208.
- [36]. Jameson S. Statistical data support prediction of death within six months on low levels of Coenzyme Q10 and other entities. *Clin Investg.* 71, 1993, 137-139.
- [37]. Fujimoto S. et al. Effects of Coenzyme Q10 administration on pulmonary function and exercise performance in patients with chronic lung disease. *Clin Investg.* 71, 1993, 162-6.
- [38]. Karisson J, Diamant B and Folkers K. Exercise –limiting factors in respiratory distress. *Respiration.* 59(2), 1992, 18-23.
- [39]. Poda M and Packer L. Ubiquinol a marker of oxidative stress in skin. *Proceedings at the 9th International Symposium on Biomedical and Clinical Aspects of CoQ10.* Ancona Italy, 1996.
- [40]. Hoppe U. Coenzyme Q10-a Cutaneous Antioxidant and Energizer. Presented at the First Conference of the International Coenzyme Q10 Association, 1998.
- [41]. Jones R and Mann T. Damage to ram spermatozoa by peroxidation of endogenous phospholipids. *Journal of Reproduction and Fertility.* 50, 1977, 261-268.
- [42]. Karlson. et al. ubiquione, Alpha-tocopherol and cholesterol in man. *International J Vit Nutr Research.* 62(2), 1992, 160-4.
- [43]. Fiorella PL. et al. Metabolic effects of Coenzyme Q10 treatment in high level athletes. In: *Biomedical and Clinical Aspects of Coenzyme Q*, Folkers K, Ymagami T, Littaru GP. (eds) Elsevier. 6, 1991, 613-520.
- [44]. Folkers K and Simonsen R. Two successful double-blind trials with Coenzyme Q10 (vitamin Q10) and muscular dystrophies and neurogenic atrophies. *Biochem Biophys Acta.* 1271(1), 1995, 281-6.
- [45]. Barbiroli B. et al. Coenzyme Q10 improves mitochondrial respiration in patients with mitochondrial cytopathies. An in vivo study on brain and skeletal muscle by phosphorus magnetic resonance spectroscopy. *Cell Mol bio.* 43(5), 1997, 741-9.