Coenzyme Q10 – A novel molecule

Pragati Kapoor*, AK Kapoor**

Abstract
Coenzyme Q10 is a fat soluble vitamin-like substance produced by the human body. It is necessary for proper functioning of many organs and for basic functioning of cells. It is found throughout the body. Coenzyme Q10 is used both as a food supplement and as an important antioxidant. It is a component of the electron transport chain and plays a key role in producing energy in mitochondria in the form of ATP that functions like a rechargeable battery in the transfer of energy. Coenzyme Q10 levels are reported to decrease with age and to be low in cardiac conditions, Parkinson's disease, cancer, diabetes, muscular dystrophies, HIV/AIDS, etc. Some drugs also lower Coenzyme Q10 levels. It is not only used as an important nutritional supplement by millions of people all over the world but is also used in a number of clinical conditions namely CHF, diabetes, gum disease, Huntington's disease, Parkinson's disease, etc. Coenzyme Q10 is fairly safe and well tolerated.

Key words: Coenzyme Q10, antioxidant.

Introduction
Coenzyme Q10 is a fat soluble vitamin-like substance found throughout the body but especially in heart, liver, kidney, and brain. Coenzyme Q10 is produced by the human body and is required for the proper functioning of many organs and chemical reactions in the body. It helps provide energy to the cells and has powerful antioxidant activity. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Ninety-five per cent of energy of the human body is generated this way. It is necessary for the basic functioning of cells as the body needs energy for cell growth and maintenance. It is vital to a number of activities related to energy metabolism. Coenzyme Q10 can be synthesised in the laboratory and is used both as a medicine and as a food supplement. CoQ10 is the third most sold dietary supplement in the United States after omega-3 fatty acids and multivitamins. Coenzyme Q10 is also known as ubiquinone, ubidecarenone, Coenzyme Q and abbreviated as CoQ10 or Q10 or Q. These days CoQ10 is being used by millions of people in Japan, Europe, Russia, Canada, and the US. It is now also available in India.

CoQ10 is used in the treatment of a variety of disorders primarily related to suboptimal cellular energy metabolism and oxidative injury. It appears most promising for neurodegenerative disorders such as Parkinson's disease and certain encephalo-myopathies for which CoQ10 has gained orphan drug status. CoQ10 levels are reported to decrease with age and to be low in patients with some chronic diseases such as cardiac conditions, muscular dystrophies, Parkinson's disease, cancer, diabetes, and HIV/AIDS. Some drugs may also lower CoQ10 levels. CoQ10 levels in the body can be increased by taking CoQ10 supplements, although it is not clear that replacing 'low CoQ10' is beneficial.

Discovery and history
Coenzyme Q10 was first discovered from beef mitochondria by Prof. Fredrick L. Crane and colleagues at the University of Wisconsin – Madison Enzyme Institute in 1957. In 1958, its chemical structure was reported by Dr. Karl Folkers. In 1961, Peter Mitchel proposed the electron transport chain of which Coenzyme Q10 is a component (being a vital proton motive role of CoQ10), and for this he was awarded the Nobel prize in 1978. From the 1980s onward, numerous scientists around the world started studies on this molecule in relation to various diseases including cardiovascular diseases (owing to demonstration of deficiency of CoQ10 in human heart diseases) and cancer. The antioxidant role of CoQ10 as a free radical scavenger was also widely studied.

Chemical property
Its molecular formula is C59H90O4 and its molecular mass 863.34 g mol⁻¹. Chemically, it is 1,4-benzoquinone where Q refers to the quinone chemical group and 10 refers to the number of isoprenyl chemical subunits in its tail. The various kinds of Coenzyme Q can be distinguished by the number of isoprenoid subunits in their side chains. CoQ10 is present in most eukaryotic cells primarily in human mitochondria, hence it is the most common CoQ10 in human beings.

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Sources of Q10

Besides endogenous synthesis, CoQ10 is also supplied to the organism by various foods.

Dietary sources

CoQ10 levels in selected food are as under:

<table>
<thead>
<tr>
<th>Food</th>
<th>Beef</th>
<th>Pork</th>
<th>Chicken</th>
<th>Fish</th>
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<tbody>
<tr>
<td>Heart</td>
<td>113</td>
<td>118-128</td>
<td>116.2-132.2</td>
<td>Red flesh</td>
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<tr>
<td>Liver</td>
<td>39-50</td>
<td>22.7-54</td>
<td>White flesh</td>
<td>11-16</td>
</tr>
<tr>
<td>Muscle</td>
<td>26-40</td>
<td>13.8-45</td>
<td>Salmon</td>
<td>4-8</td>
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<table>
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<tr>
<th>Oils</th>
<th>Nuts</th>
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<tbody>
<tr>
<td>Soyabean</td>
<td>54-280</td>
</tr>
<tr>
<td>Olive</td>
<td>4-160</td>
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<tr>
<td>Sunflower</td>
<td>4-15</td>
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<td></td>
<td>Pistachio</td>
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<td></td>
<td>Hazelnuts</td>
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<td>Almonds</td>
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<table>
<thead>
<tr>
<th>Vegetables</th>
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<tr>
<td>Parsley</td>
<td>8-26</td>
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<tr>
<td>Broccoli</td>
<td>6-9</td>
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<tr>
<td>Cauliflower</td>
<td>2-7</td>
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<tr>
<td>Spinach</td>
<td>10</td>
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<tr>
<td>Chinese Cabbage</td>
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CoQ10 levels are particularly high in organ meats such as heart, liver and kidney, as well as beef, soy oil, sardines, mackerel and peanuts; In short, meat and fish are the richest sources of dietary CoQ10. Dairy products are poor sources of CoQ10. Vegetable oils are also good sources. Vegetables (except parsley) and fruits (except avocado) are poor sources of CoQ10. CoQ10 is manufactured by fermenting beets and sugarcane with special strains of yeast. The estimated daily intake of CoQ10 is 3 - 6mg per day derived primarily from meat. Cooking by frying reduces CoQ10 content by 14 - 32%.

Biosynthesis

The endogenous biosynthesis is quite a complex process. Starting from acetyl-CoA, a multi step process of mevalonate pathway produces farnesyl-PP (FPP), the precursor for cholesterol, CoQ10 and isoprenylated protein. The pathway involves HMG Co-A reductase The long isoprenoid side-chain of CoQ10 is synthesised by condensing FPP by enzymes. The next step involves condensation of this polyisoprenoid side-chain with 4 hydroxybenzoate, catalysed by polypropyl-4 hydroxybenzoate transferase. Hydroxybenzoate is synthesized from tyrosine or phenylalanine. In addition to mitochondria, these initial reactions also occur in the endoplasmic reticulum and peroxisomes indicating multiple sites of synthesis. Increasing the endogenous biosynthesis of CoQ10 is an important strategy to fight CoQ10 deficiency.

Physiological role

1- CoQ10 is a component of electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. CoQ10 plays a key role in producing energy in mitochondria in the form of ATP. Thus, CoQ10 has a role in producing ATP, a molecule in body cells that functions like a rechargeable battery in the transfer of energy. 95% of the human body’s energy is generated this way. Thus, those organs with the highest energy requirement such as heart, liver, and kidney have the highest CoQ10 concentrations. There are three redox states of Coenzyme Q10, fully oxidized (ubiquinone), semiquinone (ubisemiquinone) and fully reduced (ubiquinol). CoQ10 exists in a completely oxidised form and completely reduced form which enable it to perform its function in electron transport chain and as an antioxidant.

As mentioned earlier, CoQ10 is primarily found in mitochondria and is also found in the membranes of many organelles. Since its primary function in cells is in generating energy, the highest concentration is found in the inner membrane of the mitochondrion. Some other organelles that contain CoQ10 include endoplasmic reticulum, peroxisomes, lysosomes, and vesicles.

CoQ10 and the electron transport chain

CoQ10 plays a unique role in the electron transport chain (ETC) and functions in every cell of the body to synthesise energy. In the inner mitochondrial membrane, electrons from NADH and succinate pass through to the ETC to the oxygen, which is then reduced to water. The transfer of electrons through ETC results in pumping of H+ across the membrane causing a proton gradient across the membrane, which is used by ATP synthase (located on the membrane) to generate ATP. CoQ10 functions as an electron carrier from enzyme complex I and enzyme complex II to complex III in this process. This is crucial in the process, since no other molecule can perform this function.
Antioxidant function of CoQ10

CoQ10 functions as an antioxidant which protects the body from damage caused by harmful molecules known as free radicals. The antioxidant role of CoQ10 as a free radical scavenger was widely studied by Lars Emster. Antioxidants such as CoQ10 can neutralise free radicals and may reduce or even help prevent some of the damage they cause like damage to cell membranes, tamper with DNA, and cell death. The antioxidant nature of CoQ10 derives from its energy carrier function. As an energy carrier, the CoQ10 molecule is continually going through an oxidation reduction cycle. As it accepts electrons, it becomes reduced. As it gives up electrons, it becomes oxidised. In its reduced form, the CoQ10 molecule holds electrons rather loosely, hence this CoQ10 molecule will quite easily give up one or both electrons, and thus act as an antioxidant. CoQ10 inhibits lipid peroxidation by preventing the production of lipid peroxy radicals. By preventing propagation of lipid peroxidation CoQ10 protects not only lipids, but also proteins from oxidation. Oxidation of the circulating LDL is thought to play a key role in the pathogenesis of atherosclerosis, which is the underlying disorder leading to heart attack and ischaemic strokes and CHD. Content of ubiquinol in human LDL affords protection against the oxidative modifications of LDL themselves, thus lowering their atherogenic potency. In addition, the reduced form of CoQ10 effectively regenerates vitamin E from, the α-tocopheroxyl radical and, thereby interfering with the propagation step. Furthermore, during oxidative stress, interaction of H₂O₂ with metal ions bound to DNA generates hydroxyl radicals and CoQ10 efficiently prevents the oxidation of bases, particularly in mitochondrial DNA. In contrast to other antioxidants, CoQ10 inhibits both the initiation and propagation of lipid and protein oxidation. It also regenerates other antioxidants such as vitamin E. The circulating CoQ10 in LDL prevents oxidation of LDL, therefore providing its benefits in cardiovascular disease. Additionally, CoQ10 is an indirect stabiliser of calcium channels to decrease calcium overload.

Coenzymes help enzymes work to digest food and perform other body processes, and they help protect the heart and skeletal muscles. It is also said to boost energy and speed recovery from exercise.

Pharmacokinetics

Absorption

CoQ10 is a crystalline powder that is insoluble in water. Absorption follows the same process as that of lipids and the uptake mechanism appears to be similar to that of vitamin E, another lipid soluble nutrient. In human beings, the process involves the secretion of pancreatic enzymes and bile into the small intestine that facilitate emulsification and micelle formation that is required for the absorption of lipophilic substances. Food intake (and the presence of lipids) stimulates bodily biliary excretion of bile acids and greatly enhances the absorption of CoQ10. Exogenous CoQ10 is absorbed from the small intestine and is best absorbed if it is taken with a meal. Peak plasma levels are achieved in 2 - 6 hours after oral administration. In some studies, a second plasma peak was also observed at about 24-hours after administration.

Improving the bioavailability of CoQ10

In order to boost the bioavailability of CoQ10 after oral administration, several approaches have been adopted:

a. Reduction in particle size

The obvious strategy is reduction of the particle size to as low as the micro-and nano-scale. This approach has so far not proved to be very successful with CoQ10.

b. CoQ10 in oil suspension

Using an emulsion to facilitate absorption from GIT and to improve bioavailability has been successful. Emulsions of soybean oil are being used in the form of oil-based soft gelatin capsules to enhance bioavailability. The significantly increased bioavailability of CoQ10 was confirmed for several oil-based formulations in most other studies.

c. Novel forms of CoQ10 with increased water solubility

Facilitating drug absorption by increasing its solubility in water is a common pharmaceutical strategy and has been shown to be successful with the use of aqueous dispersion of solid CoQ10 with tyloxapol polymer formulations based on various solubilising agents, i.e., hydrogenated lecithin and complexation with cyclodextrin. Besides, some other novel carrier system like liposomes, nano-particles, dendrimer, etc., can be used to enhance the bioavailability of Coenzyme Q10.

Metabolism

Limited data are available. It appears CoQ10 is metabolised in all tissues, while a major route for its elimination is biliary and faecal excretion. The elimination half-time is 33 hours.
Measurement of CoQ10 levels

CoQ10 levels can be measured in plasma and these measurements reflect dietary intake rather than tissue status. Currently, CoQ10 levels are measured in cultured skin fibroblasts, muscle biopsies, and in blood mononuclear cells. Cultured fibroblasts can be used to evaluate the rate of endogenous CoQ10 biosynthesis by measuring the uptake of 14C–labelled p-hydroxybenzoate.

Inhibition of synthesis by statins and beta-blockers

Coenzyme Q10 shares a common biosynthetic pathway with cholesterol. The synthesis of an intermediary precursor of CoQ10, mevalonate, is inhibited by some beta-blockers and statins. Statins can reduce serum levels of CoQ10 by up to 40%. Thus, it is logical to supplement CoQ10 as a routine to any treatment that may reduce endogenous production of CoQ10. It may be emphasised that till date there are no conclusive reports that support the role of CoQ10 deficiency in the pathogenesis of statin-related myopathy.

Deficiency of CoQ10

There are two major factors that lead to deficiency of CoQ10 in human beings:

1. Reduced biosynthesis
2. Increased utilisation by the body.

Biosynthesis is the major source of CoQ10. Biosynthesis requires at least 12 genes and mutations in many of them cause CoQ10 deficiency. A few other genetic defects such as mutations of mitochondrial DNA can also influence, while the role of statins is controversial. Some chronic diseases such as cancer, heart disease, etc., may also reduce the biosynthesis and increase the demand for CoQ10 in the body.

It may be mentioned that CoQ10 levels are highest during the first 20 years of life. By age 80 years, the levels of CoQ10 are lower than that at birth. It is not only time that uses up the body’s store of CoQ10, smoking does, too.

Dose

The observed safe level (OSL) is intake up to 1,200 mg/day. However, the usual dose is 100-200 mg/day in deficiency states and other disease states.

Are there safety concerns?

CoQ10 is considered to be safe for most adults, and possibly safe for children when taken by mouth or when applied directly to the gums. Most people tolerate CoQ10 well, i.e., it causes minimal side effects.

Indications

CoQ10 is being used by millions of people all over the world not only as a nutritional supplement but also in treating a variety of clinical conditions such as cardiac, neurologic, and immunologic disorders. It is being used for treating heart and blood vessel conditions like CHF, angina, high BP, and heart problems linked to certain cancer drugs. It is also used for diabetes, gum disease, breast cancer, Huntington’s disease, Parkinson’s disease, muscular dystrophy, chronic fatigue syndrome (CFS), Lyme disease and to treat hair loss related to warfarin. Coenzyme Q10 has also been tried for treating inherited or acquired disorders that limit energy production in the cells of the body (mitochondrial disorders), for improving exercise performance, for strengthening the immune systems of people with HIV/AIDS, male infertility, migraine headache and countering muscle pain sometimes caused by statins. Besides, it has also been tried for increasing the life span, since with advanced age CoQ10 levels decrease.

According to the Mayo Clinic, use of CoQ10 remains controversial and unproven as a treatment in many clinical conditions though it is approved for use as an orphan product in the treatment of Huntington’s disease and mitochondrial cytopathies.

However, the effectiveness ratings for Coenzyme Q10 based on the Natural Medicines Comprehensive Database are as follows:

1. Likely effective –
   i. In cases of Coenzyme Q10 deficiency - Rare condition, 150 mg/day is administered.
   ii. Inherited or acquired disorders that limit energy production in the cells of the body (mitochondrial disorders). Improvement in symptoms are slow and the treatment 50 mg/day has to be continued for six months. CoQ10 is being approved for use as an orphan drug in mitochondrial cytopathies. Additionally, CoQ10 has shown positive trends in reducing symptoms associated with selected mitochondrial abnormalities including encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome, Kearns-Sayre syndrome, and the myoclonus epilepsy with ragged-red fibers (MERRHF) syndrome.

2. Possibly effective –
   i. Congestive heart failure (CHF):
In CHF there is increased oxidative stress as well as there is evidence of CoQ10 deficiency as confirmed by tissue assays. CoQ10 taken alone may not be effective in CHF, but it can be helpful when taken in combination with other medications of heart failure. CoQ10 is thought to increase energy production in heart muscle. Recent human studies, however, have not supported these. Studies show that CoQ10 has little or no effect in treating heart failure or angina. A more recent trial using CoQ10 in combination with carnitine and taurine did find modest clinical improvement. However, CoQ10 has been approved in Japan since 1974 for use in heart failure. Recently, CoQ10 plasma concentrations have been demonstrated as an independent predictor of mortality in chronic heart failure.

ii. Decreasing the risk of additional heart problems in people who have had a recent myocardial infarction:
When started within 72 hours of MI and taken for one year, CoQ10 significantly lowers the risk of heart-related events including non-fatal MI. Dose is 120 mg/day BD.

iii. Preventing blood vessel complications caused by coronary by-pass surgery:
There is some evidence that taking CoQ10 orally for a week before surgery might help to reduce blood vessel damage. Further, its use following cardiac surgery demonstrated improvements in myocardial isoenzyme levels, left ventricular functions, and post-operative recovery time (n=20).

iv. Lowering high blood pressure:
Combining CoQ10 with other antihypertensive agents may permit decrease of antihypertensive dose as it can enhance the effects of antihypertensive medications. A recent meta-analysis (2007) concluded that CoQ10 in hypertensive patients can lower systolic blood pressure by up to 17 mm of Hg, and diastolic blood pressure by up to 10 mm of Hg without significant side effects. Dose of CoQ10 is 120 - 200 mg/day BD.

v. In isolated systolic hypertension:
Taking CoQ10 orally may lower systolic blood pressure by about 26% after 12-weeks of therapy in some people. Dose is 60 mg BD.

vi. Huntington’s disease:
Ubiquinol, an altered form of CoQ10 has been granted, “orphan drug status” by the US FDA. However, taking CoQ10 in doses of 600 mg/day orally or less does not seem to be effective in slowing the progression of this rare neurological disorder.

vii. Preventing migraine headache (prophylaxis):
Oral CoQ10 helps in preventing migraine headache (prophylaxis). It can decrease the frequency of headaches by about 30%. However, CoQ10 does not seem to be effective in treating migraine once it has developed. Dose is 100 mg TDS. It has been used effectively in prophylaxis of migraine (300 mg/day) in combination with magnesium citrate 500 mg/day and riboflavin 400 mg/day.

viii. Parkinson’s disease:
Lower levels of CoQ10 have been observed in people with Parkinson’s disease. Increasing CoQ10 may increase the level of dopamine, which is thought to be lower in people with Parkinson’s disease. It has also been suggested that CoQ10 might protect brain cells from damage by free radicals. The results of a 16-month trial suggested that CoQ10 – especially at 1,200 mg/day dose – had a significant reduction in disability compared to those who took placebo. A randomised, double blind, placebo controlled multicentre study of 80 patients observed that 1,200 mg/day of Coenzyme Q10 was associated with up to 44 per cent less functional decline in patients with Parkinson’s disease, including activities of daily living. However, the results need further confirmation.

Oral CoQ10 may slow the decline in people with early Parkinson’s disease but not in people with mid-stage Parkinson’s disease.

ix. Improving the immune system of people with HIV/AIDS:
CoQ10 is being used for strengthening the immune system of people with HIV/AIDS.

x. Muscular dystrophy:
Oral CoQ10 seems to improve physical performance in this inherited disorder in some patients. Dose is 100 mg/day.
3. CoQ10 has been used or recommended for use in the following conditions though more evidences and additional studies are required for its effectiveness –

i. Dental (periodontal) disease:
   When applied directly to the teeth and gums or else oral administration of CoQ10 improves gingival health. Studies have shown that diseased gum tissue is deficient in CoQ10. Thus CoQ10 may improve gingival health, immune response in gum tissues and reversal of the diseased gum conditions. In addition to oral supplementation, topical application of CoQ10 on gum tissues has been shown to improve periodontitis and gingivitis conditions.

ii. Atherosclerosis:
   Preliminary data imply benefit in the setting of atherosclerosis. As mentioned earlier, oxidation of the circulating LDL is thought to play a key role in the pathogenesis of atherosclerosis, which is the underlying disorder leading to heart attack, ischaemic strokes, and CHD. It has been demonstrated that the content of ubiquinol in human LDL affords protection against the oxidative modifications of LDL themselves, thus lowering their atherogenic potency.

iii. In post-MI cases:
   In a randomised, placebo-controlled trial of 73 patients following MI who were administered 120 mg/day of coenzyme 10 for one year, it was observed that coenzyme Q10 group demonstrated a significant decrease in total cardiac events including nonfatal MI and cardiac deaths. This improvement has been attributed to possible attenuation of endothelial dysfunction.

iv. In cardiac arrest:
   A recent study shows a survival benefit after cardiac arrest if CoQ10 is administered in addition to commencing active cooling of the body to 32 - 34°C.

v. Angina:
   CoQ10 might improve exercise tolerance in angina. Evidences in angina pectoris cardiomyopathy and physical exercise capacity show conflicting results and require further study.

vi. Hypertrophic cardiomyopathy:
   CoQ10 orally seems to decrease the thickness of heart wall and decrease symptoms of shortness of breath and fatigue. Several small trials have found CoQ10 may be helpful for certain types of cardiomyopathy.

vii. Cancer:
   CoQ10 is being investigated as a treatment for cancer and as a relief from cancer treatment side-effects. The AHRQ found no evidence to assess the efficacy of coenzyme Q10 for this use. Animal studies have shown that CoQ10 helps the immune system work better and makes the body better able to resist certain infections and types of cancer. In breast cancer, the results are not very conclusive, though oral CoQ10 might be helpful in advanced breast cancer along with surgery and conventional treatment plus other antioxidants and omega-3 and omega-6 fatty acids as relief from cancer treatment side-effects. Clinical trials have shown that CoQ10 helps protect the heart from the damaging side-effects of doxorubicin and daunorubicin (anti-cancer agents), or other anthracycline medications.

viii. Radiation injury:
   CoQ10 dietary supplementation in rats reduced radiation damage to animal’s blood.

ix. Improving athletic or exercise performance and reducing fatigue:
   CoQ10 might help increase energy. This is because CoQ10 has a role in producing ATP. Thus, CoQ10 has been tried for treating inherited or acquired disorders that limit energy production in the cells of the body (mitochondrial disorders) and for improving exercise performance or athletic performance and reducing the sensation of fatigue. The physical performance of subjects was found to increase in those who had taken 300 mg of CoQ10 and the subjects also reported feeling less fatigued.

x. Enhancing anti-inflammatory effects:
   CoQ10, a powerful antioxidant produced by the human body, helps to reduce inflammation. It is observed that in elderly individuals, the anti-inflammatory effects of eating a Mediterranean-style diet – one rich in olive oil, fruits, and vegetables – are enhanced by addition of a daily 200 mg supplement of CoQ10, and that CoQ10 supplementation acts in synergy with a Mediterranean diet to control inflammatory responses and oxidative stress within cells.

xi. Improving blood sugar control in diabetics:
The effectiveness of CoQ10 in diabetes is controversial. A more recent trial using 100 mg CoQ10 twice daily suggested significantly improved blood pressure and glycaemic control. However, two randomised controlled studies conducted earlier found that CoQ10 supplementation failed to find any effect on glycaemic control.

xii. Male infertility:
There is some evidence that CoQ10 treatment can improve the movement and density of sperm in men with certain type of infertility. Dose: 200 - 300 mg/day.

xiii. Statins-induced myopathy:
Statins sometimes cause muscle pain. Oral CoQ10 might reduce this pain.

xiv. Reduction in muscle damage from exercise:
Too much exercise or strenuous exercise can cause oxidative stress, inflammation, and muscle damage. CoQ10 supplementation before strenuous exercise may lower the oxidative stress and inflammation in the body, lowering the chance of muscle damage. CoQ10 group of runners showed a reduction in oxidative stress as suggested by milder increase in 8-OHdG levels, a decrease in isoprostanes generation and an increase in catalase and antioxidant status. Besides, CoQ10 decreased creatinine production, creatinine being the end-product of muscle metabolism and a key marker of muscle damage.

xv. Prevention of pre-eclampsia:
Evidences show that women who are at risk for developing this condition have a lower chance of getting it if they take oral CoQ10 from 20 weeks of pregnancy until delivery. Dose: 100 mg/d.

xvi. In hair loss related to use of the warfarin:
Research is continuing to assess the potential of CoQ10 in this condition.

xvii. In Lyme disease.

xviii. Life span:
Low dosages of CoQ10 reduce oxidation and DNA double strand breaks, and a combination of a diet rich in polyunsaturated fatty acids and CoQ10 supplementation leads to a longer life span in rats. Yet a few studies reported no increase in life span or decrease in ageing in mice or rats supplemented with CoQ10.

Contraindications
No absolute contraindications are known for CoQ10.

Adverse effects
Adverse effects with CoQ10 are quite rare. Toxicity is not usually observed with high doses of CoQ10. A daily dose up to 3,600 mg is found to be well-tolerated by healthy as well as unhealthy persons though very high intakes are associated with mostly GIT adverse effects such as stomach upset, loss of appetite, nausea, vomiting, and diarrhoea. On an average, mild gastrointestinal discomfort is reported in less than one per cent of patients in clinical trials. It can also cause allergic reactions and may lower BP in some people. Dividing the total daily dose by taking smaller amounts two or three times a day can reduce the side effects.

Precautions
i. Not enough is known about the use of CoQ10 during pregnancy or in breast feeding mothers or in young children. Hence it is better to avoid its use in them.

ii. CoQ10 might interfere with blood pressure control during and after surgery; hence stop using CoQ10 at least 2 weeks before a scheduled surgery. It may increase the effects of medications used to lower BP; hence monitoring is advised.

iii. Because of CoenzymeQ10’s potential hypoglycaemic effects, monitoring is advised when using adjunctively with prescription medications.

iv. Smoking can use-up the body’s store of CoQ10.

v. CoQ10 has not been carefully tested in combination with chemotherapy to see if it is safe and effective.

Drug Interactions
i. Antihypertensive agents:
CoQ10 seems to decrease BP. Taking CoQ10 along with other antihypertensive agents may cause BP to go too low.

ii. Warfarin:
Warfarin is used to decrease blood clotting while CoQ10 might increase blood clotting; thus CoQ10 might decrease the effectiveness of warfarin and increase the risk of dangerous clots. Potential interactions with warfarin causing decreased international normalised ratio (INR) has been reported in case studies. However, a prospective placebo controlled trial of 24 stable patients taking warfarin and 100 mg CoQ10 over four weeks found no changes.
in prothrombin time and INR levels.

iii. Oral contraceptives:
These agents significantly decrease serum levels of CoQ10 and alpha-tocopherol, the most biologically active form of vit E. This is the outcome of a cross-sectional study conducted on 55 pre-menopausal women with regular menstrual cycles.

iv. Cancer chemotherapy:
CoQ10 being an antioxidant, it might decrease the effectiveness of some medications used for cancer, but it is too early to pass a judgement. Several doxorubicin trials, mostly in animal models have workers observed a reduction in cardiac coenzyme Q10 depletion and cardiotoxicity associated with co-administration of coenzymeQ10. The clinical implications on disease state and adverse reaction profile with coenzymeQ10 supplementation in depleted states requires further investigation.

v. Statins:
Statin drugs or HMG-CoA reductase inhibitors which are used to lower cholesterol, may interfere with the body’s production of CoQ10. A recent cross-over trial found no significant coenzyme Q10 drop after initiation of selected statins.

vi. Tricyclic antidepressants:
Including amitryptyline, doxepin, and imipramine can lower the levels of CoQ10 in the body.

vii. Red yeast:
Red yeast might reduce CoQ10 levels. However, there are no known interactions with foods.

Dosage and standardisation
The majority of coenzyme Q10 products are synthesised in Japan. It is available in various formulations. This exhibits variation in bioavailability, bioequivalence, and dosage consistency.

Current status
CoQ10 has been used, recommended, or studied for numerous clinical conditions, but remains controversial as a treatment in many areas. It is a safe but expensive supplement with preliminary benefit in Parkinson’s disease and mitochondrial cytopathies, and inconsistent results in cardiovascular disease requiring further multicentric research evaluations.

References
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