Ancient Science of life Vol: XXII (2) October / 2002 Pages 49 - 55

COENZYME Q 10: A REVIEW

Deependra singh , Vandana Jain, Swarnlata Saraf, S. Saraf,
B.R. Nagata College of Pharmacy, Mandsur, 458001 M.P.

Received: 12.10. 2002 Accepted: 20. 10. 2002

ABSTRACT: *Ubiquinone or Co Q_{10} is essentially a vitamin like substance and is a cofactor of an enzyme. It is an integral part of the memberanes of mitocondria where it is involved in the energy production. It is a nutrient necessary for the function of every cell of the body especially vital organs of the body like heart, liver, brain etc. Studies have shown that coenzyme Q_{10} alters the natural history of cardiovascular illness and has the potential of prevention of cardiovascular diseases through the inhibition of LDL cholesterol oxidation by maintenance of optimal cellular and mitochondrial function throughout the ravages of time internal and external stress.*

INTRODUCTION

Ubiquinone is found in most body tissues, the highest amount is found in the heart, liver Kidney pancreas and lungs. It is an integral part of the membrance of the mitochondria. Ubiquinone is vitamin like substance (simlar to vitamin A and E) and is coenzyme for at least three mitochondrial enzyme (complex I,II,III) involved in oxidative phosphorylation for the other part of the cell. Its electron and proton transfer function is of importance in electron transport side chain.[1-7]

Co Q is the nutrient necessary for the function of every cell of our body, without Co Q the food we eat cannot be converted to energy or it can be said that Co Q is especially related with energy production in cell with high metabolic demand. Apart from this main function, it also serves as an efficient antioxidant. [8-11].

Upiquinone is only lipid soluble coenzyme of mitochondria and can migrate freely in the lipid mass of the mitochondria and can easily accept electron and protons from various dehydrogenase system with the reversible formation of dehydroubiquinone thus is get reduced and can oxidized other biomolecules. The reduced and can dehydroubiquinone can undergo oxidation and reconverted to oxidized form i.e. ubiquinone by cytochrome b and like substances in the body and further propagates the electron transport chain. [12]

The energy released during various stages of this redox system is conserved in the presence of ADP and inorganic Phosphate resulting in the formation of ATP, whish can be utilized for several metabolic needs thus making it essential for ht survival of living beings.

CHEMISTRY:

Chemically ubiquinone has a quinoid structure, one at 2^{nd} and one at 3^{rd} position, a methy1 group at 5^{th} position and a isoprenoid side chain at 6^{th} position of quinoid ring. The number of isoprenoid nuit in the side chain varies from 6-10 for Co

Q_{10}, the number is 10. The physiologically active form has all Trans configuration. [13,14.]

CLINICAL INDICATION :

The usefulness of ConQ_{10} in heart diseases is slowly but steadily been established in the past 30 years, after the discovery of Co Q_{10} by frederick crane et al. in 1957,others investigators and its first use in heart failure [15-17]

Co Q_{10} is know to be highly concentrated in heart muscle cells, as cardiac cells have high metabolic demands in term of energy and Co Q $_{10}$ is associated with energy production. Co Q_{10} has received particular attention in the prevention and treatment of various cardiovascular diseases like congestive heart failure, hypertension, arthymia's ischemia, reperfusion injury and to hasten post cardiac surgery recovery.

HYPERTENSION:

Hypertension has always been associated with cardiac complications or development of other cardiac problems, studies have provided evidences that Co Q_{10} supplementation reduces blood levels of epinephrine (Adr) and other catecholamines. This is stated to be responsible of reduction of blood pressure and it protects the vascular endothelium from free radical induced damages. The property of reducing number of platelets and its size is also helpful in the management of hypertension. [18-20.]

CONGESTIVE HEART FAILURE:

The efficacy and safety of Co Q $_{10}$ in the treatment of CHF, whether related to primary cardiomyopathies or secondary forms of heart fail appears to be well established. [21, 22.]

Co Q $_{10}$ treatment in CHF revealed a significant important cardiac parameters such as ejection fraction, stroke volume, cardiac output cardiac index and end diastolic volume index [23.]

DIASTOLIC DYSFUNCTIONNING:

Use of Co Q $_{10}$ improves diastolic function in all categories of cardiac disease and this improvement occurs earlier and is more consistent than improvement is systolic function. Diastolic dysfunction often precedes more advanced stages of congestive heart failure and is commonly seen in a wide variety of clinical syndromes, including symptomatic hypertensive heart diease with left ventricular hypertrophy , symptomatic mitral prolapse, hypertropic cardiomyopathy, aging heart etc. and often seen in fatigue status such as chronic fatigue syndromes. 24 Co Q $_{10}$ has shown improvement in diastolic function, a decrease in myocardial thickness and also improvement in functional classification, Load induced diastolic dysfunction is also normalized by CoQ_{10} supplementation, is also causes lessening in hypertrophy and improvement. In functional status of patients with hypertropic cardiomyopathy with overall improvement in diastolic function. 25 Co Q_{10} supplementation no only causes improvement in NYHA classification and left ventricular hypertrophy but a significant improvement in diastolic function of hypertensive heart patients and also of that associated with aging heart [26,27.]

ISCHEMIC HEART DISEASES:

Study have shown that Co Q $_{10}$ supplementation in chronic stable anginal patients improves myocardial function measurements, improves exercise capacity, significant reduction in the number of anginal episodes and nitrate consumption. Since the Co Q_{10} treatment causes no

significant alteration in heart rate or blood pressure thus indication that the mechanism of action is directly related to myocardial metabolism 28 30 Co Q $_{10}$ related to frequency of angina attack. Study has proved that Co Q $_{10}$ reduces frequency of angina attack up to 46% while improving the capacity of physical activity for those patients[31.]

OXIDATION (LDL CHOLESTEROL)

: it is generally believed that the oxidation of LDL cholesterol is of primary importance in the development of artersclerosis. Supplementation of Co Q $_{10}$ prevents the oxidant effect of alpha tocopherols [32]. Supplementation with vitamin E alone results in LDL, which was more prone to oxidation. Supplementation of Co Q_{10} and vitamin E which increases the resistance to oxidation, Supplementation of Co Q_{10} increases the amount of Co Q $_{10}$ and lowered the peroxidiazibility of the LDL. [33-34].

PRE AND POST OPERATIVE RECOVERY:

Preoperative Co Q_{10} administration in patients undergoing heart valve replacement has significantly reduced the incidence of low cardiac output state during post operative recovery period[35]. Administration of Co Q 10 prior to coronary artery bypass graft, cardiopulmonary by pass surgery, has shown a significant improvement of left ventricular stroke work index postoperatively [36]. In patients undergoing coronary artery by pass surgery with valve replacement , a pre-operative Co Q $_{10}$ administration has shown significant improvement in post operative cardiac index an left ventricular ejection fraction with a significant reduction in post –operative recovery time and also significant decrease in postoperative markers of oxidative damage. A low in cadence of ventricular arrhythmia is also seen during recover period [32, 38].

The same improvement was observed with CoQ_{10} supplementation in left atrial pressure and low cardiac output state during postoperative period and a right and left ventricular myocardial ultrastructure was better prevented.

A significant decrease in markers of peroxidative damage was observed in Co Q_{10} treated patients[40].

CoQ_{10} protects the myocardium form ischemic reperfusion injury by its ability to increase aerobic energy production, protects creatine kinase form oxidative inactivation as well as its activity as an antioxidant [41-43].

Improved cardiovascular morbidity and mortality have been observed in several clinical studies of dietary supplementation with Co Q_{10} One attraction theory links Co Q_{10} with the inhibition of Platelets, Significant inhibition of vitronectin receptor is a direct evidence of link between dietary Co Q $_{10}$ intake, platelets and homeostasis[44]

CANCER AND OTHER DISEASES:

Apart from the benefits in various cardiovascular diseases Co Q $_{10}$ also shown light of hope in the treatment of cancer, neurogenerative diseases and problems associated with weight gain.
Preliminary evidences suggests that Co Q_{10} may suppress the proliferation of cancer cells and boost factor that kill cancer cells. Even a suppress the proliferation of cancer cells and boost factor that kill cancer cells. Even a spontaneous regression of breast cancer has been observed in some patients.

CoQ_{10} deficiency was noted in both carcinomas and non-malignant lesions [45 46.]

Studies have shown that the administration of Co Q $_{10}$ resulted in significant increase in cerebral cortex mitochondrial concentration of Co Q $_{10}$ Oral administration of Co Q $_{10}$ markedly attributed striatal lesions produced by systemic administration of 3 nitro propionic acid and significantly increased life span. These results shows that oral administration of Co Q_{10} increases both brain and brain mitochondrial concentrations Co Q_{10} can exert neuro protective action. Co Q_{10} can attenuate the MPTP induced loss of striatal dopamine and dopaminergic axon in aged mice and suggests that Co Q_{10} may be useful in the treatment of Parkinson's disease. Studies indicate that oral administration of Co Q $_{10}$ significantly reduces increased concentration of lactate in the occipital cortex of Huntington's disease patients. These findings suggest that Co Q_{10} may be useful in treating neuro degenerative disease[47]. various studies have shown that obese peoples are always deficient in Co Q_{10} levels (50%) and like people can lose weight simple with the addition of Co Q $_{10}$ This enzyme increases metabolic fuel efficiency within the cell thereby stimulate the natural weight loss[48.]

CONCLSION:

Thus it can be concluded that coenzyme Q_{10} through a simple molecule but it's a essential requirement for the survival of human beings, Being involved in almost all energy related metabolic processes, Co Q_{10} supplementation has proved a beneficial effect in several metabolic disorders, most common among them are related with cardiovascular system. Apart from the beneficial effect in congestive heart failure, it has proved to be equally effective in ischemic heart diseases, hypertension and diastolic dysfunctioning, it has been also found to improve the postoperative recovery in several cardiac surgeries.

Besides these, studies are showing evidences for its effect in carcinomas, Parkinsonism and problems associated with weight gain. Hence further attention should be provided on this essential coenzyme Q_{10}, as the best preventive measure from several severe diseases.

REFERENCE

1. Gian paolo Littarru's Energy And Deference, Casa Editrice Scientifica Internazionaale, 1994, 1-91.

2. Y.Yamammura, jpn. Cire J331 197, 168.

3. Y.Yamammura, T.Ishiyama, Y.Morita and Yannagami, Sogo Rinsho 16,1967,1564-1572.

4. Y.Yamammura, T.Ishiyama, Y.Morita and Yannagami, Sogo Rinsho Vol. 17,1968,1057-1065.

5. G. Lenaz, J. Membr. Biol. 104,1988,193-209.

6. G. Lenaz ., R.Fato, C. Casteluccio, M.Battino, M.Cavazzoni, H.Rauchova and G. .P.Castelli, Vol6, E.lsevier Amsterdam, 1991,11-18.

7. P. Mitchell, J. Theor, Biol. 62,1976, 327-367

8. R.F. Beyer, L. Ernster, G. Lena, O, Barnabei, A. Rabbi and Battino, Eds, Tatlor and Francis, London, 1990, 191-213.

9. L. Ernster, P. Formark-Andree, S.A. Mortensen G.P. Littarru, T. Yamagami and G. Lenaz. Eds, The Clinical Insvestigator, 71(8), 1993, S60-S65.

10. T. Ozawa, G. Lennaz., John Wiley and Sons, 1985, Chapter XXI, 441-456.

11. J.M. Villaba, F.Navaro, C. Gornez-Diaz, A.Arroyo, R.I. Bello and P. Navas, Molecular Aspects of Medicine, Vol, 18, 1997, 7-13.

12. F.L.Crane, I.L.Sun, R. Barr, D.J. Morre, Y.Yamamura, Eds Vol. 4, Elsevier, Amsterdam, 1984, 77-86.

13. Lehninger AlbertL., Nilson David L., Principels of Biochemistry, CBS Publishers and Distributers, 1993, 546=553.

14. Pant M.C., Essentials of Biochemistry, Kedar Nath Ram Nath and Co. Publishers, 158.

15. F.L. Crane, Y. Hatefi, R.I. Lester and C. Widmer, Biochim. Biophs. Acts 25, 1957, 2201.

16. Ra Morton, G.M. Wilson, J.S. Lowe and W.M.F. Leat, Chemical Industry, 1957, 1649.

17. Y.Yamammura, Jpn. Circ. J,31 1967,168.

18. M.Nagano, N. Saito, S. Mochizuki, S.A. Nazawa, S. Tomiuka M.Kawamura and H. Aoki.J. Adult Dis 6, 281-286.

19. Littaru G.P., Liippa S., Molecular Aspects of Medicine, 18 Suppl : 1997, 195-203.

20. T. Yamagami, M. Takagi, H.Akagami, H.Kubo, S.Toyama, T. Okamoto, T.Kishi and K. Folkers, Vol.5, Elsevier, Amsterdam, 1986,337-343.

21. P.H.Langsjoen, S.Vadhana vikit and K. Folkers, Proceedings of The National Academy of Sciences USA, 82,1985, 4250-4244.

22. H.A.Langsjoen, P.h Langsjon, P.H.Langsjoen R. Willis and K. Folkers, Moleculer aspects of Medicine, 15, 1994, 265-272.

23. Oradei A., British Journal od Pharmacology, 124(7), Aug 1998, 1500.

24. P.H.Langsjoen S.A. Mortenses, G.P. Littarru, T. Yamagami and G. Lenaz, Clinical Investigator, 71,1993,140-144.

25. P.H.Langsjoen A. Langsjoen , R. Willis and K.Folkers, Molecular Aspects of Medicine, 18,1997,145-151.

26. P.H.Langsjoen A. Langsjoen , R. Willis and K.Folkers, Molecular Aspects of Medicine, 15 (suppl), 1994,145-151.

27. P.H.Langsjoen A. Langsjoen , R. Willis and K.Folkers, Molecular Aspects of Medicine, Theraputics, Health Quest Publications, 1997,113-120.

28. T. Kamikawa, A.Kodbyashi, T.Yamashita, H.Hayashi and N. Yamazaki, American journal of Cardiology, Vol.56,1985,247-251.

29. M.F. Wilson, W.H. Frishman, T.Giles G., Sethi S.Greenberg and J.Brackett, Vol.6, Elsevier, Amsterdam, !991,339

30. G. Serra, F.Lissoni, C.P. Peimonti and C. Mazzolo, Vol. 6, Elsevier, Amsterdam, 1991,327-338.

31. Yamamura Y. Cardiovasular Drugs and Therapy, 1991, 235-241.

32. S.R. Thomas, J. Neuzil and R. Stocker, Arterioscler. Thromb. Vasc. Biol 16(5), 1996, 687-696.

33. R., Aejmelaeus, T Metsa-Ketela, P. Laipala, H. Alho and T.Solakvi, Molecular Aspects of Medicine, 18 (Suppl), 1997,113-120

34. S.R. Thomas, J. Neuzil and R. Stocker, Molecular Aspects of Medicine, 18 (Suppl), 1997, 85-103.

35. J. Tannaka, R. Tominaga, M.Jenkins, J. Hooper, L. Hadjinikolas, M. Kemp, D. Hue and G. Bennett, Annals of Thoracic surgery, 33(2) 1982, 145-151.

36. M. Sunomori, H. Tanaka, T.Maruyama, I.Sultan, T.Sakamoto and A., Suzuki, Cardiovasc. Drugs Ther., 2(Suppl.) 1991,297-300.

37. W.V. Judy, W.W. Stogsdill and K. Folkers, Clinical Investigator, 71 (8), 1993, 155-161.

38. M. Chello, P. Mastroroberto, R.Romano, E.Bevacqua, D. Pantaleo, R.Ascione, A.R. Marchese and N.Spampinato, Ann. Thorac. Surg. 58 (5). 1994, 1427-1432.

39. Y.F. Chen, Y.T.Lin and S.c. Wu, J.Thorac. Cardiovasc.Surg. 107(1), 1994, 242-247.

40. M. Chello, P.Mastroroberto, R. Romano, P. Castaldo, E.Becacqua and A.R. Marchese, J. Cardiovasc. Surg. 37(3), 229-245.

41. A. Constantinescu, J.J. Maguire and L.Packer, Molecular Aspects of Medicine, 15 (suppl), 1994,56-65.

42. F.L Crane, I.L Sun, R.Barr and D.J Morre, Biomedical and Aspects of Coenzyme Q, Vol 4, Elsevier, Amsterdam, 1984, 77-86.

43. K. Folkers, G.P. Littarru, L.Ho, T.M. Runge, S.Havanonda, D.Coley, Int. S. Vitaminforsch, 40(3), 1970, 380-390.

44. Ursini, F., Biomedical an clinical "Aspects of Coenzyme Q, Vol. 6 Eds. Amsterdam, Elsevier, 19981, 235-241.

45. Kulklinshki B., International Journal of Clinical Pharmacology and therapeutics 36(9), 1998, 506-509.

46. Proceedings of The National Academy of Sciences of the United States of Amercia, 95 (15), Jul 21. 1998, 8892-8892-8897.

47. Manto A., Brath Research, Feb 1998,109-114.

48. Ursini F., Greenberg and Frishman, Journal of clinical pharmacology, Vol 5, 1990, 57-60.