

**COENZYME Q10 ATTENUATES INCREASES IN
OXIDATIVE STRESS, INFLAMMATION, INSULIN
RESISTANCE, AND BLOOD PRESSURE IN
DEVELOPING METABOLIC SYNDROME MODEL RATS**

*M Kunitomo¹, Y Yamaguchi¹, S Kagota¹, K Otsubo²

¹School of Pharmacy and Pharmaceutical Sciences,
Mukogawa Women's University, Hyogo, Japan

²Fine Chemicals Division, Asahikasei Pharma Corporation, Japan

*Correspondence: masaru@mukogawa-u.ac.jp

Metabolic syndrome is associated with a cluster of disorders such as abdominal obesity, insulin-resistance, hyperglycemia, hypertension, hyperlipidemia, and also chronic subclinical inflammation. We have previously reported that oxidative stress and inflammation enhance with the development of such metabolic disorders in an animal model of metabolic syndrome, SHR/NDmcr-cp /cp (SHR-cp) rats. Coenzyme Q10 (CoQ10) plays an important part as an electron and proton transfer agent in mitochondrial ATP production and in maintaining the optimal pH of lysosomes. Its reduced form, ubiquinol, is an effective fat-soluble antioxidant. The present study investigated whether CoQ10 acts to scavenge oxidant species, and thereby reduces oxidative stress and inflammation, and prevents characteristic symptoms of metabolic syndrome in SHR-cp rats. Six-week-old male SHR-cp rats (Japan SLC, Hamamatsu) were maintained on a Quick Fat diet (CLEA Japan, Inc., Tokyo) supplemented with 0.07, 0.2 and 0.7% CoQ10 for 26 weeks. Oxidative stress was assessed by thiobarbituric acid reactive substances (TBARS), oxidatively modified low-density lipoprotein (LDL), 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 3-nitrotyrosine levels. Inflammation was assessed by 3-chlorotyrosine and high-sensitivity C-reactive protein (hsCRP) levels in the serum. Serum from rats supplemented with CoQ10 displayed a markedly high level of ubiquinol-10 (reduced form of CoQ10) at 8 weeks of age and this level persisted until the end of the experiment. Supplementation with CoQ10 significantly attenuated the increased serum levels of oxidative stress markers and inflammation markers in SHR-cp rats in a dose-dependent manner. CoQ10 prevented elevated insulin levels in serum, although it did not affect the elevated glucose, triglyceride and free fatty acid levels. CoQ10 also reduced the elevated blood pressure after 16 weeks of age, but did not affect body weight gain. In the aorta of SHR-cp rats, vascular endothelial function was impaired and the 3-nitrotyrosine concentration increased compared to that in the genetic control WKY rats. This suggests that superoxide anion (O₂⁻) produced in endothelial cells reacts with nitric oxide (NO) to form peroxynitrite (ONOO⁻), which nitrates tyrosine residues of the endothelial cell proteins. CoQ10 improved the impaired endothelium-

dependent relaxation in the mesenteric artery. This improvement of endothelial dysfunction by CoQ10 may be related to its hypotensive response. The present study demonstrated that CoQ10 supplementation ameliorates systemic oxidative stress, inflammatory state, hypertension and hyperinsulinemia in the metabolic syndrome model rats. This implies that CoQ10 may help prevent and treat the progression of metabolic syndrome.

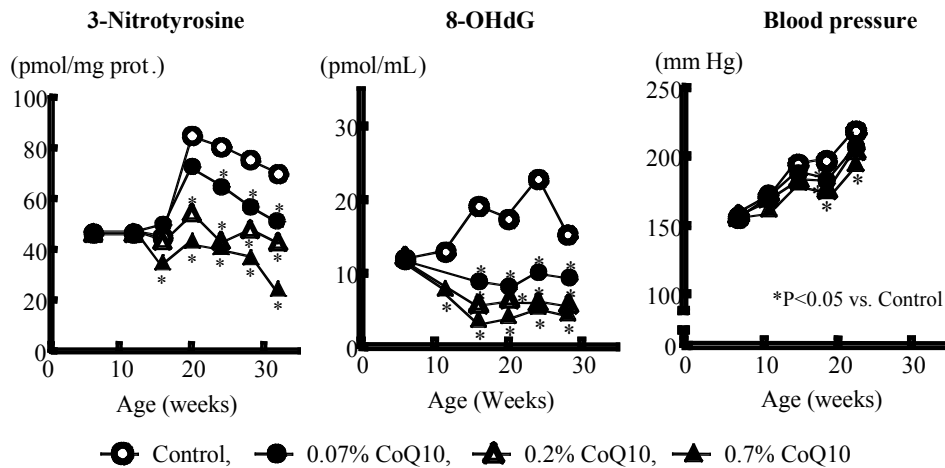


Fig. 1. Effects of CoQ10 supplementation on circulating oxidative stress markers and blood pressure in SHR-cp rats, a model of metabolic syndrome.