



A Review on Ultrasome Drug Delivery Systems

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Abstract

Coenzyme Q10 (ubiquinone), is a natural fat-soluble antioxidant with promising usage in cardiac disorders as adjunctive treatment and to protect neurons against age-related diseases when undergoing degeneration, it is very lipophilic and poorly absorbed by the gut. CoQ10's was formulated using the patented drug delivery system of Ultrasome™ which is encapsulated of CoQ10 demonstrating high efficacy in drug tapping and increased invitro efficiency, release profile, and better oral bioavailability relative to generic CoQ10. Besides, many clinical trials and experimental testing, Ultrasome-CoQ10™ has played a role in the quality of patients life with end-stage heart failure undergoing cardiac transplantation, in the healing of persistent skin lesions, in the regeneration of patients with hip fracture surgery, and in the defense against 6-hydroxydopamine mediated nigra lesions in rats that suggest potency majority in Parkinson's and other neurodegeneration diseases without any sort of side effects.

Keywords: Coenzyme Q10; Ultrasome™; Fat soluble antioxidant; patented drug delivery system.

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1. Introduction

Coenzyme Q10 (CoQ10) is a compound that is available naturally in our body and its high amount present in the heart, pancreas, liver and kidney [1]. It is also present everywhere in nature and because of its quinone structure which is similar to vitamin-k. CoQ10 is also called ubiquinone (lipophilic metabolite) [2]. Ubiquinone is a metabolite that functions as an electronic carrier in mitochondrial oxidative phosphorylation, which demonstrated that CoQ10 plays an important role as an electron carrier in mitochondrial oxidative phosphorylation. Due to its major involvement in ATP synthesis, this coenzyme affects all tissues and organs. CoQ10 has several advantages due to its increased adenosine levels which prevent loss of cardiac cells [3] and its functions as an intercellular antioxidant which has high stabilizing properties [4] and cellular properties to treat several diseases which helps in improving mitochondrial antioxidant as well. Many studies have considered the profit of CoQ10 supplementation which has already possessed antioxidant properties improves

more energy production and enhancing cardiac muscle contractility which reduces LDL levels [5-8]. More clinical trials reported that there are lower levels of it in systolic and diastolic blood pressure [9]. The CoQ10 will explore the neurologic demonstration effects in Alzheimer's, Huntington's, and Parkinsonism diseases [10,11]. The peculiarity of mitochondrial, encephalomyopathy, stroke-like episodes / MELAS syndrome, myoclonus epilepsy and in mitochondrial abnormalities [12, 13]. Regarding diabetes, this CoQ10 enhances glycaemic control which reduces oxidation stress [14, 15]. CoQ10 lowers the acute toxic effect of chemotherapeutic compound doxorubicin which has its antioxidant properties leads to inhibition of CoQ10 related enzymatic factors that are present in cardiac tissues [16]. More number of studies has shown a significant impact of CoQ10; which proved its supplementation in providing proper improvement in muscular injury and oxidative stress during exercise performance [17-18] and physical fatigue sensation [19].

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2. STRUCTURE OF CoQ10:

The CoQ10 structure consisting of a quinone ring which is attached to the variable terpenoid side. The structural chains containing one to ten monounsaturated trans-iso prenyl units. The side chain will be highly fat-soluble, which allows CoQ10 to be incorporated inside cells and it is practically insoluble in water [20]. Finally, the oral bioavailability of CoQ10 is very Low, which was found to be related to the dissolution rate of the formulation. Microemulsions and emulsions are more useful as vehicles for the oral delivery of lipophilic drugs which improves oral bioavailability for the insoluble compounds [21, 22]. The major objective of this ongoing work is to analyze the oral bioavailability which is formulated with CoQ10 using Ultrasome TM technology (Fig.1.).

3. ULTRASOMES:

Ultrasomes are of the advanced type of lipid particles that acts as a hybrid system between lipid nanoparticles and oil-in-water (o/w) emulsions. These particles have a lipid type of assembly consisting of a hydrophobic core in o/w emulsions and it is rounded by one or more phospholipid bilayers of these liposomes. Ultrasome technology will be representing a new molecule which is a type of lipoidal drug vehicle and its success will be incorporated with a high amount of lecithin (5-10%) which is compared to standard emulsions (0.5-2%), and the use of triglycerides which are solid at room temperature instead of using the oils, and the usage procedure by high-pressure emulsification method. Based upon these mixing ratios and the technology used in manufacturing will form the lipid particles which are submicron range and stable.

4. ULTRASOME COQ10:

In enhancing the oral bioavailability of Ultrasome CoQ10 drug delivery system it was compared with the generic CoQ10 in elderly patients by performing double-blind studies and in this study, the results were reported as effectiveness is more in younger patients as 9-10 folds which are higher than the elderly patients. The Ultrasome CoQ10 drug delivery system treatment was most effective in case of chronic wounds majority studied in elderly patients aged 76.9 Yrs. above shows very positive results and the drug is given in the amount of 400 mg of Ultrasome CoQ10TM drug delivery (60 mg of CoQ10) for about the duration of 20-60 days. The Ultrasome CoQ10 drug delivery system treatment was very much useful in end-stage heart failure patients ready for cardiac transplantation. During this study as of placebo, the drug is given as 400mg of Ultrasome CoQ10TM drug delivery (60 mg of CoQ10) this study shows significant improvement in the case of 6min walk test which has properly reduced dyspnoea. For the effectiveness of the action of hip fracture replacement, all the patients in the group are given 400 mg of Ultrasome CoQ10TM drug delivery (60 mg of CoQ10) and the pain intensity is less than ($p < 0.001$) which results in less pain in

their entire stay in the hospital. The Ultrasome CoQ10 drug delivery system treatment in case of athletes has proven effective when randomly taken 30 athletes and given a dose of 400mg of Ultrasome CoQ10TM drug delivery (60 mg of CoQ10) for about one week their results are reported after physical activity having low muscle soreness and fatigue ($p < 0.05$).

5. FORMULATING ULTRASOME COQ10:

The CoQ10 was taken and mixed up with the lipid materials like solid triglyceride, phospholipids, tocopherol succinate in the ethanol was dissolved together with the lipid ingredients (solid triglyceride, tocopherol succinate, and phospholipids) in ethanol. This mixture solvent was evaporated until it is prone to dryness after this drug combination was hydrated using the aqueous phase by using a mechanical shaker. The final dispersed mixture is homogenized by using a high-pressure homogenizer to lower the particle size until it reaches the sub-micron level. The solvents like ethyl alcohol and water (EtOH + H₂O) were evaporated by using a spray drying method to obtain the final Ultrasome CoQ10 dry powder. Ultrasomes are a modern method of lipid particles known to be an interim or hybrid mechanism between liposomes and oil-in-water emulsions. Ultrasound particles have a new form of lipid assembly consisting of a hydrophobic core, in typical oil-in-water emulsions, but surrounded and stabilized by one or more phospholipid bilayers as in liposomes. Ultrasome technology represents a new entity as a lipoidal drug vehicle and its successful production has been accomplished by the integration of a relatively new product. Strong lecithin content (5-10 %) compared to normal lecithin. Emulsions (0.5-2 %), the use of fats or triglycerides that are strong in the space. Temperature instead of oils and use of high-pressure emulsification. This is the Combination of complex lipid structure and production technology results. In the formation of stable lipid particles within the submicron scale.

6. DISSOLUTION STUDIES OF ULTRASOME COQ10:

Release of CoQ10 from UltrasomeTM in vitro- Preparation of the CoQ10 and commercial Product (generic CoQ10) (Fig.3) demonstrates the patterns of in vitro release of CoQ10 from the formulation of UltrasomeTM-CoQ10 and the generic formulation of CoQ10 in simulated gastric fluid. The percent release of CoQ10 from the marketed formulation was poor compared to a large release (50 percent after 2 hours) from the formulation of UltrasomeTM-CoQ10. After capsule disruption in the activated gastric fluid, large aggregates or clusters of CoQ10 have been found, which may describe the low dissolution of CoQ10 in the release medium. Fig 3. shows the particle size of UltrasomeTM-CoQ10 (A) compared to generic CoQ10 (B). The particle size is one of the factors that affect the dissolution rate. UltrasomeTM-CoQ10 represented by small, homogenous and uniform particles compared to



large and heterogeneous particles of generic CoQ10

ORAL BIOAVAILABILITY IN ELDERLY PATIENTS BY ULTRASOME COQ10:

The findings of this study show the efficacy of Ultrasome™ CoQ10 with substantially improved oral bioavailability of CoQ10 compared to generic CoQ10 for geriatric patients with many chronic diseases. Increased plasma response to additional treatment with Ultrasome™ CoQ10 is clinically and statistically significant. CoQ10 deficiency has been identified in patients with diabetes mellitus, extreme ischaemic heart disease, and in patients undergoing cholesterol-lowering by statins. Supplementary CoQ10 therapy is effective in the treatment of congestive heart failure. Dyslipidaemia, complications of diabetes, Parkinson's disease. Improved oral absorption of Ultrasome™ CoQ10 is especially relevant for elderly patients diagnosed with chronic and debilitating conditions. It is considered to have low gastrointestinal absorption.

BENEFITS OF ULTRASOME COQ10:

When a very low amount of CoQ10 is released from the body due to issues that are particularly related to aging and to provide basic benefits we are supplementing with CoQ10. The major advantage produced in related to anti-aging, fatigue and energy which shows a healthy outcome regarding CoQ10 with a daily intake of 10 to 30 mg daily is often profitable under the age 30-40 yrs., which gives positive effects regarding for energy boost up. So finally, the patients will be given 200-400 mg which should be under the supervision of medical and beyond the level of dose 600 mg is given in clinical trials.

To heart: A weak heart-patients with congestive heart failure due to myocardial infarction, cardiomyopathy, or even hypertension-indicates that the heart is inadequately functioning and the pumped blood flow becomes very low with all the undesired side effects: shortness of breath, fluid in the lungs, heavy legs, etc. There has been a strong association between ATP material of myocardial tissue, systolic, and diastolic in case of Left ventricular indicators of heart disease. Patients with a Dilated and restrictive cardiomyopathy is of poor blood flow and myocardial concentrations of CoQ10. The underlying energy deficiency can be explained in the Heart muscle, associated with impaired function of the heart, and possible gain of additional CoQ10 in improving Performance of energy generation in human heart tissue [24-26]. There is strong evidence to prove that CoQ10 acts as the mitochondrial stage to increase performance and energy generation in human heart tissue [27]. This is illustrated by CoQ10 localization and relative abundance. In mitochondria and the central function of the CoQ10 with mitochondrial bioenergetics. The inotropic action of the CoQ10, which increases the contractile strength of the heart to increase cardiac output, was also suggested as another interesting function of CoQ10 which is used to help heart function

in heart failure [28]. Suggested that additional CoQ10 could also boost Usage of oxygen at the cellular level, and possibly Gain patients with coronary artery insufficiency.

To immune system:

The advantage of the development of immune system energy and the efficient immune response will be reduced according to a lower CoQ10 content, as the immune system requires an enormous amount of ATP to mount defences aggressively.

In statins Therapy:

Statin therapy induces a 40-50 percent reduction in CoQ10 levels. Several studies have shown that external CoQ10 is effective in countering statin side effects.

In Parkinson's disease: Advanced research suggests that supplementation with CoQ10 can help increase levels of dopamine, a deficient neurotransmitter, in people with Parkinson's disease. Some clinical testing, even with very high levels of supplementation, is carried out.

In skin lesions:

A prospective demonstration study on patients who have undergone more than 20 days of either non-healing or worsening full-thickness skin lesion. Although there is no scientific evidence, several anecdotal CoQ10. Benefits are reported as of migraine due to hypertension, headache etc.

APPLICATIONS OF ULTRASOME COQ10:

Ultrasomes Q10 supplementation for CoQ10™ treatment in cardiac transplantation patient, hip fracture replacement, persistent wounds and in treatment for athletes after physical activity.

In cancer therapy:

A lipophilic antioxidant, CoQ10, exhibits various biological activities such as immune-boosting, scavenging of free radicals, and DNA defence. CoQ10 administration studies have revealed promising results in cancer prevention and/or treatment. Positive effects of breast cancer have been documented in patients who use CoQ10 [29- 32].

In lipid metabolism:

Clinical human and animal studies have indicated that dietary supplementation with CoQ10 [33] increases the metabolism of cholesterol in mammals. In the long-term CoQ10 feeding experiment, decreased cholesterol synthesis with cholesterol catabolism suppression was observed, resulting in the return of hepatic cholesterol to normal levels [34]. Long-term (0-42 days) CoQ10 supplementation at 20 and 40 mg/kg decreased serum total cholesterol, however, total cholesterol levels and LDL serum cholesterol levels. The reduction in serum LDL cholesterol due to



CoQ10 supplementation was due to the reduced form of CoQ10 (H₂), which induces characteristic patterns of gene expression that are translated into lower levels of LDL cholesterol in human subjects. CoQ10 reduced the plasma metabolism of cholesterol in patients with myocardial infarction.

7. DISCUSSION:

Herbamed [35] has developed a special proprietary Ultrosome™ program for improved oral lipophilic compounds such as CoQ10 bioavailability. Ultrasones are a new type of Lipid particles between liposomes which are known as intermediate or "Hybrid" systems of o/w emulsions; a new form of lipid is found in ultrasones particles. In standard o/w emulsions, but with a fat-soluble assembly much as in liposomes, surrounded and stabilized by one or more phospholipid bilayers. In vitro and in vivo, the efficacy of the formulation was tested. The dissolving apparatus was used for the in vitro assay and tested for oral bioavailability. Geriatric patients, hospitalized, undertaking continuing therapy with various drugs. The percent release from the marketed product of CoQ10 was very poor. Compared to a very critical release from the Ultrosome™ (50 % after 2 hours) the CoQ10. In the simulated gastric fluid after capsule disturbance, large CoQ10 aggregates or clusters have been observed, which may explain the small Dissolution of CoQ10 into the discharge medium. Since the size of particles is a limiting factor as a consequence of the rate and degree of drug absorption

from the gastrointestinal tract, the oral bioavailability of CoQ10 from the commercial product, as opposed to the commercial product, is poor. To the formulation of the Ultrasones-CoQ10™ the findings of a report on human oral bioavailability involving oral ingestion of 90 mg CoQ10 in encapsulated (Ultrasones™) formulation -CoQ10,) as well as the generic variant is provided. The (Ultrasones™) Research CoQ10) has shown good Tolerability was noted and there were no side effects. This study shows that high drug-tapping has been shown by Ultrasones-CoQ10™ Efficacy and increased oral delivery of CoQ10 also in geriatric patients hospitalized, CoQ10 is a material that is naturally present in nearly every aspect of cell in the body. For cellular respiration and ATP manufacture, CoQ10 has also been reported to be an important intercellular antioxidant due to a lack of CoQ10 nutritional deficiencies that might result in impaired synthesis. A hereditary or acquired deficiency in CoQ10 synthesis or consumption, such as vitamin B6, Increases the needs of tissue arising from a specific disease. CoQ10 on the other hand with advancing age and using medications such as statins, levels may decline. CoQ10 reduces numerous diseases like a cardiovascular disease which can benefit from supplementation; Muscular dystrophy, linked to diabetes mellitus, and Parkinson's disease. Furthermore, supplementation with CoQ10 can benefit the quality of the Good subjects' lives, such as athletes and those who perform physical exertion. Depending on the formulation used, absorption and bioavailability vary greatly.

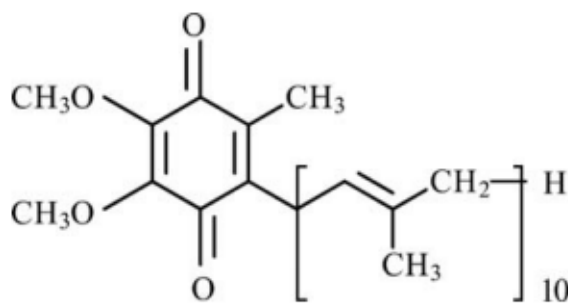


Fig 1. Chemical structure of CoQ10

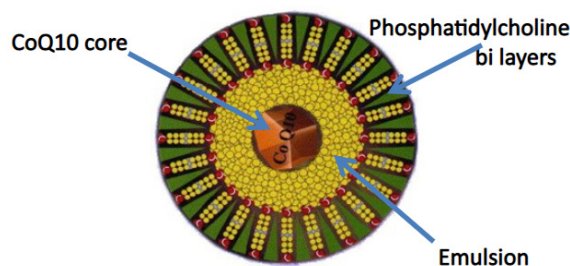


Fig.2. Typical structure of Ultrasones.



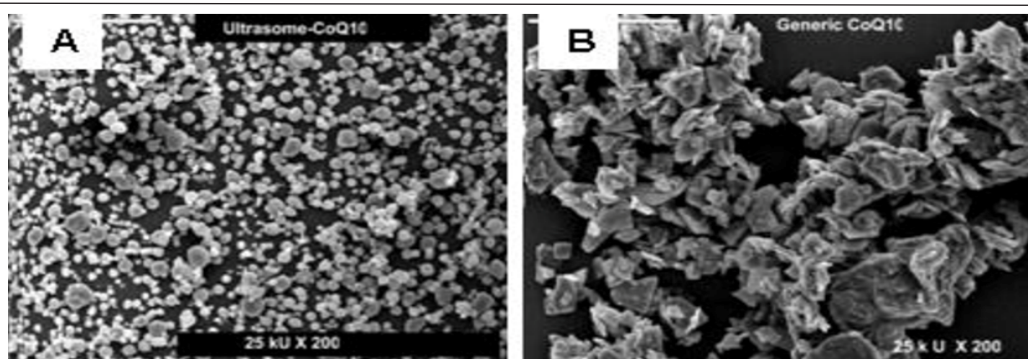


Fig 3. Particle size of Ultrasome™-CoQ10 (A) compared to generic CoQ10 (B)

CONCLUSION:

Using the Ultrasome™ patented drug delivery technology, CoQ10 was formulated. The outcomes of this indicates the efficacy of Ultrasome CoQ10™ with the majority in enhancing oral bioavailability of CoQ10 with generic CoQ10 compression and it is provided to geriatric patients with multiple chronic illnesses and weak absorption capacity of gastrointestinal has shown the increased reaction of plasma with supplementary therapy by this Ultrasomes™, which proved a positive value for quality to life with CoQ10.

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