

Potential uses for coenzyme Q10

Neither classified as a vitamin nor as a mineral, coenzyme Q10 is exempt from the EC Directive on Food Supplements. In this article,

Pam Mason gives an overview of this biochemical

Coenzyme Q (ubiquinone) is a naturally occurring enzyme cofactor found in mitochondria. Several types of coenzyme Q have been identified and numbered from zero upwards. The variety found in human tissue is coenzyme Q10. It can be obtained from the diet or from food supplements but it is also produced endogenously.

Meat and fatty fish products are the most concentrated sources of coenzyme Q10, although smaller quantities are found in wholegrain cereals, soya beans, nuts and vegetables, particularly spinach and broccoli. Absorption of coenzyme Q10 from the diet (or supplements) occurs in the small intestine and is influenced by the presence of food and drink. It is better absorbed in the presence of a fatty meal.

After absorption, coenzyme Q10 is transported to the liver where it is incorporated into lipoproteins and bound principally to very low density lipoprotein cholesterol and low density lipoprotein cholesterol. It is then concentrated in the tissues. One study showed that coenzyme Q10 from both foods and supplements significantly raised serum concentrations.¹

The relative contribution of endogenous synthesis and dietary intake to coenzyme Q status has not been established. Coenzyme Q10 is produced from tyrosine in all the cells of the body, but specifically in the heart, liver, kidney and pancreas where it plays an indispensable role in intracellular energy production. Several co-factors are involved in its synthesis, including vitamin B₂, vitamin B₆, folic acid, vitamin B₁₂, niacin, pantothenic acid and vitamin C. The ability to make coenzyme Q10 decreases with age — concentration in human tissue peaks at 20 years of age.

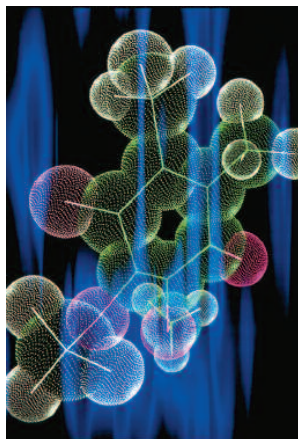
Functions

Coenzyme Q10 has the following functions:

- It plays a vital role in intracellular energy production — it is involved in the transport of electrons and protons, and supports adenosine triphosphate synthesis in the mitochondrial membrane and is essential for normal myocardial function.
- It is a fat-soluble antioxidant that helps to stabilise cell membranes, preserving cellular integrity and function. It also helps to regenerate vitamin E to its antioxidant form.
- It has immunostimulant activity.

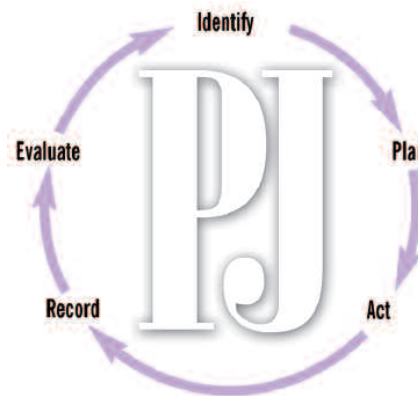
Potential clinical uses

Because coenzyme Q10 is not classed as a vitamin or mineral, no dietary reference value or recommended daily allowance has been



Alfred Jasieka/SPL

Ubiquinones are present in mitochondria. They form part of the electron transfer chain in cells



Identify knowledge gaps

1. What is coenzyme Q?
2. What conditions has coenzyme Q10 been linked with?
3. Why is coenzyme Q10 combined with magnesium?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "dietary products" (see appendix 4 of "Plan and record").

established. However, there is increasing speculation (based on serum and biopsy samples) that some signs and symptoms are associated with a lack of coenzyme Q10. Deficiency has been linked to congestive heart failure (CHF), ischaemic heart disease, cardiomyopathy, hypertension, hyperthyroidism and breast cancer. It has also been linked to the use of statins.

Whether the observed lack of coenzyme Q10 in these conditions contributes to the development of the disease or is caused by the disease itself is unclear. In heart failure, those with the most advanced disease have lower coenzyme Q10 levels than those with less advanced disease.

Deficiency can occur as a result of:

- Inadequate intake, particularly if requirements are increased due to disease
- Inadequate production caused by aging or deficiencies of nutrients required for synthesis
- Genetic or acquired defects in synthesis or metabolism
- Interactions with medicines — beta-blockers, clonidine, gemfibrozil, hydralazine, hydrochlorothiazide, methyl-dopa, statins and tricyclic antidepressants can reduce coenzyme Q10 levels

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Coenzyme Q10 interactions

Statins Simvastatin and pravastatin have been shown to reduce the endogenous synthesis of coenzyme Q10. Statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A reductase. Inhibition of this enzyme appears also to inhibit the intrinsic biosynthesis of coenzyme Q10. This reduces coenzyme Q10 concentrations and, therefore, presents a potential further risk for cardiovascular disease. Supplementation may increase coenzyme Q10 levels without adversely affecting drug efficacy.

Warfarin Case reports suggest that coenzyme Q10 may decrease international normalised ratio in patients previously stabilised on anticoagulants. Although a double blind crossover study in 24 patients on long-term warfarin found that oral coenzyme Q10 (100mg daily) had no significant effect on INR or warfarin levels, in patients on warfarin, high doses of coenzyme Q10 should be used with caution.

Cardiovascular disease The potential role of coenzyme Q10 in cardiovascular disease has been studied over more than 30 years. Studies increasingly look at its role in specific conditions but an open study in 424 patients, published in 1994, indicated that coenzyme Q10 supplementation may have benefits in cardiac function in patients with a range of cardiovascular disorders, including ischaemic cardiomyopathy, primary diastolic dysfunction, hypertension, valvular heart disease and mitral valve prolapse.²

Congestive heart failure There is substantive evidence suggesting a role for coenzyme Q in CHF. Oxidative stress is believed to play a role in the aetiology of CHF. It has been suggested that low coenzyme Q10 levels found in patients with CHF contribute to the disease while supplementation with preparations which include coenzyme Q10 may produce an improvement.

In one double-blind, placebo-controlled study 322 patients with CHF were randomly assigned to receive coenzyme Q10 2mg/kg/day, or placebo, for one year. The number of episodes of pulmonary oedema or cardiac asthma was significantly lower in the intervention group than in the placebo group. The group receiving coenzyme Q10 also had fewer admissions to hospital.³ A meta-analysis of eight clinical trials of coenzyme Q10 in patients with CHF showed that supplemental treatment of CHF resulted in significant improvements in stroke volume, ejection fraction, cardiac output, cardiac index and diastolic volume index.⁴

Not all clinical trials have produced positive results. In a double blind, placebo-controlled crossover study, 30 patients with chronic left ventricular dysfunction were randomised to receive coenzyme Q10 or a placebo for three months each. Plasma levels of coenzyme Q10 increased to more than



Coenzyme Q10 supplements have been investigated for their effect on athletic performance and in Parkinson's disease

Studies have also looked at the use of coenzyme Q10 supplements before cardiac surgery

twice baseline values, but there were no significant differences in left ventricular ejection fraction, cardiac volumes, haemodynamic indices or quality of life measures.⁵

In another randomised controlled trial (RCT) 55 patients with CHF received 200mg coenzyme Q10 or placebo daily for six months. Patients receiving the supplement had higher serum concentrations of coenzyme Q10, but there were no differences in cardiac performance, peak oxygen consumption and exercise duration between the treated group and the placebo group.⁶

Angina Coenzyme Q10 levels tend to be low in patients with ischaemic heart disease and several clinical trials have been conducted in patients with angina. Overall, coenzyme Q10 appears to delay the onset of angina and increases patients' stamina on a treadmill.

In one RCT, 144 patients were given 120mg coenzyme Q10 or a placebo daily for 28 days, starting within three days after a heart attack. There was a significant improvement in angina pectoris, total arrhythmias and poor left ventricular function in the intervention group. Total cardiac events, including cardiac deaths and non-fatal infarction, were also significantly lower in this group.⁷

Hypertension Coenzyme Q10 has been investigated for hypertension both as a stand-alone treatment and as an adjunct to conventional anti-hypertensive drugs. In one randomised double-blind study involving 83 patients, an oral dose of 60mg taken twice a day over 12 weeks produced a mean reduction in systolic blood pressure of 17.8 ± 7.3 mmHg.⁸ Another study in 59 patients with hypertension showed that adding 120mg coenzyme Q10 daily to existing medication caused an additional reduction in systolic and diastolic blood pressure after eight weeks.⁹

Cardiac surgery Studies have also looked at the use of coenzyme Q10 supplements before cardiac surgery. Oral supplementation with coenzyme Q10 for two weeks before cardiac surgery has been shown to improve post-operative heart function and shorten hospital stays. However, supplementation with 600mg coenzyme Q10 12 hours before surgery did not improve myocardial protection in patients undergoing coronary revascularisation.

Exercise performance Coenzyme Q10 is essential in energy metabolism and has, therefore, been investigated for its effect on athletic performance. Controlled trials using doses of 60 to 150mg daily over 28 days to eight weeks have generally shown no improvements in physical performance. However, in one double-blind crossover trial, there were positive results on both objective and subjective parameters of physical performance — 94 per cent of athletes thought that coenzyme Q10 improved their performance and recovery times compared with 33 per cent taking a placebo.¹⁰

Parkinson's disease Studies suggest that oxidative damage, inflammation and mitochondrial impairment may play a role in Parkinson's disease. In a multicentre RCT comparing three different doses of coenzyme Q10 (300mg, 600mg, 1,200mg) in 80 patients with early Parkinson's disease, significant improvements were reported after nine months in the group taking 1,200mg daily.¹¹ A new trial by the same research group is scheduled to start this year.

Huntingdon's chorea A randomised, double-blind study involving 347 patients with early Huntington's chorea showed that a dose of coenzyme Q10 600mg daily taken over 30 months produced a trend towards slow decline and beneficial improvements in some parameters. However, changes were not significant.¹²

Cancer Observational studies of women diagnosed with breast cancer have reported

reduced blood coenzyme Q10 concentrations. There have been several case reports of remissions or partial remissions in patients with tumours who take coenzyme Q10. However, there are no controlled studies to show the effectiveness of coenzyme Q10 in cancer.

Migraine An open trial investigated the effects of coenzyme Q10 150mg daily for three months in 32 individuals with a history of migraine. Coenzyme Q10 was associated with a significant reduction in both the frequency and duration of attacks.¹³

Doses and safety

Coenzyme Q10 is sold in capsules and tablets in strengths of 10–150mg. Doses used in studies investigating use in cardiovascular disease and prevention of migraine have ranged from 100–150mg daily. However, higher doses have been used in angina (up to 600mg daily) and Parkinson's disease (up to 1,200mg daily). Doses used to prepare for heart surgery have

The potential benefits of a product containing coenzyme Q10 and magnesium

Products containing coenzyme Q10 sometimes also contain magnesium. These tend to be promoted for maintenance of energy levels and nutritional support. However, magnesium also has potential roles in cardiovascular disease and migraine.

Magnesium is the second most abundant intracellular cation in the body and is involved in more than 300 enzymatic reactions. It interacts with other electrolytes, plays a role in neuromuscular function and is involved in the growth and maintenance of bone. It also stabilises the structure of adenosine triphosphate in ATP-dependent enzyme reactions and is, therefore, involved in energy metabolism. In the heart, it acts as a calcium channel blocker.

Poor magnesium status can result from renal dysfunction, malabsorption, use of loop diuretics, excessive diarrhoea, chronic alcoholism, diabetes mellitus and endocrine disorders. Low magnesium levels are associated with several cardiovascular disorders.

The UK reference nutrient intake for adult females is 270mg daily and for adult males it is 300mg each day. Evidence from the most recent National Diet and Nutrition Survey in adults suggest that significant numbers of individuals in the UK, particularly young adults, do not achieve the RNI, and around 10 per cent do not achieve the lower reference nutrient intake (the level below which deficiency is more likely). Good sources of magnesium are whole grains, dark green leafy vegetables, nuts, legumes and fish.

Doses of 300–600mg of magnesium daily have been used in cardiovascular disease and migraine. Guidance on the likely safe total daily intake from supplements alone (established by the Food Standards Agency Expert Vitamins and Mineral Group) is 400mg daily.

Cardiovascular disease A multinational prospective RCT showed that six months' supplementation with oral magnesium (365mg daily) in patients with coronary artery disease resulted in significant improvement in exercise tolerance, exercise-induced chest pain and quality of life.¹⁴

In a study involving 141 patients with mitral valve prolapse hypomagnesaemia was found in 60 per cent of the patients.¹⁵ These patients were then followed in a randomised double-blind crossover study. Five weeks of magnesium supplementation (255mg magnesium daily for the first week, followed by 170mg daily until the fifth week) was associated with alleviation of symptoms of weakness, chest pain, dyspnoea, palpitations and anxiety.

Controlled trials investigating the mineral's effect on blood pressure have produced variable results — effects on hypertension are, at best,

moderate. A meta-analysis of 20 randomised trials involving 1,220 subjects showed that magnesium supplementation produced a modest dose-dependent blood pressure lowering effect. For each 250mg daily increase in magnesium intake, systolic blood pressure fell by a further 4.3mmHg and diastolic blood pressure by 2.3mmHg.¹⁶

Migraine People who suffer from repeated migraines have been found to have lower magnesium levels than those who do not. According to one review, 50 per cent of patients have lowered levels of ionised magnesium during an acute migraine attack. The author suggested that the potential role of magnesium in migraine was related to its influence on serotonin receptors, nitric oxide synthesis and release, and other migraine-related receptors and neurotransmitters.¹⁷ Pilot studies have suggested that low magnesium may be responsible for hyperexcitability of neuronal tissue in migraine patients.

In a double-blind, placebo-controlled, prospective multicentre study 69 patients experiencing two to six migraine attacks per month without aura and a history of migraine for at least two years were randomised to receive 480mg daily of magnesium in two divided doses for 12 weeks. There were no differences in the number of migraine attacks or number of days when attacks were suffered.¹⁸

Another trial in 81 subjects showed that 576mg magnesium daily over 12 weeks significantly reduced self-reported attack frequency by 41.6 per cent compared with 15.8 per cent in the placebo group. Effects were observed after week 9. Treatment also decreased the duration of migraine.¹⁹ Results from other studies investigating the role of magnesium in migraine are promising but further research is needed.

Oral magnesium (360mg daily) has also been shown to reduce the number of days with migraine headache in women who experience migraine premenstrually.

Exercise performance Magnesium, like coenzyme Q10, has been investigated for a potential role in enhancing performance. Well-controlled trials do not generally support improved performance as an effect of magnesium supplementation.

Labelling and promotion Any potential benefits in terms of cardiovascular disease or other conditions cannot be mentioned on any labelling or promotional materials because these products are sold as foods.

varied between 30mg and 100mg daily for one to two weeks before surgery and a month afterwards.

Conclusion

People who wish to try coenzyme Q10 for cardiovascular conditions or migraine prevention should be advised it may take 10–12 weeks to have an effect. However all patients with cardiovascular conditions should consult their prescriber before taking coenzyme Q10.

Coenzyme Q10 seems to be safe and relatively well tolerated in doses of 10–200mg daily. There are occasional reports of gastrointestinal discomfort, dizziness and skin rash, but these tend to occur with doses higher than 200mg daily.

Safety in pregnancy has not been established.

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Key points

- Coenzyme Q10 is generally a safe supplement with few reported side effects.
- Blood concentrations of coenzyme Q10 fall with age.
- Evidence that supplements slow the ageing process is lacking.
- Evidence from human studies suggests that coenzyme Q10 supplementation may have benefits in improving the symptoms of congestive heart failure and angina and reducing high blood pressure. It may also improve the outcomes of cardiac surgery. Further research is needed to clarify the dosage and duration of treatment.
- Coenzyme Q10 does not appear to enhance athletic performance.
- There are no controlled trials to support the use of coenzyme Q supplementation in cancer prevention or management.
- The use of coenzyme Q10 supplementation in Parkinson's disease shows promise, but further controlled trials are needed.
- High dose coenzyme Q10 supplements should not be taken by patients on warfarin without monitoring.
- A supplement providing 100–150mg daily of coenzyme Q10 with or without magnesium 300mg daily may be helpful in cardiovascular conditions and migraine. Further research is needed to confirm these effects. Patients with these conditions should seek their doctor's advice.

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Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Cascade the information in this article to your staff.
2. Read the packaging and any information leaflets of coenzyme Q10 products in your pharmacy.
3. Discuss with another pharmacist other biochemicals that might be beneficial in heart disease or migraine.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities.

Answer the following questions:

What have you learnt?

How has it added value to your practice? (Have you applied this learning or had any feedback?)

What will you do now and how will this be achieved?