



## Coenzyme Q<sub>10</sub>; Importance, Effective Sources and Improving its Bioavailability

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### ABSTRACT

Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>), a lipid-soluble endogenous pro-vitamin found naturally in the mitochondria, is present in many organisms. It has crucial roles in many biochemical pathways and important health functions. It has an essential role as a vital intermediate of the electron transport system in mitochondria. CoQ<sub>10</sub>, as an electron and proton carrier for energy coupling leads to adenosine triphosphate (ATP) formation. CoQ<sub>10</sub> also acts as a potent antioxidant and scavenger of reactive oxygen species and is involved in multiple aspects of cellular metabolism. Furthermore, in medicine, the pharmacological use of CoQ<sub>10</sub> has received increasing attention following the reports of its benefits in treating cardiovascular and degenerative neurologic diseases. CoQ<sub>10</sub> is a hydrophobic compound with a molecular weight of ۸۶۳ Da. The long isoprenoid side chain is responsible for its water insolubility. Because of its hydrophobicity, its bioavailability is low and application of CoQ<sub>10</sub> in aqueous foods and drugs is limited. Various approaches such as emulsion and nanoemulsion formulations have been developed to improve its water solubility. CoQ<sub>10</sub> is found in plants such as soya bean, peanut, palm oil and litchi pericarp and in animals such as pelagic fish, beef and pork hearts. Various analytical methods have been published for the extraction and analysis of CoQ<sub>10</sub> from different matrices. The most common methods for extracting CoQ<sub>10</sub> from different samples are liquid-liquid or ultrasound extraction. CoQ<sub>10</sub> also can be produced by chemical synthesis and microbial fermentation. Microbial production offers an environmentally benign option based on the enzymatic catalysis at



the cellular level for CoQ<sub>10</sub> assembly. Moreover, this approach is attractive to the industry because the process is easy to control at a relatively low production cost. This review provides an overview of CoQ<sub>10</sub> importance, health benefits and its effective sources. Improving of CoQ<sub>10</sub> bioavailability are also discussed and future growth prospects and recommendations are also given for areas of future research.

**KEYWORDS:** CoQ<sub>10</sub>, adenosine triphosphate (ATP), mitochondrial enzymes, bioavailability, microbial fermentation

## INTRODUCTION

Coenzyme Q<sub>10</sub> (۲,۳ dimethoxy, ۵-methyl, ۶-decaprenyl benzoquinone, CoQ<sub>10</sub>), a lipid-soluble endogenous pro-vitamin found naturally in the mitochondria, is present in many organisms (Xue, ۲۰۱۲). Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>), also known as ubiquinone or ubiquinone-۱۰, and its active form is ubiquinol, occurs widely in animals, plants, and the cells of microorganisms (Yuan et al., ۲۰۱۲). It plays a crucial role in the transfer of electrons between respiratory complexes of the electron transport chain, located within the inner mitochondrial membrane (Cluis et al. ۲۰۱۲). Coenzymes are cofactors upon which the comparatively large and complex enzymes absolutely depend for their function. CoQ<sub>10</sub> is the coenzyme for at least three mitochondrial enzymes (complexes I, II and III) as well as enzymes in other parts of the cell. Mitochondrial enzymes of the oxidative phosphorylation pathway are essential for the production of the high-energy phosphate, adenosine triphosphate (ATP), upon which all cellular functions depend. Mitochondria, specialized compartments present in every cell of the body (except red blood cells), produce ۹۰% of the energy needed to support growth and sustain life [Marin, ۲۰۱۵]. Recently CoQ<sub>10</sub> has received great attention for its application as therapeutic agent as well as in related fields such as a potential antioxidant (Tokdar et al., ۲۰۱۴). Despite of many advantages of CoQ<sub>10</sub>, because of its hydrophobicity, application of CoQ<sub>10</sub> in aqueous foods and drugs is limited and its bioavailability is low. Various approaches such as emulsion and nanoemulsion formulations have been developed to improve its water solubility.[]

CoQ<sub>10</sub> is naturally produced in the body, but its levels decrease as we age and may be low in people with cancer, genetic disorders, diabetes, heart problems, and Parkinson's disease. Symptoms of CoQ<sub>10</sub> deficiency include heart failure, high blood pressure, and chest pain. CoQ<sub>10</sub>, can be produced by chemical synthesis, extraction from biological tissues (plants and animal). CoQ<sub>10</sub> is naturally present in small amounts in a wide variety of foods, but is particularly high in organ meats such as heart, liver and kidney, as well as beef, soy oil, sardines, mackerel, and peanuts (Langsjoen, ۱۹۹۴). CoQ<sub>10</sub> can also be produced by microbial fermentation including bacteria, molds, yeasts, etc. Microbial biosynthesis offers several advantages over chemical synthesis and extraction including specificity towards the all-trans biologically active isomer of CoQ<sub>10</sub>, and the reduced production of environmentally hazardous waste based on the enzymatic catalysis at the cellular level for CoQ<sub>10</sub> assembly, (Cluis, ۲۰۱۲).

The present study aimed to discuss about importance, benefits of CoQ<sub>10</sub> and also its effective sources. Moreover, improving of CoQ<sub>10</sub> bioavailability was mentioned and future growth prospects and recommendations were given for areas of future research.

In the body CoQ<sub>10</sub> exists in either an oxidized (ubiquinone) or reduced form (ubiquinol and hydroquinone). Mainly in its reduced form, CoQ<sub>10</sub> is also known as a very effective antioxidant (Pravst et al., ۲۰۱۰). The chemical structure of CoQ<sub>10</sub>, elucidated by Dr. Karl Folkers and his group. Fig. ۱ shows chemical structures of ubiquinone and ubiquinol and properties of them are summarized in table ۱.

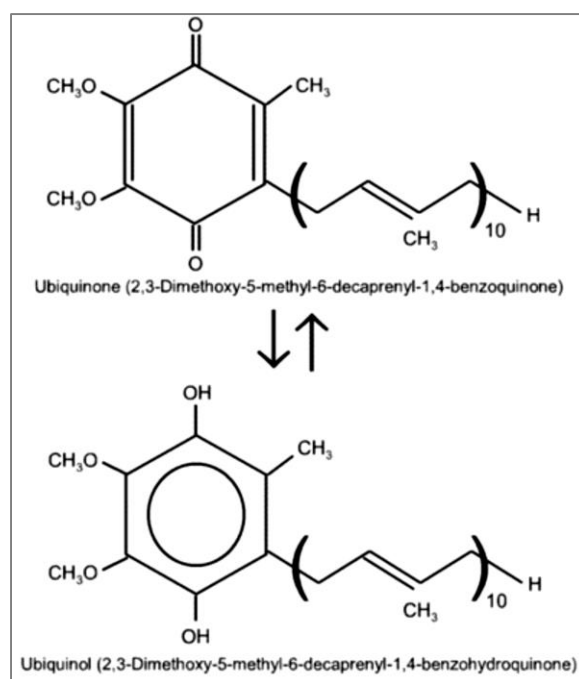


Fig. ۱. Structures of CoQ<sub>10</sub>; Ubiquinone (۲,۳-dimethoxy-۵-methyl-۶-decaprenyl-۱,۴-benzoquinone) and ubiquinol (۲,۳-dimethoxy-۵-methyl-۶-decaprenyl-۱,۴-benzohydroquinone)

Table ۱. Properties of Ubiquinone (CoQ<sub>10</sub>) and Ubiquinol (CoQ<sub>10</sub> H<sub>2</sub>)

|                   | Ubiquinone (CoQ <sub>10</sub> )                | Ubiquinol (CoQ <sub>10</sub> H <sub>2</sub> )  |
|-------------------|--|--|
| Appearance        | Orange crystals (at room temperature)          | White to very pale yellow crystalline powder   |
| Empirical formula | C <sub>59</sub> H <sub>90</sub> O <sub>۴</sub> | C <sub>59</sub> H <sub>92</sub> O <sub>۴</sub> |
| Molecular weight  | ۸۶۳,۳۵۸  | ۸۶۵,۳۷   |
| Melting point     | ۴۹۰ °C   | ۴۹۵ °C   |
| Solubility        | Insoluble in water                             | Practically insoluble in water.                |
|                   | Limited solubility in oils and fats            | Limited solubility in oils and fats.           |
|                   | Soluble in nonpolar solvents                   | Soluble in nonpolar solvents.                  |

#### IMPORTANCE OF COQ<sub>10</sub>

For several years, the study of CoQ<sub>10</sub> in foodstuffs and animal tissue has attracted special attention owing to its crucial roles in many biochemical pathways and important health functions (Rodriguez, ۲۰۰۶). CoQ<sub>10</sub> is the coenzyme for at least three mitochondrial enzymes (complexes I, II and III). CoQ<sub>10</sub> as shown in Fig. ۲ is a core component of cellular energy production and respiration, shuttling electrons down the electron transport chain to produce the key energy-rich molecule ATP. Due to its involvement in ATP synthesis, CoQ<sub>10</sub> affects the function of every cell in the body, making it important for the health of all tissues and

organs. CoQ<sub>10</sub> has been shown to have quite powerful antioxidant potential. Therefore, it can effectively defend against reactive oxygen species and free radical damage, protects the body from damage caused by harmful molecules (Ruiz, ۲۰۰۷) through protecting membranes and proteins from oxidation by scavenging free radicals and by regenerating pools of tocopherols (Cluis, ۲۰۱۲). There is evidence that CoQ<sub>10</sub> is involved in the transcriptional regulation of genes, some of which play roles in inflammatory responses and in cholesterol metabolism (Schmelzer et al, ۲۰۰۷).

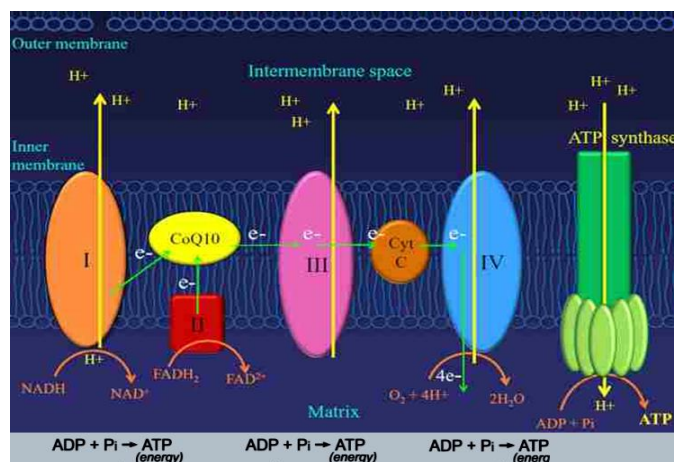


Fig. ۲. Central role of CoQ<sub>10</sub> in electron transport chain

### Health benefits and clinical conditions of CoQ<sub>10</sub>

CoQ<sub>10</sub> is naturally produced in the body, but its levels decrease as we age and may be low in people with cancer, genetic disorders, diabetes, heart problems, and Parkinson's disease. Symptoms of CoQ<sub>10</sub> deficiency include heart failure, high blood pressure, and chest pain. On the other hand, the concentration of CoQ<sub>10</sub> in the body decreases year by year, indicating that it has a close relationship with aging (Fig. ۲.). For these reasons, some people rely on CoQ<sub>10</sub> supplements. The daily intake of CoQ<sub>10</sub> is suggested as ۱۲ mg kg<sup>-1</sup> (Rujiralai, ۲۰۱۴).

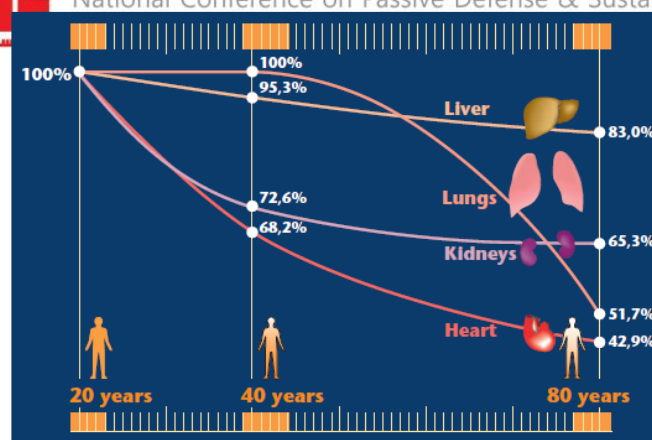


Fig. ۳. CoQ10 decline with age (Littarru and Lambrechts, ۲۰۱۱)

Nowadays, in medicine, the pharmacological use of CoQ10 has received increasing attention following the reports of its benefits in treating cardiovascular and degenerative neurologic diseases (Weant and Smith, ۲۰۰۵). Recently, some natural health products and commercial nutraceutical supplements containing CoQ10 have gained increasing popularity in health management [Buettner et al., ۲۰۰۷].

There is a large body of data on the beneficial effects of CoQ10 supplementation in various disease states. CoQ10 supplements have been demonstrated to have positive effects on patients suffering from certain cardio-vascular conditions (such as conjunctive heart failure, congestive heart failure, angina pectoris, arrhythmias, mitral valve prolapse, hypertension, atherosclerosis and cardiotoxicity) and neurodegenerative diseases (such as Huntington, parkinson, alzheimer) (Hodgson et al., ۲۰۰۲; Yang et al., ۲۰۱۰).

It has been proved that CoQ10 helps treat muscular dystrophy, amyotrophic lateral sclerosis, neuromuscular, mitochondrial cytopathies, ataxias, diabetes, cancer, chronic obstructive pulmonary disease, asthma, migraine, immune disorders, HIV/AIDS, chronic fatigue syndrome, male infertility and periodontal disease. It is also said to boost energy and speed recovery from exercise. Some people take it to help reduce the effects certain medicines can have on the heart, muscles, and other organs. Furthermore, early research has suggested that CoQ10 supplementation may benefit patients suffering from male infertility, neurodegenerative disease and diabetes-associated nephropathy (Yang et al., ۲۰۱۰; Mancini and Balercia ۲۰۱۱)

#### IMPROVING BIOAVAILABILITY OF CoQ10



CoQ<sub>10</sub> is a hydrophobic compound with a molecular weight of ۸۶۳ Da. The long isoprenoid side chain which is responsible for its water insolubility (<۴ ng/mL) generates yellow color. Because of its hydrophobicity, application of CoQ<sub>10</sub> in aqueous foods and drugs is limited and its bioavailability after intake is low (Kim et al., ۲۰۱۲). In addition to insolubility in water, the solubility of CoQ<sub>10</sub> in lipids is also limited and CoQ<sub>10</sub> is thus very poorly absorbed (Pravst et al., ۲۰۱۰). The literature is flooded with the various reports regarding the modification of physiochemical properties to improve its oral bioavailability. There have been various approaches to improve water solubility of CoQ<sub>10</sub>. Among those, emulsion formulations of CoQ<sub>10</sub> using additives have been largely studied. Latest technical developments reveal that encapsulation of CoQ<sub>10</sub> in nanoemulsions results in a significantly enhanced bioavailability ((Kim et al., ۲۰۱۲). In addition, multiple nanoemulsions prepared according to a patented process even allow the administration of several incompatible substances at the same time. In the formation of nanoemulsions and nanoparticles mechanical processing, such as ultrasound, high pressure, homogenisation and microfluidization are common techniques (Cheuk et al., ۲۰۱۵). Schematic models of various novel forms of CoQ<sub>10</sub> is presented in fig.۳.

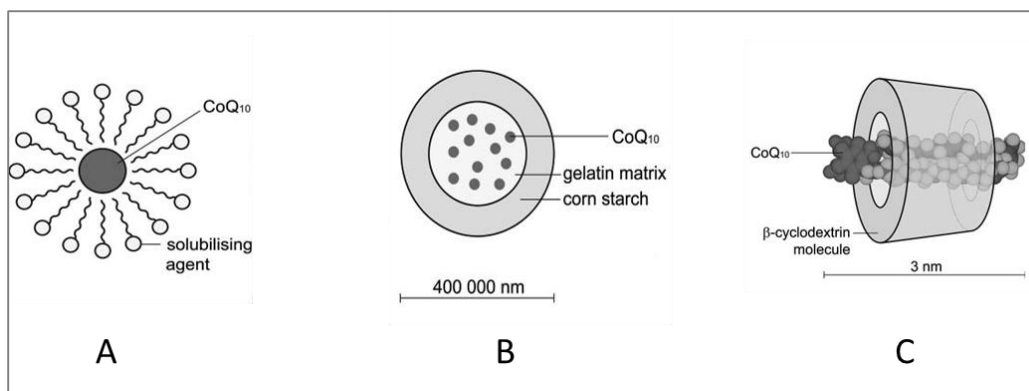


Fig.۴. Schematic models of various novel forms of CoQ<sub>10</sub>: (A) nanomicelles, (B) CoQ<sub>10</sub> beadlets finely dispersed in a water-soluble fish gelatine matrix and coated with starch-based granules (C) CDQ<sub>10</sub> - inclusion complex of CoQ<sub>10</sub> in  $\beta$ -cyclodextrin (Pravst et al., ۲۰۱۰)

The increased water-solubility of otherwise insoluble compounds not only allows the fortification of aqueous based products but also contributes to their improved absorption, which is a common pharmaceutical strategy (Pravst et al., ۲۰۱۰)

### CoQ<sub>10</sub> EFFECTIVE SOURCES

CoQ<sub>10</sub> can be produced by chemical synthesis, extraction from biological tissues (plants and animal) and microbial fermentation (Laplante et al., ۲۰۰۹). CoQ<sub>10</sub> compounds are widely distributed in nature, from microorganisms to plants and animals.



Animal products such as beef, pork and chicken are relatively good sources of CoQ10. As a general rule, tissues with high energy demands contain relatively high amounts of CoQ10. It is particularly high in organ meats such as heart, liver and kidney, CoQ10 is naturally present in small amounts in a wide variety of foods, but it is high in soy oil, palm oil, sardines, mackerel, and peanuts (Langsjoen, ۱۹۹۴). Among foods of plant origin, broccoli and spinach contain significant amounts of CoQ10.

Table ۱- Overview of CoQ10 contents in various foods (Pravst et al., ۲۰۱۰)

| Food           | CoQ10<br>concentration [mg/kg] | Food              | CoQ10<br>concentration [mg/kg] |
|----------------|--------------------------------|-------------------|--------------------------------|
| <b>Beef</b>    |                                | <b>Nuts</b>       |                                |
| heart          | ۱۱۳                            | peanuts           | ۲۷                             |
| liver          | ۳۹-۵۰                          | walnuts           | ۱۹                             |
| muscle         | ۲۶-۴۰                          | sesame seeds      | ۱۸-۲۳                          |
| <b>Pork</b>    |                                | pistachio nuts    | ۲۰                             |
| heart          | ۱۱,۸-۱۲۸,۲                     | hazelnuts         | ۱۷                             |
| liver          | ۲۲,۷-۵۴,۰                      | almond            | ۵-۱۴                           |
| muscle         | ۱۳,۸-۴۵,۰                      | <b>Vegetables</b> |                                |
| <b>Chicken</b> |                                | parsley           | ۸-۲۶                           |
| heart          | ۱۱۶,۲-۱۳۲,۲                    | broccoli          | ۶-۹                            |
| <b>Fish</b>    |                                | cauliflower       | ۲-۷                            |
| sardine        | ۵-۶۴                           | spinach           | up to ۱۰                       |



|             |        |                 |     |
|-------------|--------|-----------------|-----|
| mackerel    |        | grape           | ۶-۷ |
| red flesh   | ۴۳-۶۷  | Chinese cabbage | ۲-۵ |
| white flesh | ۱۱-۱۶  | <b>Fruit</b>    |     |
| salmon      | ۴-۸    | avocado         | ۱۰  |
| tuna        | ۵      | blackcurrant    | ۳   |
| <b>Oils</b> |        | strawberry      | ۱   |
| soybean     | ۵۴-۲۸۰ | orange          | ۱-۲ |
| olive       | ۴-۱۶۰  | grapefruit      | ۱   |
| grapeseed   | ۶۴-۷۳  | apple           | ۱   |
| sunflower   | ۴-۱۵   |                 |     |

#### MICROBIAL SOURCES OF COQ10

CoQ10 can be produced by microbial fermentation including bacteria (e.g. *Agrobacterium*, *Paracoccus*, *Cryptococcus*, *Rhodobacter*, *Tricosporon*), molds (e.g. *Neurospora*, *Aspergillus*), yeasts (e.g. *Candida*, *Sporidobolus*, *Rhodotorula*), etc. Moreover, presence of CoQ10 in *Artemia* samples as a Crustacean was investigated (Rujiralai, ۲۰۱۴). Microbial production offers an environmentally benign option based on the enzymatic catalysis at the cellular level for CoQ10 assembly. Moreover, this approach is attractive to the industry because the process is easy to control at a relatively low production cost (Tokdar et al., ۲۰۱۴). However, due to the limits of CoQ10 accumulation in cells, strain improvements have been made using genetic engineering (using recombinant nucleic acid technology), chemical mutagenesis, and high hydrostatic pressure treatment (Kim et al., ۲۰۱۵).

#### CONCLUSION AND FUTURE TRENDS





CoQ10, a lipid-soluble endogenous pro-vitamin found naturally in the mitochondria, is present in many organisms. It has crucial roles in many biochemical pathways and important health functions. Levels of CoQ10 decrease as we age and may be low in people with cancer, genetic disorders, diabetes, heart problems, and Parkinson's disease. For these reasons, some people rely on CoQ10 supplements. CoQ10 is a hydrophobic compound with a long isoprenoid side chain which is responsible for its water insolubility, application of CoQ10 in aqueous foods and drugs is limited and its bioavailability is low. So developing various approaches to improve its water solubility could also be evaluated in the future. Also, it is important to establish a suitable extraction and analysis method for determining the content of CoQ10 in different sources including foods and microorganisms. Moreover, types of reactors that provides high cell concentrations, high productivity, and easy separation of the products for development of CoQ10 production in a better microorganism, could be determined from further research.

## REFERENCES

- Buettner, C., R.S. Phillips, R.B. Davis, P. Gardiner and M.A. Mittleman. ۲۰۰۷. Use of dietary supplements among United States adults with coronary artery disease and atherosclerotic risks. The American journal of cardiology, ۹۹(۵): ۶۶۱-۶۶۶. DOI:10.1016/j.amjcard.۲۰۰۶.۰۹.۱۱۶.
- Cheuk, S.Y., F.F. Shih, E.T. Champagne, K.W. Daigle, J.A. Patindol, C.P. Mattison, and S.M Boue., ۲۰۱۵. Nano-encapsulation of coenzyme Q 10 using octenyl succinic anhydride modified starch. Food chemistry, ۱۷۴: ۵۸۵-۵۹۰. DOI:10.1016/j.foodchem.۲۰۱۴.۱۱.۰۳۱
- Cluis, C.P., A.M. Burja, and V.J. Martin. ۲۰۰۷. Current prospects for the production of coenzyme Q10 in microbes. Trends in biotechnology, ۲۵(۱۱): ۵۱۴-۵۲۱. DOI:10.1016/j.tibtech.۲۰۰۷.۰۸.۰۰۸.
- Cluis, C.P., D. Pinel and V.J. Martin. ۲۰۱۲. The production of coenzyme Q10 in microorganisms. In Reprogramming Microbial Metabolic Pathways (pp. ۳۰۳-۳۲۶). Springer Netherlands. ISBN: ۹۷۸-۹۴-۰۰۷-۵۰۵۵-۵.
- Hodgson, J.M., G.F. Watts, D.A. Playford, V. Burke and K.D. Croft. ۲۰۰۲. Original Communication-Coenzyme Q10 improves blood pressure and glycaemic control: a controlled trial in subjects with type ۲ diabetes. European Journal of Clinical Nutrition, ۵۶: ۱۱۳۷-۱۱۴۲. DOI:10.1038/sj.ejcn.۱۶۰۱۴۶۴.
- <http://wikybrew.com/wp-content/uploads/۲۰۱۴/۱۱/co-q10-in-the-body.png>
- Langsjoen P.H. (۱۹۹۴) Introduction to coenzyme Q10.pdf. <http://faculty.washington.edu/ely/coenzq10.html>.
- Laplanche, S., N. Souchet and P. Bry. (۲۰۰۹). Comparison of low-temperature processes for oil and coenzyme Q10 extraction from mackerel and herring. European Journal of Lipid Science and Technology, ۱۱۱(۲): ۱۳۵-۱۴۱. DOI: 10.1002/ejlt.۲۰۰۸.۰۱۳۳.



Littarru, G.P. and P. Lambrechts ۲۰۱۱. Coenzyme Q ۱۰: multiple benefits in one ingredient. Oléagineux, Corps gras,

DOI: ۱۰,۱۰۵۱/ocl.۲۰۱۱,۰۳۷۴ Lipides, ۱۸(۲), pp.۷۶-۸۲.

Kim, E.A., J.Y. Kim, H.J. Chung and S.T. Lim. ۲۰۱۲. Preparation of aqueous dispersions of coenzyme Q۱۰ nanoparticles with amylo maize starch and its dextrin. LWT-Food Science and Technology, ۴۷(۲): ۴۹۳-۴۹۹. DOI:

DOI:۱۰,۱۰۱۶/j.lwt.۲۰۱۲,۰۲,۰۱۳.

Kim, T.S., J.H. Yoo, S.Y. Kim, C.H. Pan, V.C. Kalia, Y.C. Kang and J.K., Lee. ۲۰۱۵. Screening and characterization of an *Agrobacterium tumefaciens* mutant strain producing high level of coenzyme Q۱۰. Process Biochemistry, ۵۰(۱):

۳۳-۳۹. DOI:۱۰,۱۰۱۶/j.procbio.۲۰۱۴,۱۰,۰۲۴.

Mancini, A. and G. Balercia. ۲۰۱۱. Coenzyme Q۱۰ in male infertility: physiopathology and therapy. Biofactors, ۳۷(۵):

۳۷۴-۳۸۰. DOI: ۱۰,۱۰۰۲/biof.۱۶۴.

Marin, S.E. and R.H. Haas. ۲۰۱۵. Coenzyme Q۱۰ and the treatment of mitochondrial disease. COENZYME Q۱۰, p.۸۵.

Pravst, I., K. Žmitek and J. Žmitek. ۲۰۱۰. Coenzyme Q۱۰ contents in foods and fortification strategies. Critical reviews in food science and nutrition, ۵۰(۴): ۲۶۹-۲۸۰. DOI:۱۰,۱۰۸۰/۱۰۴۰۸۳۹۰۹۰۲۷۷۳۰۳۷.

Rodriguez-Estrada, M.T., A. Poerio, M. Mandrioli, , G. Lercker, A. Trincherro, M.R. Tosi and V. Tugnoli. ۲۰۰۶. Determination of coenzyme Q۱۰ in functional and neoplastic human renal tissues. Analytical Biochemistry, ۳۵۷(۱):

۱۵۰-۱۵۲. DOI: ۱۰,۱۰۱۶/j.ab.۲۰۰۶,۰۶,۰۱۳.

Ruiz-Jiménez, J., F. Priego-Capote, J.M. Mata-Granados, J.M. Quesada and M.L. de Castro. ۲۰۰۷. Determination of the ubiquinol-۱۰ and ubiquinone-۱۰ (coenzyme Q۱۰) in human serum by liquid chromatography tandem mass spectrometry to evaluate the oxidative stress. Journal of Chromatography A, ۱۱۷۵(۲): ۲۴۲-۲۴۸.

DOI:۱۰,۱۰۱۶/j.chroma.۲۰۰۷,۱۰,۰۵۵.

Rujiralai, T., R. Nirundorn, C. Wilairat, N. heewasedtham and C. Chonlatee. ۲۰۱۴. Development of an effective

extraction process for coenzyme Q۱۰ from Artemia. Chemical Papers. ۶۸ (۸): ۱۰۴۱-۱۰۴۸. DOI:۱۰,۲۴۷۸/s۱۱۶۹۶-

۰۱۴-۰۵۵۸-۲.

Schmelzer C., I. Lindner, C. Vock, K. Fujii, F. Doring. ۲۰۰۷. Functional connections and pathways of coenzyme Q۱۰-inducible genes: an in-silico study. IUBMB life, ۵۹: ۶۲۸-۶۳۳. DOI: ۱۰,۱۰۸۰/۱۵۲۱۶۵۴۰۷۰۱۵۴۵۹۹۱.



Tokdar, P., P. Ranadive, R. Kshirsagar, S.S. Khora and S.K. Deshmukh. ۲۰۱۴. Influence of Substrate Feeding and Process Parameters on Production of Coenzyme Q10 Using *Paracoccus denitrificans* ATCC ۱۹۳۶۷ Mutant Strain P-۸۷. *Advances in Bioscience and Biotechnology*, ۵(۱۲): ۹۶۶-۹۷۷. DOI: ۱۰,۴۲۳۶/abb.۲۰۱۴.۵۱۲۱۱۰.

Weant, K.A. and K.M. Smith. ۲۰۰۵. The role of coenzyme Q10 in heart failure. *Annals of Pharmacotherapy*, ۳۹(۹): ۱۵۲۲-۱۵۲۶. DOI: ۱۰,۱۳۴۵/aph.۱E۵۵۴.