[11:30 - 12:10]

Industrialization of CoenzymeQ10

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Since the first isolation of Coenzyme 10 by Dr. Frederick Crane in 1957, achievements in both academic and industrial fields were made to enhance the availability and usage of Coenzyme Q10. The first large volume production of Coenzyme Q10 was accomplished in the early 1970's by Japan's Nisshin Flour and Milling. Nisshin was able to synthetically prepare Coenzyme Q10 from a tobacco plant extract called Solanesol . Other Japanese companies followed Nisshin with fermentation methods to produce Coenzyme Q10 and since then Coenzyme Q10 production was exclusively from Japan. As research data showing the effectiveness against various illness and possible application to other fields were published, the popularity of Coenzyme Q10 increased. This popularity and regulatory changes in Japan triggered a major supply shortage of the raw material causing the price of the raw material double or triple in a matter of months. However new producers did not appear because industrialization of Coenzyme Q10 production was very difficult due to heavy financial investments for fermentation routes and difficult to synthesize or industrialize for synthetic routes.

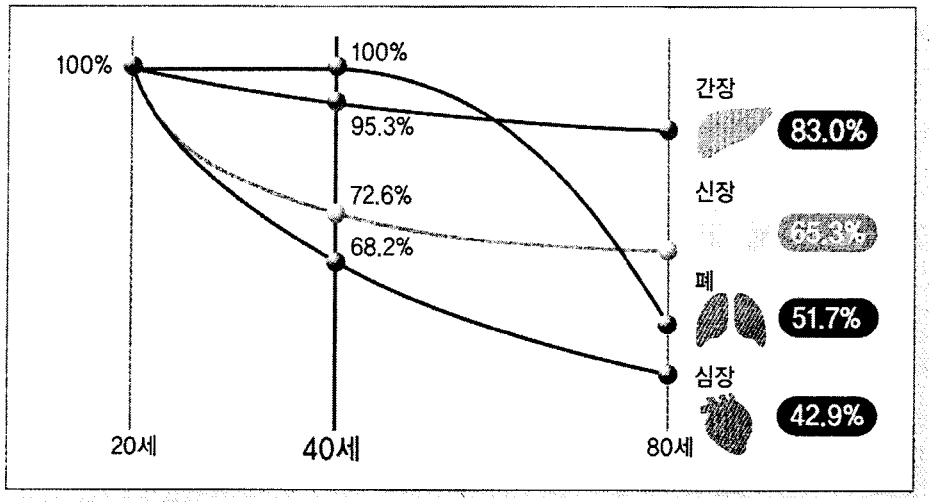

Figure 1. Research data showing the decrease of Coenzyme Q10 in human organs

Although Nisshin's synthetic method was obscurely known to the public it was difficult to replicate it. Alternative methods for synthesis of Coenzyme Q10 were researched by various pharmaceutical companies and prominent researchers but were eventually not applied for large scale production due to cost, impurities or its difficulties in application.

In the winter of 2003 Daewoong Chemical became the 2nd company in the world and the 1st in Korea to successfully industrialize Coenzyme Q10 using natural solanesol. Daewoong's process is made up of unique methods which enable the process to be cost effective, easy to industrialize and free of impurities. Cis isomer is a major impurity that can be found in synthetic methods of Coenzyme Q10 synthesis depending on their synthetic methods. Although there are no known toxicity or effect on human body fermentation companies uses this as means to promote their superiority in quality over synthetic products. However not all synthetic methods produce cis-isomer as impurities and Daewoong's process prevents the formation of cis-isomer during the process and has no cis-isomers existing. The only impurity detectable was CoQ9, a compound similar to CoQ10 except for one deficient isoprenoid unit. CoQ9 which are often found in lower animals such as rats and rabbits, functions as same as Coenzyme Q10 inside

the animals' body. CoQ9 is found both in synthetic and fermentation methods but are known to have no toxicity nor have any effect on the human body. Even this CoQ9 can be completely eliminated from Coenzyme Q10 with intense purification procedure.

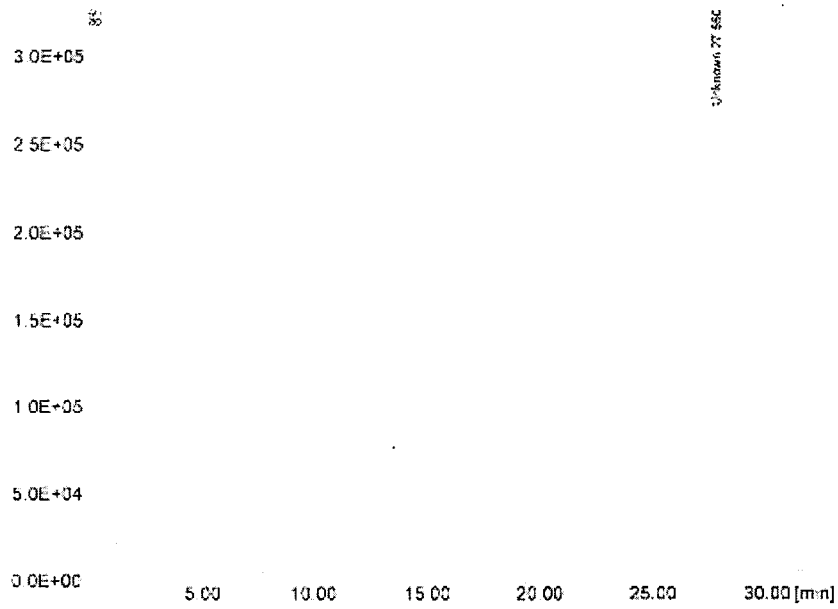

Figure 1. HPLC analysis chart of Daewoong Coenzyme Q10

Other impurities referred to in the European Pharmacopoeia such as 2,3-dimethoxy-5-methylbenzene-1,4-diol, ubqiquinone-7 (CoQ7), ubiquinone-8, ubicromenol were not found in Daewoong's Coenzyme Q10 at all.

The assay of Daewoong's synthetic Coenzyme Q10 is similar to those of Japan's products. Where most of the regulations (KP, EP, USP, JP) require assay not less than 98% Daewoong's Coenzyme Q10 assay was found to be in the range of 98.5% to 100.0% where higher assay could be obtained with additional purification. Unlike other companies purification Daewoong's process requires no silica gel and uses only traditional crystallization method. Cautions for residing solvents were eliminated when none or the least amount of solvents were residing in the product. No solvents except for the final crystallizing solvent were detected and even the final solvent was usually below detection level or not more than 30 ppm when rarely existing.

Because Nisshin developed and launched synthetic Coenzyme Q10 three decades ago the clinical data used for the registration or studies are difficult to be found or does not follow appropriate protocols. Animal studies were independently done by Daewoong with Daewoong's synthetic Coenzyme Q10. Single dose oral toxicity test on beagles and SD rats gave no abnormality and the lethal dosage was determined to be more than 5,000mg/kg. Other studies such as chromosome aberration test, micronucleus test, and reversion mutation test all tested to be negative. Repeated oral dose toxicity study in rats is under progress but has no observable abnormality and seems to have similar results with single dose toxicity test.

Daewoong's synthetic CoQ10 is as good as Japanese synthetic or fermented product and is not only good in quality but also safe. With this above standard quality Daewoong has made sales of more than $25 million to the US and Japan, where it is used as nutritional supplement, in the year of 2005. Also Daewoong Coenzyme Q10 was honored as the No. 1 API produced in Korea last year. We hope to develop the nutritional market of Coenzyme Q10 in Korea and enable our fellow citizens to take advantage of the miracle medicine in the future.