Coenzyme Q10 And Its Function – A Review

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Abstract- *Coenzyme Q10, also known as ubiquinone, or coenzyme Q (CoQ10 or Q10), is a coenzyme that is ubiquitous in animals and most bacteria. It is present in all respiring eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, which generates energy in the form of ATP. It protects the membrane phospholipids and proteins from lipid peroxidation by scavenging free radicals directly and/or regenerating tocopherol levels. CoQ10 regulates mitochondrial permeability transition pores and the activation of the mitochondrial uncoupling proteins and inhibits lipid peroxidation in mitochondria, protein oxidation, and DNA oxidation. It also has potential redox activity in both the Golgi apparatus and lysosomes, and regulates the NADH oxido-reductase activity in the plasma membrane.Coenzyme Q10 is also proven to have many functions that include antioxidant, anti-hypertensive, anti-aging, nephroprotective, cardioprotective, anti-cancer effect and many more. Therefore, the aim of this review is to expose the different roles of coenzyme Q10 in a short manner.*

Keywords- Coenzyme Q10; antioxidant; anti-cancer effect; anti-hypertensive; cardioprotective effect

I. INTRODUCTION

Coenzyme Q is 2,3-dimethoxy,5-methyl, 6-polyisoprene parabenzoquinone. The coenzyme Q10 found in humans has a polyisoprene chain containing 10 isoprene units (5 carbons each) or a total of 50 carbons [1]. The all trans polyisosoprene ensures an affinity for the interior of cell membranes. The two methoxy groups contribute to the specificity in enzyme action as may the methyl group. The fully substituted quinone ring does not allow addition reactions with thiol groups in the cell such as glutathione, thioredoxin or thioctic acid. The functional group is the quinone ring [2].

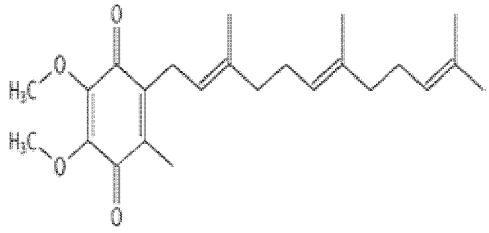

Figure 1: Structure of Coenzyme Q

CoQ is a central component in the mitochondrial electron transport chain (ETC) located in the inner mitochondrial membrane where it transports electrons from complexes I and II to complex III to provide energy for proton translocation to the intermembrane space. CoQ is also a structural component in complexes I and III and is essential in the stabilization of complex III in yeast Coenzyme Q is distributed in all membranes throughout the cell [3].

II. IMPORTANCE OF COENZYME Q10

2.1 Anti-oxidant role of coenzyme Q10

Coenzyme Q10 serves as a powerful antioxidant. This has been proven by many studies. One such study was the effect of an oral dose of 90 mg/day coenzyme Q10 on the antioxidative status in 22 healthy young subjects (9 men and 13 women) subjected to oxidative stress by fish oil supplementation. The levels of oxidised and reduced coenzyme Q10, alpha-tocopherol, ascorbate, TBARS and the fatty acid composition of phospholipids were determined in plasma. The total amount of plasma coenzyme Q10 increased significantly from 0.7 +/- 0.1 mumol/l before supplementation to 1.7 +/- 0.3 mumol/l after one week of supplementation while the redox status (reduced CoQ10/total CoQ10) remained constant, even during a following fish oil supplementation. The level of TBARS decreased during the first 2 weeks of CoQ10 ingestion while the content of alpha-tocopherol increased in the second week and ascorbate did not change. The decrease of TBARS and the presence of the majority of the orally supplemented CoQ10 in the reduced form in plasma seem to indicate an antioxidative role of CoQ10 in blood plasma [4].

2.2 Anti-hypertensive role of coenzyme Q10 through scavenging of free radicals

Patients with hypertension frequently have a significant deficiency of the antioxidant CoQ10. Furthermore, reactive oxygen species are overproduced in the nucleus tractus solitarii (NTS) during the cardiovascular regulation of hypertension in vivo. However, the molecular mechanisms by which CoQ10 modulates cardiovascular functions in the NTS are unclear. In this study, the effects of CoQ10 on superoxide generation, downstream NO signaling in the NTS, and blood pressure were evaluated in rats with fructose-induced

hypertension. Treatment with oral CoQ10 for 4 weeks abolished nicotinamide adenine dinucleotide phosphate-oxidase (NADPH oxidase) activation, decreased p38 phosphorylation, and increased superoxide dismutase 2 production in the NTS of fructose-fed rats. The serum levels of uric acid decrease in response to CoQ10 treatment in fructose-fed rats. Oral CoQ10 reduced blood pressure by inducing Akt and nNOS phosphorylation in NTS of fructose-induced hypertensive rats. Oral CoQ10 decreases blood pressure by negatively regulating fructose-induced NADPH oxidase levels, abolishing ROS generation, reducing p38 phosphorylation, and enhancing the Akt-nNOS pathway in the NTS. These results support the beneficial effects of CoQ10 in oxidative stress associated hypertension [5].

2.3 Effect of coenzyme Q10 supplementation for type 2 diabetes mellitus patients

In a study, they have investigated the effects of CoQ10 intervention on cardiovascular disease (CVD) risk factors in overweight/obese patients with type 2 diabetes mellitus (T2DM). Fourteen eligible trials with 693 overweight/obese diabetic subjects were included for pooling. CoQ10 interventions significantly reduced fasting blood glucose (FBG; -0.59 mmol/L; 95% CI, -1.05 to -0.12; P=0.01), hemoglobin A1c (HbA1c; -0.28%; 95% CI-0.53 to -0.03; P=0.03), and triglyceride (TG) levels (0.17 mmol/L; 95% CI, -0.32 to -0.03; P=0.02). Subgroup analysis also showed that low-dose consumption of CoQ10 (<200 mg/d) effectively reduces the values of FBG, HbA1c, fasting blood insulin, homeostatic model assessment of insulin resistance, and TG. CoQ10 treatment was well tolerated, and no drug-related adverse reactions were reported. These findings provide substantial evidence that daily CoQ10 supplementation has beneficial effects on glucose control and lipid management in overweight and obese patients with T2DM [6].

2.4 Anti-cancer activity of coenzyme Q10 against experimentally induced liver cancer

The therapeutic potential of coenzyme Q10 was investigated in rats with hepatocellular carcinoma induced by trichloroacetic acid (0.5g/kg/day, p.o., for five days). Coenzyme Q10 treatment (0.4mg/kg/day, i.p.) was applied for four weeks following trichloroacetic acid administration. Coenzyme Q10 significantly suppressed lipid peroxidation, prevented the depletion of reduced glutathione and superoxide dismutase activity, and decreased the elevations of tumor necrosis factor-α and nitric oxide in liver tissue of rats with hepatocellular carcinoma. Also, the histopathological dysplastic changes induced by trichloroacetic acid in liver tissue were ameliorated by coenzyme Q10. Immunohistochemical analysis revealed that coenzyme Q10 significantly decreased the expression of hepPar-1, alpha-fetoprotein, inducible nitric oxide synthase, cyclooxygenase-2 and nuclear factor-κB in liver tissue of rats with hepatocellular carcinoma. From this study, it can be concluded that coenzyme Q10 may represent a potential therapeutic option for liver carcinogenesis [7].

2.5 Coenzyme Q10 prevents cadmium induced reproductive toxicity

Adult male Wistar rats were exposed to an acute dose of Cd (25 mg/kg bwt; Cd group), Cd+CoQ10 (25 mg/kg bwt Cd+10 mg CoQ10; Cd-Q10 group) and distilled water (control) in vivo for 15 consecutive days and semen quality was assessed. A significant reduction was noted in sperm concentration, progressive motility, morphology and DNA integrity in both Cd- and Cd-Q10 groups in comparison to control indicating Cd-induced testicular lipid per oxidation (LPO) and decline in indigenous antioxidant defense system as measured by total antioxidant capacity (TAC) ($p<0.05$). However, simultaneous co-administration of CoQ10 along with Cd (Cd-Q10 group) was able to improve sperm concentration, motility, progressive motility, morphology, DNA integrity, and testicular TAC as well as lower LPO compared to Cd group ($p<0.05$). This study indicated that used dose of CoQ10 is capable of moderately ameliorating reproductive toxicity of Cd by improving semen quality and reducing testicular oxidative stress [8].

2.6 Coenzyme Q10 prevents nephrotoxicity induced by doxorubicin and cyclosporine

Nephrotoxicity is one of the limiting factors for using doxorubicin (Dox) as an anticancer chemotherapeutic, as well as cyclosporine as an immunosuppressant drug. Results showed that the dose of CoQ10 succeeded in reversing Dox as well as cyclosporine induced nephrotoxicity to control levels. Histopathological and immunohistochemical analysis of renal tissues confirmed the nephroprotective effect of coenzyme Q10. This could be due to the antioxidant effect of coenzyme Q10 in protecting against the free radicals (oxidative stress) generated during doxorubicin and cyclosporine induced toxicities [9-10].

2.7 Coenzyme Q10 protects against selenite induced experimental cataract

The molecular interaction between liposomes and Coenzyme Q10 was examined using differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FTIR).

Rat pups were randomly divided into six groups comprising 15 pups. Group (1), control group. Group (2), untreated model of cataract, received a single subcutaneous injection of sodium selenite. Instillation of pure CoQ10 (Group 3), CoQ10 encapsulated into neutral (Group 4), positive (Group 5) and negative (Group 6) Dipalmitoyl phosphatidylcholine (DPPC) liposomes on the opacification of lenses in rat pups after sodium selenite injection was topically received. The incorporated CoQ10 is probably associated with lipid bilayers where it interacts to a large extent and perturbs them. This results in strong broadening and shift to lower temperature (94°C) of the major characteristic endothermic peak of pure DPPC at 105°C. FTIR showed that the incorporation of CoQ10 into DPPC induces a conformational change in the polar region of DPPC. Ophthalmological and Biochemical studies revealed that CoQ10 alone followed by negatively charged liposomes doped with CoQ10 are more effective in reducing the progress of cataract as well as improving the lens soluble proteins levels and total antioxidant capacity. The interactions of CoQ10 with membrane systems may contribute to a better understanding of CoQ10 physiological properties and the development of therapeutically [11].

III. CONCLUSION

Thus it is concluded that coenzyme Q10 is just not a coenzyme that helps in mitochondrial electron transport chain, it also have diverse cellular functions. This review will further pave way to study the molecular mechanisms of coenzyme Q10 in a detailed approach.

REFERENCES

[1] Crane FL: New functions for coenzyme Q. Protoplasma, 213:127–133, 2000.
[2] Lenaz G, Faro R, DeBernardo S, Jarreta D, Costa, A, Genova ML, Parenti Castelii G: Location and mobility of coenzyme Q in lipid bilayers and membranes. Biofactors 9:87–94, 1999.
[3] Cramer WA, Soriano GM: Energy transduction function of the quinone reactions in cytochrome bc complexes. Biofactors 9:81–86, 1999.
[4] Weber C, Sejersgård Jakobsen T, Mortensen SA, Paulsen G, Hølmer G. Antioxidative effect of dietary coenzyme Q10 in human blood plasma. Int J Vitam Nutr Res. 1994;64(4):311-5.
[5] Chen HH, Yeh TC, Cheng PW, Ho WY, Ho CY, Lai CC, Sun GC, Tseng CJ. Antihypertensive Potential of Coenzyme Q10 via Free Radical Scavenging and Enhanced Akt-nNOS Signaling in the Nucleus Tractus Solitarii in Rats. Mol Nutr Food Res. 2019;63(6):e1801042.
[6] Huang H, Chi H, Liao D, Zou Y. Effects of coenzyme Q10 on cardiovascular and metabolic biomarkers in overweight and obese patients with type 2 diabetes mellitus: a pooled analysis. Diabetes Metab Syndr Obes. 2018;11:875-886.
[7] Fouad AA, Al-Mulhim AS, Jresat I. Therapeutic effect of coenzyme Q10 against experimentally-induced hepatocellular carcinoma in rats. Environ Toxicol Pharmacol. 2013;35(1):100-108.
[8] Saha R, Roychoudhury S, Kar K, Varghese AC, Nandi P, Sharma GD, Formicki G, Slama P, Kolesarova A. Coenzyme Q10 ameliorates cadmium induced reproductive toxicity in male rats. Physiol Res. 2019;6;68(1):141-145.
[9] El-Sheikh AA, Morsy MA, Mahmoud MM, Rifaai RA, Abdelrahman AM. Effect of coenzyme-q10 on Doxorubicin-induced nephrotoxicity in rats. Adv Pharmacol Sci. 2012;2012:981461.
[10] Sato T, Ishikawa A, Homma Y. Effect of reduced form of coenzyme Q10 on cyclosporine nephrotoxicity. Exp Clin Transplant. 2013;11(1):17-20.
[11] Shafaa MW, Elshazly AH, Dakrory AZ, Elsyed MR. Interaction of Coenzyme Q10 with Liposomes and its Impact on Suppression of Selenite – Induced Experimental Cataract. Adv Pharm Bull, 2018, 8(1), 1-9.