[10:30 - 11:10]

Microbial production of coenzyme Q10

Jung-Woo Suh

Fermentation R&D center, Yungjin Pharm. Co., Ltd.

239-3, Galgot-ri, Jinwi-myun, Pyeongtaek-si. Gyeonggi-do, Korea

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 CoQ10 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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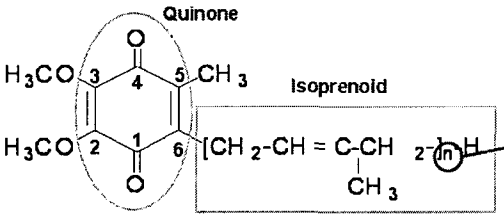
Coenzyme Q10 ? (2)

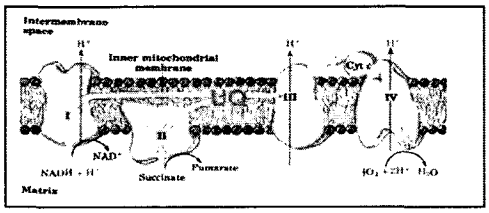
■ **Chemical structure and characteristics**



▷ Composed of two units : Quinone head, Isoprenoid side chain

▷ Designated as Q_6, Q_7, Q_8 ... 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

Efficacy	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
Dosage	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 doses 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

▽

Strain development

▽

Fermentation process

▽

purification process

▽

Scale-up process

▽

Plant production

Various Microoranisms producing CoQ10

Strain	Researchers
Rhodosporidium sphaerocarpum *Trichosporon cutaneum*	Ajinomoto
Trichosporon JY-155	Jujo Paper
Cryptococcus laurentii *Rhodotorula glutinis* *Sporobolomyces salmonicolor* *Oosporidium margaritiferum*	Ko Aida
Paracoccus denitrificans *Rhodobacter sphaeroides* *Agrobacterium tumefaciens* *Pseudomonas sp.*	Kyowa

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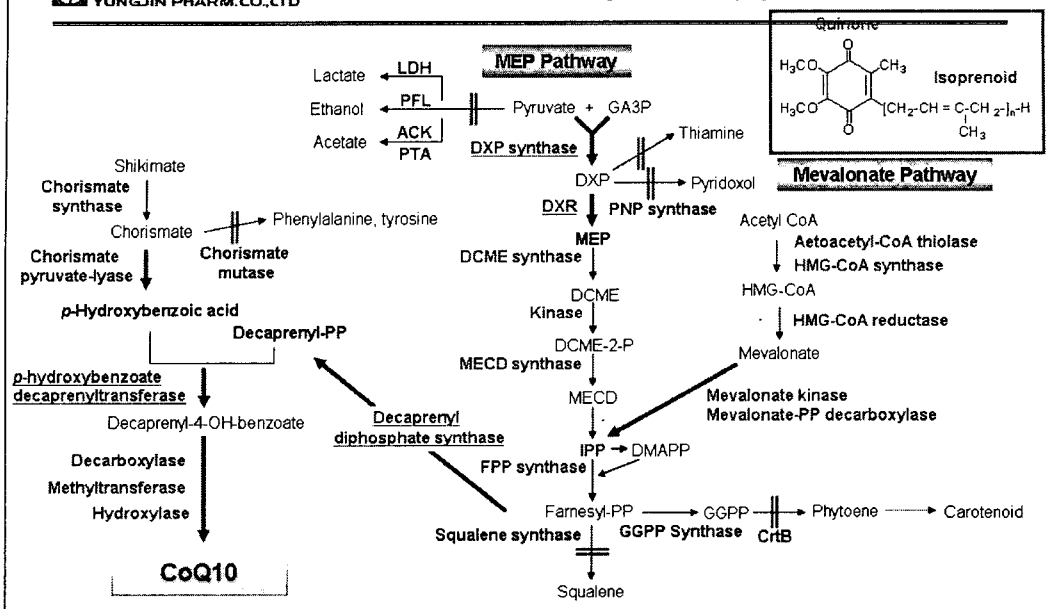
Strain development (1)



IPP: Isoprenoid building block

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※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 development process - Determination of antioxidant activity	-Determination of Life-span - Analyze the effect on germ cell	

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