Microbial production of coenzyme Q10

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Abstract

Coenzyme Q10(CoQ10) is a biological quinine compound that is widely found in living organisms including yeast, plants, and animals. CoQ10 has two major physiological activities:(a)mitochondrial electron-transport activity and (b)antioxidant activity. Various clinical applications are also available: Parkinson's disease, Heart disease, diabetes. Because of its various application filed, the market size of CoO10 is continuously expanding all over the world. A Japanese company, Nisshin Pharma Inc. is the first industrial producer of CoQ10(1974). CoQ10 can be produced by fermentation and chemical synthesis. In several companies, these two methods are used for the production of CoQ10:chemical synthesis - Yungjin, Daewoong, Nishin Parma; fermentation - Kaneka, Kyowa, Yungjin, etc. Researchs in microbial production of CoQ10 have several steps: screening of producing microorganisms, strain development, fermentation process, purification process, scale-up process, plant production. Several strategies are available for the strain development: Random mutation and screening, directed metabolic engineering. For the optimization of fermentation process, various conditions (nutrient, aeration, temperature, culture type, etc.) are considered. Purification is one of the most important step because the quality of final products entirely depends on its purity. The production cost will be reduced and the quality of the CoQ10 will be impoved by continuous researches in strain development, fermentation process, purification process.

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Coenzyme Q10 ? (1)

■ General Fact

- Natural product (discovered by Frederic Crane in 1957)
- Vitamin-like compound which has major two physiological activities
 - a) Mitochondrial electron transport activity
 - b) Antioxidant activity
- Naturally existed in human body, but remakably decrease after fourty years old
- Nissin Pharma Inc. : First industrial producer (1974)
- Application fields: medicin, functional foods and cosmetics

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Coenzyme Q10 ? (2)

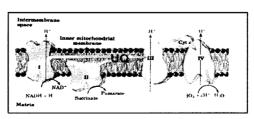
Chemical structure and characteristics

Quinone

H₃CO 3 4 5 CH₃ Isoprenold

H₃CO 2 6 [CH₂-CH = C-CH₂-h]

- \triangleright Designated as Q₆, Q₇, Q₈ ... by the number of
 - isoprenoid units in the side chain
- ▷ Lipid-soluble components of membrane-bound electron-transport chains



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Clinical application



Parkinson's disease and mitochondrial cytopathies: Preminary evidence for benefit

Congestive heart failure, hypertension, and ischemic heart disease: conflicting or preliminary evidence
Diabetes: conflicting evidence for improvement in glycemic control

Adverse effect Rare: gastrointestinal upset reported in less than 1 % of study patients



Mitochondrial cytopathies: 150 mg/day or 2 mg/kg with titration up to 3,000 mg/day in some patients

Parkinson's disease: 200 to 1,200 mg/day in four divided

Cardiovascular:typically 50 to 200 mg/day

Diabetes: 100 to 200 mg/day

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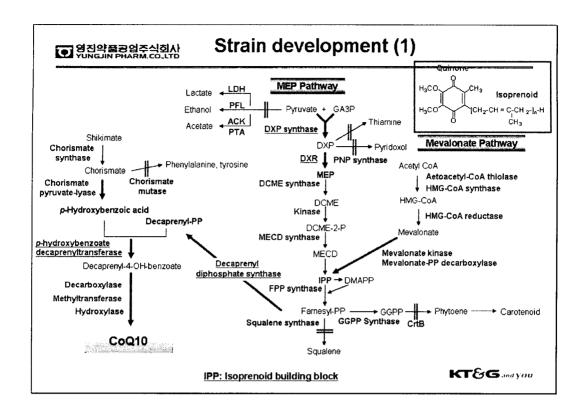
Microbial Production of CoQ10

■ Development flow-chart of Microbial production of CoQ10

Screening of Microorganism strains

Various Microoranisms producing CoQ10

- Mary Control of the	Strain	Researchers
Strain development	Rhodosporidium sphaerocarpum	Ajinomoto
	Trichosporon cutaneum	
Fermentation process	Trichosporon JY-155	Jujo Paper
	Cryptococcus laurentii	
	Rhodotorula glutinis	
purification process	Sporobolomyces salmonicolor	Ko Aida
	Oosporidium margaritiferum	
Scale-up process	Paracoccus denitrificans	
	Rhodobacter sphaeroides	Kyowa
Plant production	Agrobacterium tumefaciens	
	Pseudomonas sp.	



● 영진약플공업주식회사 YUNGJIN PHARM.CO_LTD *** Research Project**

- Project name: Examination of bioactivities of CoQ10 using C.elegans
- Purpose
 - Verification of antioxidative activity of CoQ10
 - Examination of effects on the lifespan of C. elegans
 - Understanding of bioactivities of CoQ10 on the molecular level

 Milestone 2006 2007 2008 Analyze the effect on -Determination of Life-span development process - Determination of antioxidant - Analyze the effect on germ cell activity KT&Gandyou