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Co-Enzyme Q10 to Treat Neurological Disorders: Basic Mechanisms, Clinical Outcomes, and Future Research Direction

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Abstract: Coenzyme Q10 (CoQ10) is critical for the cell power supply in mitochondria. CoQ10 shuttles electrons from complexes I and II to complex III, and can be anti-oxdiative. Neurons require high energy for synaptic transmission and therefore the mitochondria dysfunction often leads to severe neuronal degeneration, as observed in many neurological disorders. CoQ10 supplementation has been widely used to treat aging, stroke, neuromuscular diseases, Alzheimer's disease, Parkinson's disease, progressive supranuclear palsy, autosomal recessive cerebellar ataxias, Huntington's disease and amyotrophic lateral sclerosis. Here we discuss a large number of preclinical and clinical trials for CoQ10 to elucidate the mechanisms underlying CoQ10 therapy. The rational applications as a therapeutic agent in neurological disorders are discussed.

Keywords: Coenzyme Q10, mitochondrial respiratory chain, neurological disorders, rational therapeutic approaches, ATP.

INTRODUCTION

Coenzyme Q (CoQ; 2,3-dimethoxy-5-methyl-6-multiprenyl1,4-benzoquinone) was discovered by Dr. Crane in 1957 [1]. However, as he said, "the discovery of CoQ was not a simple accident as sometimes mentioned". In fact, it's based on all previous investigations into the biological energy conversion [2]. We can trace the origin of this discovery back to the work of Warburg and Keilin in biological oxidation and Chance (1954) [3]. Moreover, the important investigations created by David E. Green to recognize the compound and its role in mitochondria [4] were fostered by the studies of Karl Folkers to investigate its medical and nutritional significance [5].

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CoQ is a lipid-soluble biomolecule which is composed of a benzo-quinone ring that is prenylated with an isoprenoid chain at various lengths (Fig. **1**). The isoprenoid chain is made up of isopentenyl diphosphate (IPP) units [6]. The methyl groups on the benzene ring are derived from S-adenosyl methionine. CoQ molecules are located in the hydrophobic domain of the phospholipid bilayer of cellular membranes [7]. The various kinds of CoQ are named according to the numbers of isoprenoid side chains they have [8]. CoQ10 the mostly common in human (named previously Q275 with an absorption peak at 275 nm) [2]. Our energetic biomolecule exists in three redox states, fully oxidized (ubiquinone), semiquinone radical (ubisemiquinone), and fully reduced (ubiquinol): however, different levels of protonation alters the possible redox forms of the quinone ring [9]. As a hydrophobic molecule, CoQ can be found in three different states : micellar aggregates, dissolved in lipid bilayers, and bound to proteins. Binding to protein is crucial in cell-free systems [10], however in the living cell CoQ is distributed in the other two forms. The synthetic pathway for

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