Coenzyme Q_{10} reduced blood glucose and intracellular inflammation in an animal model of type 2 diabetes mellitus

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Yong-Jae Lee

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ABSTRACT

Coenzyme Q_{10} reduced blood glucose and intracellular inflammation in an animal model of type 2 diabetes mellitus

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Objectives: We examined the effects of coenzyme Q_{10} supplementation on metabolic parameters including fasting plasma glucose, insulin sensitivity, and intracellular inflammation in *db/db* mice, a diabetic animal model.

Materials and Methods: Mice were divided into 3 groups: normal control mice with chow diet (n=6), *db/db* mice with high-fat diet (n=9), and *db/db* mice with high-fat diet and coenzyme Q_{10} administration (20 mg/kg/day) for 12 weeks (n=9). After 12 weeks, metabolic parameters including fasting blood glucose concentrations, hemoglobin A_{1C} ($HbA1_c$), insulin and lipid profiles were determined using high-performed liquid chromatography. The expression of mitochondrial biogenesis markers including PGC-1α and T-fam were measured in cardiac and skeletal muscle tissues. Similarly, inflammatory markers such as IL-6, COX-2,

and CRP were measured in liver tissues.

Results: After 12 weeks of treatment, the glucose index including fasting blood glucose levels, $HbA1_C$, and homeostatic model assessment of insulin resistance (HOMA-IR) were significantly decreased in coenzyme Q_{10}-treated *db/db* mice compared with untreated control *db/db* mice. Compared with normal controls, the expressions of proteins related to mitochondrial biogenesis such as PGC-1α and T-fam were higher in *db/db* control mice, whereas the expressions of these proteins were significantly decreased in *db/db* mice treated with coenzyme Q_{10}. Coenzyme Q_{10} treated *db/db* mice exhibited a significant decrease in the mRNA expression of IL-6, COX-2, and CRP compared with normal control and *db/db* control mice. We calculated inflammatory scores by summing the mRNA levels of IL-6, COX-2, and CRP, and found that while scores were significantly increased in untreated *db/db* control mice, they tended to decrease in coenzyme Q_{10}-treated *db/db* mice.

Conclusion: We observed significant decreases in fasting blood glucose levels and insulin resistance associated with significant reductions in inflammatory markers in coenzyme Q_{10} treated *db/db* mice.

Key words: coenzyme Q_{10}, diabetes mellitus, antioxidant, oxidative stress, inflammation, insulin resistance

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I. INTRODUCTION

Mitochondria generate high-energy intermediate adenosine triphosphate (ATP) using chemical energy liberated during the oxidation of organic nutrients by molecular oxygen, and are also the major sources and targets of reactive oxygen species (ROS).[1,2] Although the underlying mechanisms of type 2 diabetes mellitus (type 2 DM) remain unclear, emerging evidence supports the hypothesis that type 2 DM is associated with mitochondrial dysfunction including mitochondrial loss and over-production of oxidants.[3-7] Furthermore, chronic low-grade inflammation is also associated with insulin resistance and type 2 DM.[8,9]

Coenzyme Q_{10}, a vitamin-like benzoquinone, plays a crucial role in the transfer of electrons from mitochondrial respiratory complexes I and II to complex III and is necessary for the production of ATP.[10-12] In addition, coenzyme Q_{10} is a functional element of all cell membranes that serves a number of biological functions including potent antioxidative protection against

lipid peroxidation, regeneration of tocopherol and ascorbic acid, and stabilization of cell membranes.[13,14] Maintaining sufficient mitochondrial nutrients in mitochondria may be an effective approach for reducing oxidative stress and mitochondrial dysfunction. Since coenzyme Q_{10} plays a vital role in energy production as a redox carrier in mitochondrial membranes, as well as being a potent antioxidant for reducing cellular oxidative stress, coenzyme Q_{10} supplementation may have therapeutic value for mitochondrial dysfunction.

The aim of this study was to investigate the effects of coenzyme Q_{10} supplementation on metabolic parameters including fasting blood glucose concentrations, insulin sensitivity and lipid profiles. We also examined whether regulation of coenzyme Q_{10} is partly mediated through mitochondrial metabolism such as biogenesis and/or decrease of intracellular inflammation levels in an animal model of type 2 DM.

II. MATERIALS AND METHODS

1. Animals

The study protocol and all procedures were approved by the Institutional Animal Care and Use Committee at the Yonsei Institude for Life Sciences, Seoul, Korea. Four-week-old C57BL/KsJ *db/db* and C57BL/KsJ *db/+* male mice were purchased from Joongang Lab (Seoul, Korea). All animals were acclimatized to the laboratory environment for 2 weeks prior to the initiation of experiments. Mice were allowed free access to drinking water and a high-fat diet under constant room temperature (22 ± 2℃) and humidity (50 ± 10%) with an automatic 12-hour light and 12-hour dark cycle. Mice were fed a high-fat diet comprised of 72% lipids, 28% protein, and <1% carbohydrates. Food intake and body weight were recorded every day and glucose concentrations were recorded weekly for 12 weeks.

2. Coenzyme Q_{10} powder preparation and administration

Coenzyme Q_{10} powder was provided by TEI Korea Co., Ltd. (Seoul, Korea). Coenzyme Q_{10} was dissolved in 1% Tween-80.[15] The coenzyme Q_{10} solution was injected intraperitoneally (IP) once daily at a dose of 20 mg/kg body weight (approximately 0.2 ml in volume). Control animals received

equimolar injections of saline solution. No detectable irritation was observed following daily administration of the extract or vehicle. No noticeable adverse effects were observed in any animal after treatment with the extract or vehicle.

3. Experimental design

The mice used in this study were allowed to acclimatize to the laboratory environment for 2 weeks before experiments were initiated. Acclimatized mice were divided into 3 groups as follows: 1) normal control mice with chow diet (n=6), 2) *db/db* mice with high-fat diet (n=9), 3) *db/db* mice with high-fat diet and coenzyme Q_{10} (n=9)

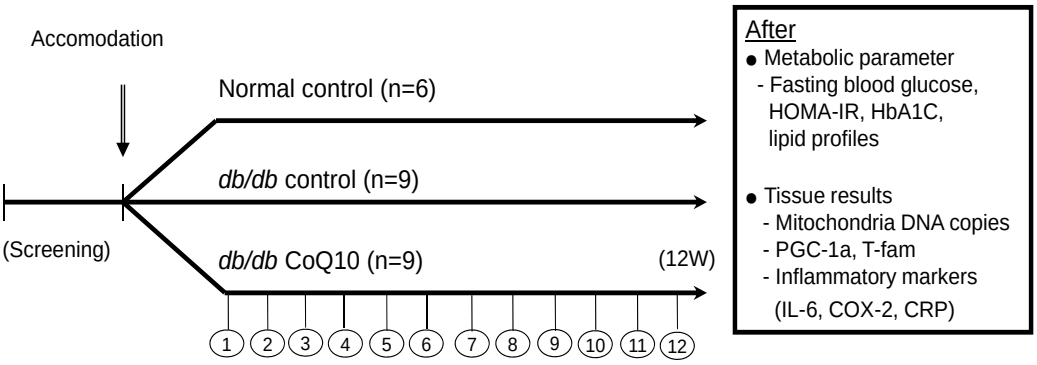

Figure 1. The framework of the current study

4. Measurement of body weight and blood glucose levels

Fasting blood glucose levels were measured by collecting blood samples drawn from tail veins on Day 0 (before treatment) and each week thereafter (Days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, and 84). All samples were obtained after animals were fasted for 4 hours starting at 7:00 AM. Blood glucose levels were determined in blood samples taken from the tail vein at 11:00 AM using a Glucose Analyzer (Hemocue AB, Angelholm, Sweden). Body weight was also measured at 11:00 AM.

5. Tissue sample preparation and biochemical analysis

At the end of the experimental period, the mice were sacrificed under light ether anesthesia and blood samples were obtained by exsanguination of the heart. Levels of fasting plasma glucose, hemoglobin $A1_C$ ($HbA1_c$), insulin, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol were determined using high-performed liquid chromatography (HPLC) with a Kamsi instrument (Kyeonggo, Korea). Insulin resistance was estimated using the homeostasis model assessment estimate of insulin resistance (HOMA-IR). Liver, cardiac, and skeletal muscles were taken and each sample was quickly frozen in liquid nitrogen and kept at -80°C until analyzed.

6. Quantitative real time PCR analysis

Total RNA was isolated from cardiac muscles with TRIzol (Invitrogen, USA) according to the manufacturer's instructions. From each sample, total RNA (3 μg) was reverse transcribed into cDNA using a reverse transcription system kit (Thermo, USA). Briefly, quantitative RT-PCR reactions were performed as described in the manufacturer's instructions and analyzed with Power SYBR green Master Mix (Applied Biosystems) using an ABI 7500 Real-Time PCR system (Applied Biosystems) with the following cycling parameters: stage 1, 50°C for 2 minutes; stage 2, 95°C for 10 minutes; stage 3, 40 cycles for 95°C for 15 seconds; 60°C for 1 minutes; and stage 4, 95°C for 15 seconds; 60°C for 15 secconds; 95°C for 15 secconds. Primers (Table 1) were designed using Primer Express software (Applied Biosystems, USA). Mouse target genes consisted of peroxisomal proliferator-activated receptor-γ coactivator-1α (PGC-1α) and mitochondrial transcription factor A (T-fam) for mitochondrial biogenesis markers,and interleukine-6 (IL-6), cyclooxygenase-2 (COX-2), and C-reactive protein (CRP) as inflammatory markers (Table 1). The linearity of dissociation curves was analyzed using ABI 7500 software, and data were analyzed by the comparative method ($2^{-\Delta\Delta Ct}$) using an internal control. Each sample was analyzed in duplicate. Inflammatory scores were the sums of mRNA levels of IL-6, COX-2 and CRP.

Table 1. Primers used for PCR analysis

Gene		Sequence
CF	Sense	5’-TGTTGTGAAGACGAGCTGATGTAAAG-3’
	Antisense	5’-TGCATTAAAAGAGAGCATGTGTTG-3’
ND5	Sense	5’-TGGATGATGGTACGGACGAA-3’
	Antisense	5’-TGCGGTTATAGAGGATTGCTTGT-3’
β-Actin	Sense	5’-GGAAAAGAGCCTCAGGGCAT-3’
	Antisense	5’-GAAGAGCTATGAGCTGCCTGA-3’
PGC1α	Sense	5’-ACTATGAATCAAGCCACTACAGAC-3’
	Antisense	5’-TTCATCCCTCTTGAGCCTTTCG-3’
Tfam	Sense	5’-AAGACCTCGTTCAGCATATAACATT-3’
	Antisense	5’-TTTTCCAAGCCTCATTTACAAGC-3’
IL-6	Sense	5’-TCCTACCCCAACTTCCAATGCTC-3’
	Antisense	5’-TTGGATGGTCTTGGTCCTTAGCC-3’
COX-2	Sense	5’-TGACCCCCAAGGCTCAAATAT-3’
	Antisense	5’-TGAACCCAGGTCCTCGCTTA-3’
CRP	Sense	5’-CCATTTCTACACTGCTCTGAGCAC-3’
	Antisense	5’-CCAAAATATGAGAATGTCGTTAGAGTTC-3’

7. Mitochondrial DNA analysis

Mitochondrial DNA (mt DNA) was measured using qPCR. Briefly, total DNA was extracted with a QIAamp DNA extraction kit (QIAGEN). The ratio of mtDNA to nuclear DNA, which reflects the tissue concentration of mtDNA per cell, was subsequently determined. Targeted genes included nuclear cystic fibrosis (CF) and mitochondrial nicotinamide adenine dinucleotide dehydrogenase-5 (ND5). For nuclear DNA quantification, 10 ng DNA was used as a template. Mouse specific primers (sequences reported in Table 1) were selected using Primer Express Software (Applied Biosystems).

8. Western blot analysis

After sacrifice, skeletal and cardiac muscles and liver tissues were immediately removed and instantly soaked in liquid nitrogen and stored at -80°C. Protein extracts were prepared in RIPA buffer (Thermo, USA). Lysates (20 μg) were electroblotted onto a PVDF membrane followed by separation using 12% SDS-polyacrylamide gel electrophoresis. Blotted membranes were incubated for 1 hour with blocking solution (tris-buffered saline/Tween-20, TBST) containing 5% skim milk (w/v) at room temperature, followed by incubation overnight at 4°C with 1:2000 diluted GAPDH (Cellsignaling, USA), PGC1-α (Abcam, USA) and T-fam (Abcam, USA) primary antibodies. Membranes were washed four times with 0.1% TBST and incubated with a 1:3000 dilution of horseradish peroxidase-conjugated goat anti-rabbit IgG secondary antibody for 1 hour at room temperature. Membranes were washed four times in TBST and then developed by ECL (Pierce, USA).

9. Statistical analysis

Results are presented as mean ± S.D or S.E. Data were compared using Student's t test. All analyses were conducted using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, NC, USA). All statistical tests were 2-sided and the threshold for statistical significance was set at P-value <0.05.

III. RESULTS

1. Changes of body weight

Changes in body weight of each group are shown in Figure 2. Body weight increased continuously among all three groups during the 12 weeks of treatment. Furthermore, there were no significant differences in body weight between the two diabetic *db/db* mice groups throughout the experiments.

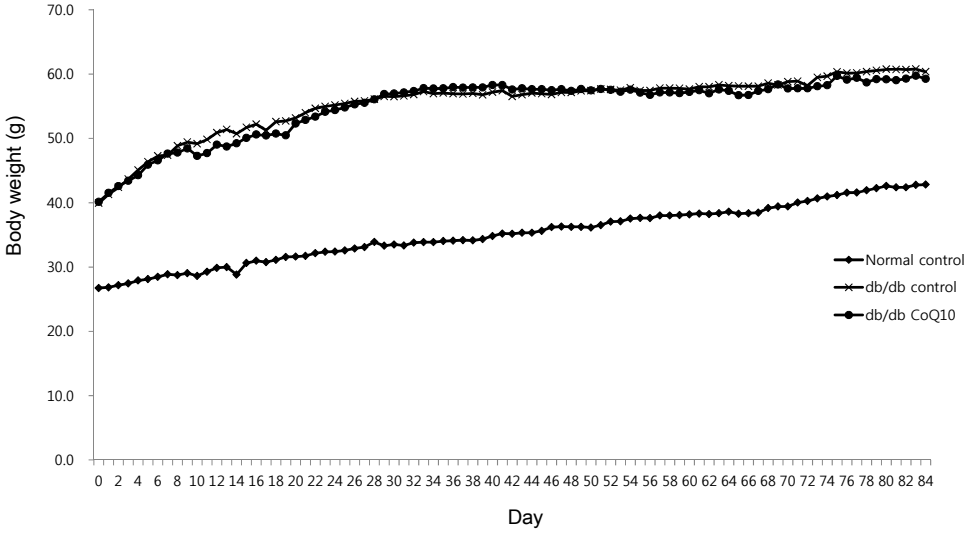

Figure 2. Changes of body weight.

2. Effects of coenzyme Q_{10} on fasting blood glucose levels

Four-hour fasting blood glucose levels were measured after daily IP administration of coenzyme Q_{10} (20 mg/kg body weight) or vehicle in *db/db* mice on a weekly basis. As shown in Figure 3, *db/db* mice had higher blood glucose levels compared with control mice. Compared with the untreated *db/db* group, fasting blood glucose levels of coenzyme Q_{10} treatment group were significantly lower during weeks 10 through 12 (Figure 3).

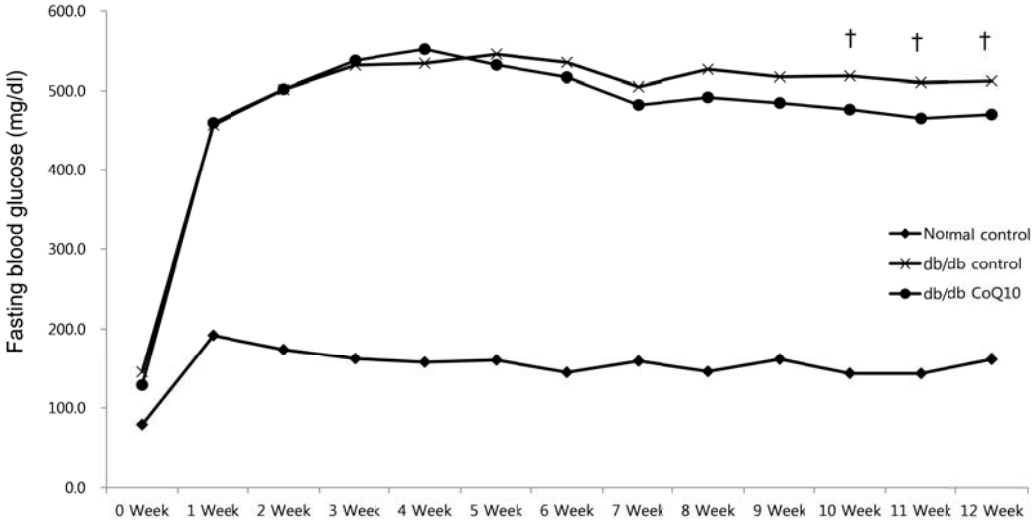

Figure 3. Effects of coenzyme Q_{10} on fasting blood glucose levels.

db/db CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice.

3. Effects of coenzyme Q_{10} on metabolic parameters

The biochemical characteristics of normal control mice and *db/db* mice are shown in Table 2. Administration of coenzyme Q_{10} significantly altered the metabolic parameters of *db/db* mice. Specifically, treatment with coenzyme Q_{10} generated significant differences in glucose index between *db/db* control mice and coenzyme Q_{10}-treated *db/db* mice. After 12 weeks of treatment, fasting blood glucose levels in coenzyme Q_{10}-treated *db/db* mice decreased to 463.6 ± 28.8 mg/dl compared with *db/db* control mice, which had fasting blood glucose levels of 540.5 ± 47.5 mg/dl (P =0.0016). Likewise, levels of HbA1c and HOMA-IR were lower in coenzyme Q_{10}-treated *db/db* mice than in coenzyme Q_{10}-treated *db/db* mice after 12 weeks. However, the changes in additional lipid profiles were not different between the two groups.

Table 2. Effects of coenzyme Q_{10} on biochemical profiles

	Normal control (n=6)	*db/db* control (n=9)	*db/db* CoQ_{10} (n=9)
Fasting glucose (mg/dl)	165.2 ± 36.8	540.5 ± 47.5*	463.6 ± 28.8*†
$HbA1_C$ (%)	3.2 ± 0.2	8.4 ± 1.5*	6.8 ± 1.8*†
Insulin (μIU/mL)	10.4 ± 2.7	15.2 ± 6.1*	12.3 ± 5.4
HOMA-IR	4.1 ± 1.0	20.3 ± 7.0*	14.8 ± 5.5*†
Total cholesterol (mg/dl)	153.2 ± 24.9	177.1 ± 53.7*	162.4 ± 20.9
Triglyceride (mg/dl)	35.3 ± 11.7	71.9 ± 53.7*	85.1 ± 34.9*
HDL cholesterol (mg/dl)	79.2 ± 12.6	83.6 ± 23.4	75.7 ± 8.7
LDL cholesterol (mg/dl)	39.5 ± 11.6	63.4 ± 23.0*	59.8 ± 15.0*

db/db CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice

†P less than .05 vs untreated *db/db* control

*P less than .05 vs *normal* control

4. Effects of coenzyme Q_{10} on mitochondrial DNA contents and proteins related to mitochondrial biogenesis

Compared with the normal control group, the mitochondrial DNA copy numbers were lower in both *db/db* control mice and coenzyme Q_{10}-treated

db/db mice (Figure 4). We also performed immunoblotting of proteins associated with mitochondrial biogenesis on the gastrocnemius muscle and cardiac muscle among the three groups (Figure 5). Compared with the normal control group, the abundance of proteins related to mitochondrial biogenesis, including PGC-1α and T-fam, were higher in *db/db* control mice, whereas the abundances of these proteins were significantly decreased in *db/db* mice treated with coenzyme Q_{10}.

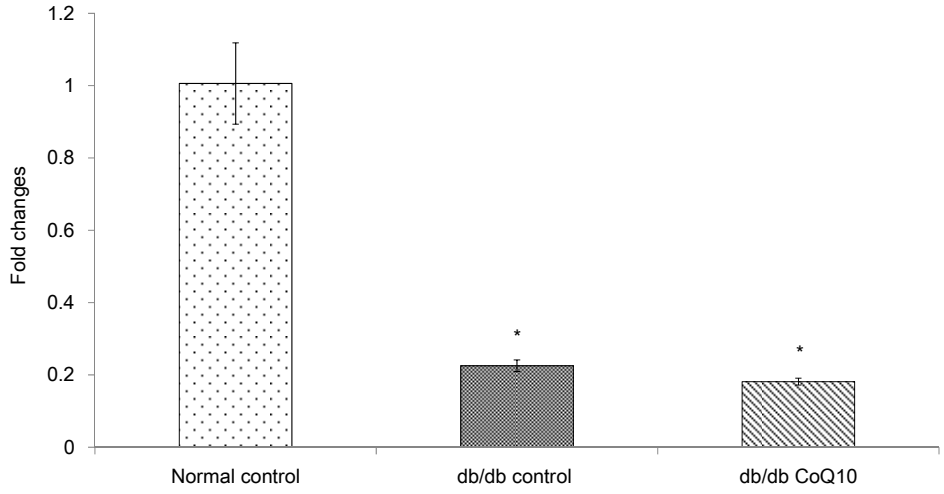

Figure 4. Effects of coenzyme Q_{10} on mitochondrial DNA copy numbers. Data are mean ± S.E. *db/db* CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice. *P less than .05 vs *normal* control.

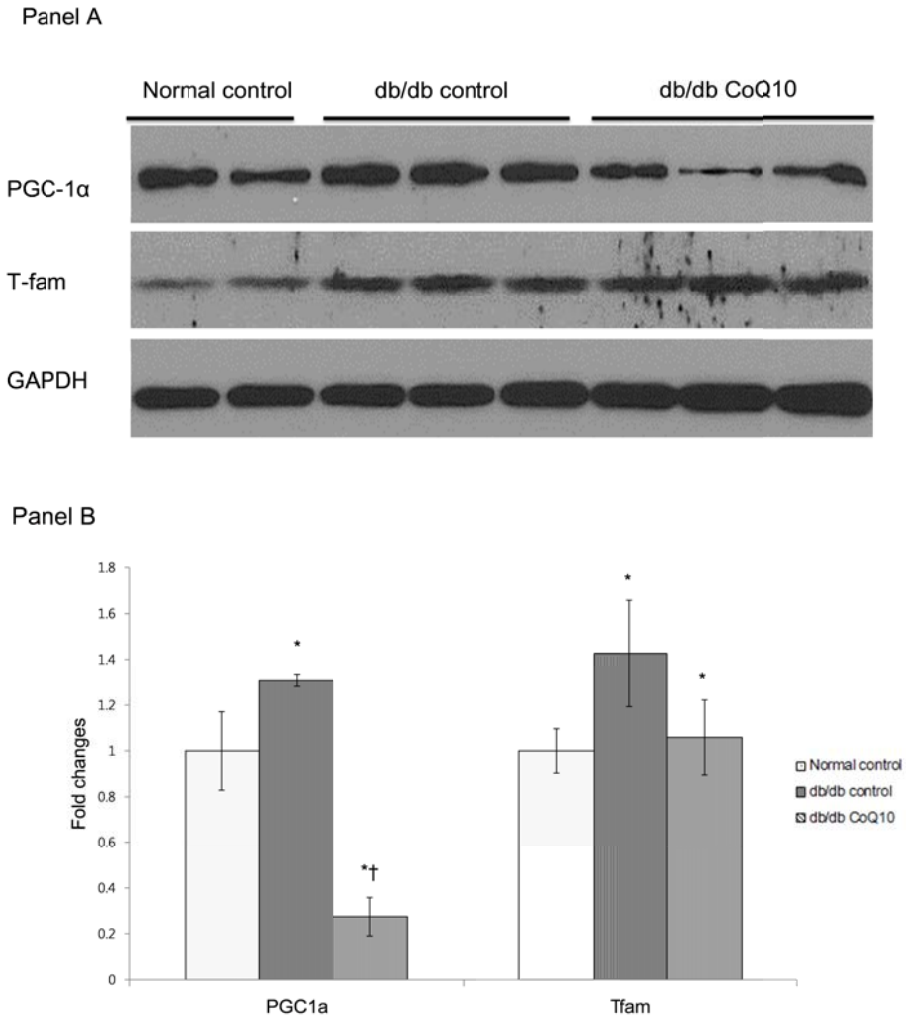

Figure 5. Effects of coenzyme Q_{10} on expression of proteins related to mitochondrial biogenesis. Data are mean ± S.E. *db/db* CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice. *P less than .05 vs *normal* control, †P less than .05 vs untreated *db/db* control.

5. Effects of coenzyme Q_{10} on inflammatory markers in the liver

Compared with the normal control group, the inflammatory protein precursors IL-6, COX-2, and CRP were increased in *db/db* control mice. Treatment of *db/db* mice with coenzyme Q_{10} resulted in a significant decrease in the expression of mRNA expression of IL-6, COX-2, and CRP compared to normal controls as well as untreated *db/db* mice (Figure 6). Finally, an inflammatory score was calculated by summing the levels of mRNA expression of IL-6, COX-2, and CRP. The resulting inflammatory scores were significantly increased in *db/db* control mice and tended to decrease in coenzyme Q_{10}-treated *db/db* mice (Figure 7).

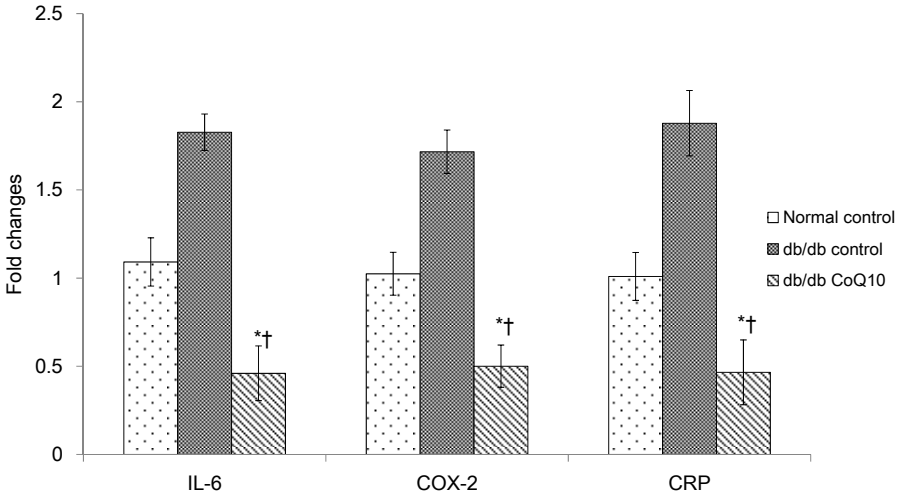

Figure 6. Effects of coenzyme Q_{10} on expression of mRNA related to inflammatory markers. Data are mean ± S.E. IL-6: interleukin 6, COX-2: cyclooxygenase 2, CRP: C-reactive protein, *db/db* CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice. *P less than .05 vs *normal* control, †P less than .05 vs *db/db* control.

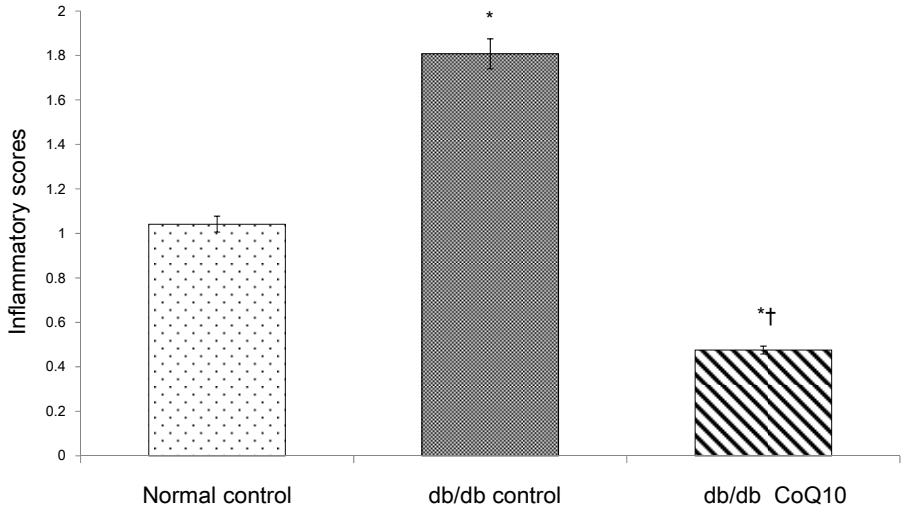

Figure 7. Effects of coenzyme Q_{10} on inflammatory scores. Data are mean ± S.E. *db/db* CoQ_{10}: coenzyme Q_{10}-treated *db/db* mice. *P less than .05 vs *normal* control, †P less than .05 vs untreated *db/db* control.

IV. DISCUSSION

In this study, we examined the effect of exogenous coenzyme Q_{10} as a therapeutic intervention to ameliorate hyperglycemia and insulin resistance in an animal model of type 2 DM. Overall, we observed significant benefits of 12 week-administration of coenzyme Q_{10} on fasting blood glucose levels and expressions of both HbA1c and HOMA-IR. Moreover, we observed significant decreases in the levels of intracellular inflammatory markers in coenzyme Q_{10}-treated *db/db* mice compared with untreated *db/db* mice.

An emerging body of evidence suggests that mitochondrial dysfunction induced by oxidative stress plays a key role in the pathogenesis of insulin resistance and type 2 DM.[3-5] Indeed, oxidative stress during diabetic status may be induced by both an increase in free radical production and a disturbance in free radical scavenging systems. Oxidative stress markers and inflammatory markers such as TNF-α, IL-6, and CRP, as well as WBC counts, are elevated in patients with type 2 DM and insulin resistance.[16-18] In our study, the total inflammation scores and the scope of mRNA expression of IL-6, COX-2, and CRP were significantly decreased in *db/db* mice after treatment with coenzyme Q_{10}. This suggests that the antioxidant agent coenzyme Q_{10} may prevent free radical chain reactions and attenuate intracellular inflammation in the *db/db* mouse model of type 2 DM (Figure 6). Furthermore, these findings suggest that coenzyme Q_{10} improves hyperglycemia and insulin resistance, at least in part, via anti-oxidant effects of coenzyme Q_{10}.

Coenzyme Q_{10} has a fundamental role in cellular bioenergetics as a cofactor in the mitochondrial electron transport chain. It is essential for generating ATP-associated energy, and is a powerful source of reactive oxygen species in the mitochondrial respiratory chain and plays a major role in the deterioration of cell structures. Indeed, coenzyme Q_{10} functions as a mobile redox agent shuttling electrons and protons in the electron transport chain.[10] As coenzyme Q_{10} is an integral part of the respiratory chain and is located where free radicals are generated, its antioxidant properties are crucial for the overall antioxidative capacity of mitochondria.[11] Therefore, coenzyme Q_{10} might reduce oxidative stress in order to inhibit the generation of superoxide in mitochondria. In this regard, maintaining a sufficient abundance of mitochondrial nutrients such as coenzyme Q_{10} may be effective in reducing oxidative stress and improving mitochondrial dysfunction.

In vitro and *in vivo* studies suggest that coenzyme Q_{10} decreases oxidative stress and increases antioxidant enzyme activity. Schmelzer et al.[19] assessed the effect of coenzyme Q_{10} *in vitro* on human and murine macrophages and observed upregulation of 17 genes functionally connected by signaling networks including G-protein-coupled receptors, JAK/STAT, integrin, and b-arrestin pathways. Five of the genes coded for by this network also encode for proteins involved in inflammation, including IL-5, thrombin, vitronectin, vitronectin receptor, and CRP. Furthermore, *in vitro* macrophage cells lines pretreated with coenzyme Q_{10} exhibited reduced TNF-α levels after

lipopolysaccharide stimulation.[20] Friedlyand et al.[21] showed that the cellular protective mechanisms against oxidative stress by coenzyme Q_{10} are capable of creating an oxidant-dependent insulin resistant state, which in turn can result in oxidant-induced mitochondrial dysfunction and subsequent lipid-dependent insulin resistance in myocytes. Similarly, Sena et al.[22] reported that supplementation of coenzyme Q_{10} and α-tocopherol lowers HbA1c and lipid peroxidation in the pancreas of diabetic rats, while, Modi et al[23] reported that coenzyme Q_{10} treatment reduced lipid peroxidation and increased antioxidant parameters such as superoxide dismutase, catalase, and glutathione in the liver homogenates of diabetic rats. On the contrary, Watts et al.[24] reported that 200 mg of coenzyme Q_{10} increased via flow-mediated dilation of the brachial artery in patients with type 2 DM and dyslipidemia failed to change any of the other markers of metabolism or oxidative stress such as lipid profile, blood pressure, blood glucose, serum insulin, hemoglobin A1c, plasma F_2-isoprostane, or oxygen radical absorbance capacity.

Another increasing hypothetical mode of action for coenzyme Q_{10} in diabetes, namely the role of pancreatic insulin secretion, must not go unnoticed. Whether coenzyme Q_{10} can improve or prevent the β-cell function of the pancreas will be an interesting possibility to explore, as deficiencies of coenzyme Q_{10} in the pancreas can impair bioenergetics, ATP generation, and synthesis of insulin. Along these lines, antioxidant treatment has been reported to be protective for β cells against glucose toxicity in diabetic mice[25,26]. In this

regard, coenzyme Q_{10} and α-lipoic acid have been described as being able to stimulate insulin secretion from pancreatic islets[27]. Importantly, correction of quantitative or qualitative abnormalities of coenzyme Q_{10} levels could have diverse therapeutic benefit on pancreatic mitochondria in diabetic subjects.

In the present study we did not observe any improvement in mitochondrial biogenesis factors with exogenous coenzyme Q_{10} administration; the reasons for this dissociation remain unclear. Mitochondria in patients with type 2 DM are known to be small, with the reduced size and content contributing to diminished electron transport activity.[28] However, mitochondrial DNA content, measured by copy number, serve as an index reflecting the stability of mitochondrial genes and mitochondrial biogenesis. Currently, we do not know the biochemical mechanisms responsible for increased expression of mitochondrial biogenesis factors in untreated untreated *db/db* mice. Tentatively, we hypothesize that there is a compensatory mechanism, possibly related to enhanced mitochondrial biogenesis in response to increased oxidative stress, particularly in the late stages of DM, where the tendency for hyperglycemia and insulin resistance is greater. Santos et al.[29] reported that the hyperglycemic insult increases mtDNA repair and biogenesis protecting the electron transport chain system and preventing the initiation of the vicious cycle of ROS. Moreover, in a recent cross-sectional study of 40 Italian women with gestational DM, Giannubilo et al.[30] reported that plasma coenzyme Q_{10} levels are higher in gestational patients compared to healthy controls. Thus, further investigations into the association

between altered mitochondrial biogenesis and DM is warranted.

V. CONCLUSION

We observed a significant decrease in glucose concentrations associated with a significant reduction in inflammatory markers in the coenzyme Q_{10}-treated *db/db* mice compared with the untreated *db/db* control mice. Those finding suggest that Coenzyme Q_{10} may improve blood glucose levels and insulin sensitivity by protecting the mitochondria function from intracellular oxidative damage. Coenzyme Q_{10} could be a useful additive nutraceutical in type 2 diabetes mellitus.

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ABSTRACT (IN KOREAN)

당뇨병 동물모델에서 코엔자임 Q_{10}의 혈중 공복혈당 개선 및 세포 내 염증지표 감소 효과

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이 용 제

목적: 이 연구의 목적은 미토콘드리아의 ATP 생성에 중요한 역할을 하며, 강력한 항산화제로 알려져 있는 코엔자임 Q_{10} 투여가 제 2형 당뇨병 동물모델에서 공복 혈당과 인슐린 감수성 및 세포 내 염증지표에 미치는 영향에 대해 조사하는데 있다.

재료 및 방법: 생후 4주령 된 정상 대조군(n=6), 당뇨병 대조군(n=9), 코엔자임 Q_{10}을 매일 20 mg/kg 농도로 투여한 당뇨병 실험군(n=6), 총 세 군으로 구분하여 12주간 사육하였다. 12주 후 세 군의 공복혈당, 당화혈색소, 인슐린저항성지수(HOMA-IR), 지질 농도를 비교하였다. 미토콘드리아의 생합성과 관련된 인자인 심장근육과 골격근육에서 미토콘드리아의 생합성과 관련된 전사인자인 PGC-1α과 T-fam의 발현을 비교하였다. 또한, 각 실험군

의 간 조직에서 IL-6, COX-2, CRP 염증지표의 전사 RNA 발현과 총 염증지수를 비교하였다.

결과: 당뇨병 대조군에 비해 12주간 코엔자임 Q_{10}을 투여 군에서 공복혈당, 당화혈색소, 인슐린저항성지수 HOMA-IR이 통계적으로 유의하게 감소하였다. 정상 대조군에 비해 PGC-1α와 T-fam의 발현은 당뇨병 대조군에서 증가하였고, 코엔자임 Q_{10}투여 군에서는 감소하였다. 또한, 당뇨병 대조군에 비해 IL-6, COX-2, CRP 염증지표의 전사 RNA 발현이 감소되었으며, 총 염증지수도 감소하였다.

결론: 당뇨병 동물 모델에서 코엔자임 Q_{10}의 투여가 혈당 및 인슐린 저항성을 개선할 수 있으며, 이는 부분적으로 코엔자임 Q_{10}의 세포 내 항산화 기능에 의한 것으로 사료된다.

핵심되는 말: 코엔자임 Q_{10}, 당뇨병, 항산화제, 산화스트레스, 염증, 인슐린 저항성