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Assessment of the Role of Coenzyme Q10 on the Spleen Histological Structure in Rats with Experimentally Induced Diabetes

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ABSTRACT

Diabetes is a widespread medical condition that afflicts individuals in Iraq and globally. This disease disrupts the metabolism of proteins, carbohydrates, and fats, thus affecting the physiology of cells throughout the body. As a result, diabetes can lead to severe health complications. Therefore, the aim of this study is to investigate the effect of diabetes on the spleen and the potential role of coenzyme Q10 (CoQ10) treatment. This study included 20 rats, which were categorized into four equivalent groups with five rats each. The control group was the first group. In the second group, animals were given CoQ10 at a dose of 10 mg/kg. The third group was the diabetes group, wherein rats were intravenously injected with 42 mg/kg alloxan. Rats treated with alloxan and CoQ10 comprised the fourth group. Treatments were continued daily for two months. This study revealed that the administration of alloxan resulted in a statistically significant increase ($P \leq 0.05$) in fasting blood sugar levels in the serum. In addition, in rats, treatment with alloxan induced histopathological changes in the spleen, including severe fatty changes and white pulp atrophy with severe red pulp congestion. However, the coadministration of CoQ10 to diabetic animals led to a significant decrease ($P \leq 0.05$) in serum blood glucose levels and restored the histological integrity of the spleen. CoQ10 may potentially offer a protective effect against alloxan-induced diabetes and spleen damage in rats. These findings may hold remarkable implications for the development of new treatment options for diabetes and related conditions.

Introduction

Diabetes mellitus is a group of metabolic disorders that results in elevated blood sugar concentrations due to insufficient insulin production. It is caused by the autoimmune destruction of insulin-producing β cells (type 1) or ineffective insulin action (type 2) [1,2,3]. The spleen is the major secondary immune organ. It can initiate immune reactions against foreign antigens. It is also responsible for cleaning foreign bodies, as well as broken and old RBCs, from the blood. White and red pulp, the two central components of the spleen, clearly differ in terms of cellular composition, vascular organization, and architecture [4].

Coenzyme Q10 (CoQ10), or ubiquinone, is a vitamin or vitamin-like molecule principally found in its reduced (ubiquinol) and oxidized (ubiquinone) forms in cell membranes and inside the mitochondria. Given that CoQ10 acts as an energy transport substance, it is present at high concentrations in the kidneys, liver, and heart, which have high metabolic rates [5,6,7]. In accordance with its chemical formula, CoQ-10 is similar to vitamin K; however, it is not a vitamin because it is formed in the body, whereas almost all vitamins are obtained by the body from external sources [8]. Alloxan molecules bind with the glucose transporter GLUT-2, inducing cell death via the generation of reactive oxygen species [9,10]. The acceptance of alloxan by GLUT2 transporters on β cells in the pancreas leads to rapid cell damage. When alloxan passes through β cells, it is converted by reactive oxygen species into dialuric acid, which can be reoxidized into alloxan and produce free radicals, like superoxide.

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Superoxide can be converted into hydrogen peroxidase. In addition, reducing Fe^{+3} results in hydroxyl radical formation, leading to DNA damage in β cells, along with fragmentation and eventual cell loss [11,12]. The protective influence of CoQ10 on the liver and kidneys of diabetic rats has been studied in previous research [13,14]. The present research aims to evaluate the ability of CoQ10 to protect spleen tissue from damage caused by alloxan, as well as its ability to control hyperglycemia in a group of Wistar rats (*Rattus norvegicus*).

Materials and Methods

Experimental design

This study included 20 male Wistar rats weighing 200–250 g. The animals were obtained from the Biotechnology Research Center at Al-Nahrain University. They were housed in special laboratory cages under standard conditions, including a temperature of 23 °C (±2 °C), regulated lighting, and ventilation. The rats were fed a standard diet obtained from the College of Veterinary Medicine, University of Baghdad. The diet consisted of soy protein, L-cysteine, sucrose, cornstarch, dextrose, *tert*-butylhydroquinone, cellulose, mixtures of minerals and vitamins, and choline butyrate [15].

The rats were divided into four experimental groups, each comprising five rats. These groups included the nondiabetic group; the CoQ10 group, wherein rats were given CoQ10 (10 mg/kg) dissolved in distilled water daily via a stomach tube; and the untreated diabetic group. In this group, a specific intravenous dose (42 mg/kg) of alloxan monohydrate solution was injected into the tail vein to induce diabetes mellitus [16]. This study also involved a group of treated diabetic rats, which received CoQ10 (10 mg/kg) daily. Treatment began at the onset of diabetes induction, and alloxan-induced diabetes mellitus was confirmed five days later by using a blood glucometer. Animals with fasting blood glucose levels greater than 250 mg/dl were considered diabetic. The practical part of this study was conducted at the Department of Biology, College of Science, University of Anbar.

Ethics and approval statement

The ethical approval committee of Anbar University in Ramadi, Iraq, approved all the research techniques used in this study.

Histological examination

After two months of treatment, rats were anesthetized by using an intramuscular dose of ketamine (100 mg/kg) and xylazine (50 mg/kg) [17]. Spleen samples were soaked in saline and fixed in 10% formalin for 24 h. Subsequently, the samples were dried in high concentrations of alcohol. The samples were embedded in paraffin, sectioned with a microtome, stained with hematoxylin and eosin, and viewed by using a light microscope.

Determination of fasting blood glucose

Blood samples were drawn from the heart, and fasting blood sugar (FBS) was determined by using LINEAR CHEMICALS S.L. (Barcelona, Spain).

Results and Discussion

Treatment with alloxan significantly increased FBS levels to 300.05 ± 40.3 mg/dl ($P \leq 0.05$). By contrast, treatment with CoQ10 for eight weeks significantly reduced FBS levels to 220.08 ± 32.6 mg/dl ($P \leq 0.05$). The mean FBS value in nondiabetics was 83.24 ± 20.5 mg/dl, whereas that in the CoQ10 group was 79.27 ± 10.2 mg/dl (Figure 1).

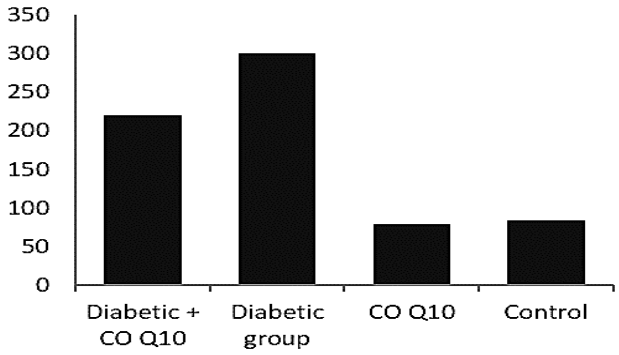
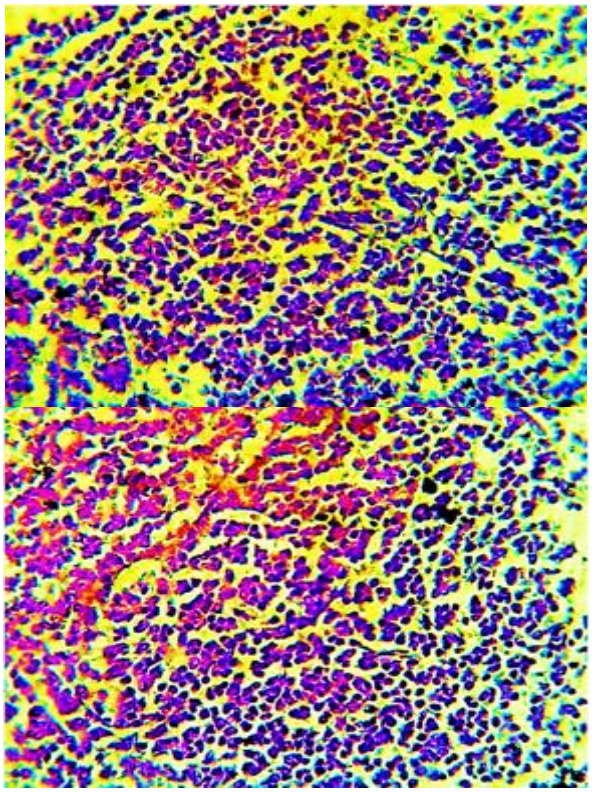


Figure 1. Mean serum concentration of FBS in the studied groups.

The histological examination of the spleen in the nondiabetic group revealed the typical appearance of red and white pulp with a well-defined marginal zone (Figure 2). The spleen in untreated diabetic rats exhibited morphological changes, such as severe fatty changes,

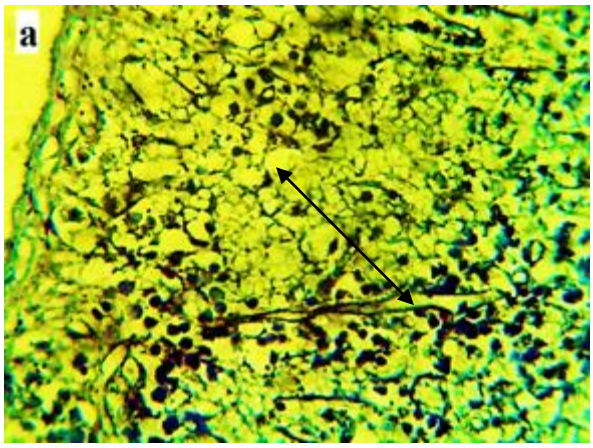
atrophy, and white pulp depletion (Figures 3 a, b, and c). In other sections, severe congestion was observed in red pulp, as well as remarkable depletion and hyperplasia in white pulp (Figures 3 d and e). The diabetic group treated with CoQ10 showed moderate hyperplasia of white pulp and moderate fatty changes in red pulp (Figure 4).

(a)



(b)

Figure 2 a,b. Histological section of the spleen of nondiabetic spleen rats displaying red pulp with a normal appearance and white pulp with a well-defined marginal zone (H&E staining under 400×).



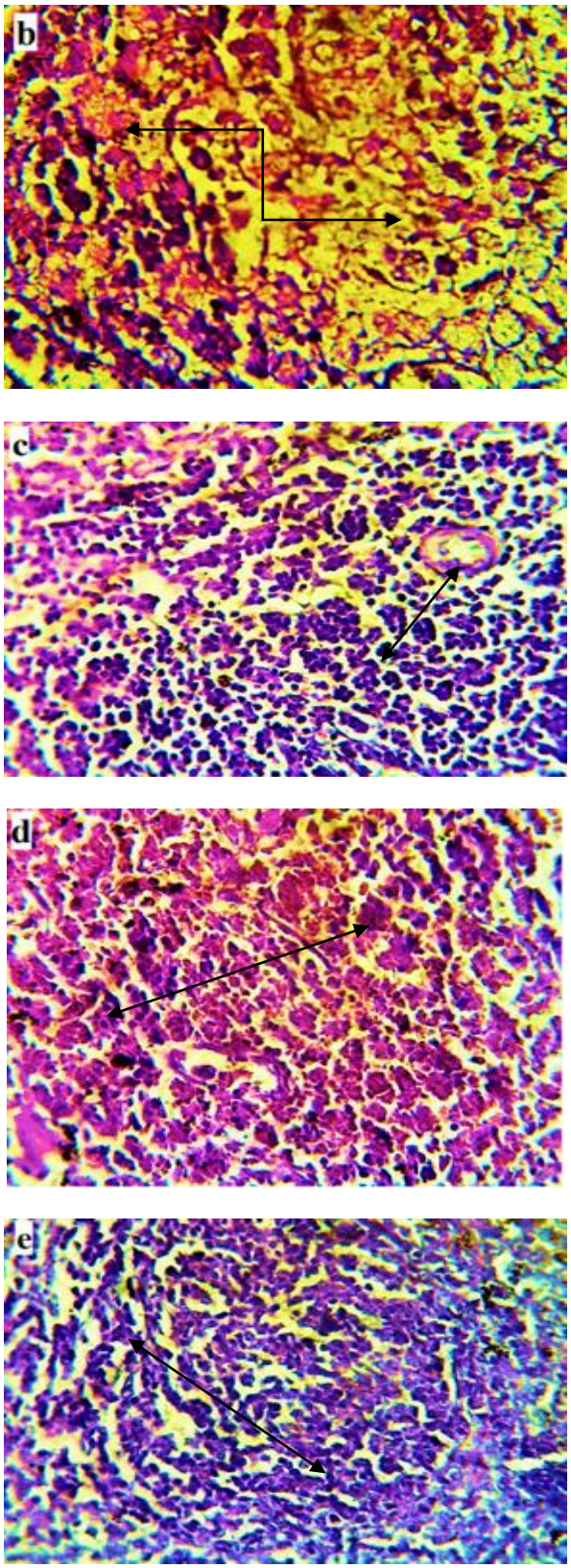
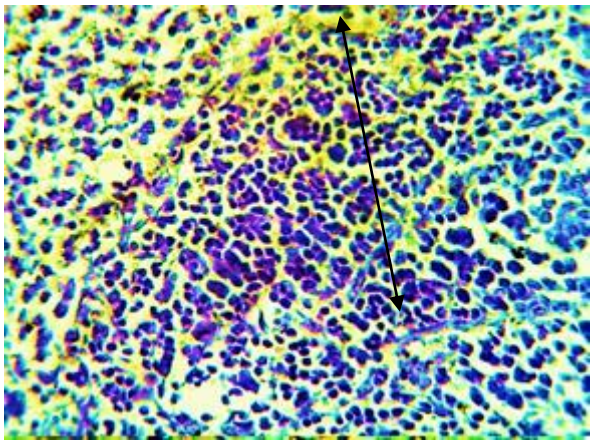
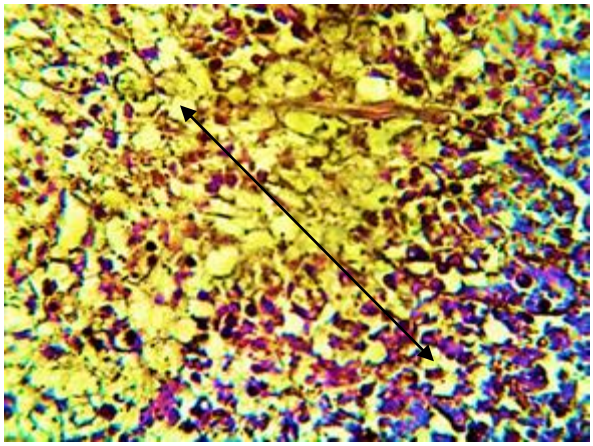


Figure 3. Spleen of untreated diabetic rats showing fatty changes with the atrophy (a), (b), and depletion (c) of

white pulp. Severe congestion in red pulp (d) and hyperplasia of white pulp (e) (H&E staining under 400×).



(a)



(b)

Figure 4. Spleen from diabetic rats treated with CoQ10 showing moderate hyperplasia of white pulp and moderate fatty changes in red pulp (a), (b) (H &E staining under 400×).

Discussion

The present study was designed to detect the influence of diabetes on the most vital immune organ, the spleen, and that of CoQ10 treatment. In rats, diabetes can induce the apoptosis of spleen cells, which is mediated by the Fas/FasL regulation pathway; this phenomenon may be considered the latent mechanism causing the immune toxicity of hyperglycemia [18]. Other studies have indicated that in diabetic rats, injury to spleen tissues results from diabetes complications and oxidative stress, which stimulate cell apoptosis by up-regulating Fas [19,20].

Hyperglycemia affects the immune organs, resulting in defects in host immunity, including phagocytosis, intracellular killing, and impaired cell migration [21,22]. It can also increase the development of advanced glycation end products and secretion of proinflammatory cytokines [23]. As observed in the present study, alloxan caused histopathological changes in the spleen in the diabetic group. These changes included severe fatty changes and white pulp atrophy with severe red pulp congestion. By contrast, in the group that received CoQ10 for eight weeks after alloxan injection, the total spleen damage decreased, with moderate hyperplasia and fatty changes observed in white and red pulp. Several studies have indicated the primary effect of oxidative stress on the pathogenesis of diabetes and its complications [24,25]. Oxidative stress is a state characterized by an increased rate of cell injury caused by oxygen and oxygen-derived oxidants, commonly known as reactive oxygen species [26]. Antioxidants, especially those with a low molecular weight, and synthetic substances may be suitable for the management of numerous pathological conditions related to diabetes mellitus [27,28]. CoQ10 exhibits potent antioxidant properties by directly reacting with free radicals in the plasma membrane, lysosome, Golgi apparatus, and mitochondria [29].

Conclusions

The present study is an experimental investigation describing the histological changes in the spleens of Wistar rats with experimentally induced diabetes after CoQ10 intake. It suggests that in diabetic rats, CoQ10 can decrease spleen damage and reduce glucose levels. This potential effect may stem from the antioxidant properties of CoQ10. Further research is needed to ascertain the antioxidant efficacy of this coenzyme.

References

[1] Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, Roh EJ, Elkamhawy A, Al-Karmalawy AA. (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine & Pharmacotherapy. 168 115734.

[2] Poznan A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. (2020). The diabetes mellitus–atherosclerosis connection: The role of lipid and glucose metabolism and chronic inflammation, Int. J. Mol. Sci. 21 (5) :1835, https://doi.org/10.3390/ijms21051835.

[3] Sakitani K, Enooku K, Kubo H, Tanaka A, Arai H, Kawazu S, Koike K. (2017). Clinical characteristics of patients with diabetes mellitus and fatty liver diagnosed by liver/spleen Hounsfield units on CT scan. J Int Med Res. Jun;45(3):1208-1220.

[4] Cesta MF. (2006). Normal structure, function, and histology of the spleen. Toxicol Pathol.;34(5):455-65.

[5] Martelli A, Testai L, Colletti A, Cicero AF. (2020) Coenzyme Q10: Clinical applications in cardiovascular diseases. Antioxidants. Apr;9(4):341.

[6] Bentinger M, Brismar K, Dallner G. (2007).The antioxidant role of coenzyme Q. Mitochondrion. Jun 1;7: S41-50.

[7] Saini R. (2011).Coenzyme Q10: The essential nutrient. Journal of Pharmacy and Bioallied Sciences. Jul 1;3(3):466-7.

[8] Bhagavan HN, Chopra RK. (2006). Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics. Free radical research. Jan 1;40(5):445-53.

[9] Queiroz LA, Assis JB, Guimarães J, Sousa ES, Milhomem AC, Sunahara KK, Sá-Nunes A, Martins JO.(2021). Endangered lymphocytes: The effects of alloxan and streptozotocin on immune cells in type 1 induced diabetes. Mediators of Inflammation. Oct 19;2021.

[10] Lenzen S. (2008). The mechanisms of alloxan-and streptozotocin-induced diabetes. Diabetologia. Feb;51(2):216-26.

[11] Macdonald Ighodaro O, Mohammed Adeosun A, Adeboye Akinloye O. (2017). Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. Medicina. Dec;53(6):365-74.

[12] Szkudelski T. (2001). The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. Physiological research. Jan 1;50(6):537-46.

[13] Salman MI, Rashied RM, Hamad HM, Hamad HS.(2020) The protective effect of coenzyme Q10 on experimental diabetic nephropathy in male rats. Eurasia J. Biosci. Aug 1; 14: 6883-8.

[14] Rashied RM, Salman MI, Hamad HS, Hamad HM.(2020). EFFECT OF COENZYME Q10 AGAINST ALLOXAN-INDUCED DIABETES AND LIVER TOXICITY IN MALE RATS. Biochemical & Cellular Archives. Oct 1;20(2).

[15] Reeves PG. (1997). Components of the AIN-93 diets as improvements in the AIN-76A diet. J. Nutr. . 127: 838S-841S.

[16] Lucchesi AN, Cassettari LL, Spadella CT. (2015). Alloxan-induced diabetes causes morphological and ultrastructural changes in rat liver that resemble the natural history of chronic fatty liver disease in humans. Journal of diabetes research. Feb 19;2015.

[17] Aledani AHE, Khudhair NA, Alrafas HR. (2020). EFFECT OF DIFFERENT METHODS OF ANESTHESIA ON PHYSIO-BIOCHEMICAL PARAMETERS IN LABORATORY MALE RATS. Bas.J.Vet.Res. 19(1): 206-214.

[18] Ebaid H, Al-Tamimi J, Metwalli A, Allam A, Zohir K, Ajarem J, Rady A, Alhazza IM, Ibrahim KE. (2015). Effect of STZ-induced diabetes on spleen of rats: Improvement by camel whey proteins. Pakistan J. Zool. Aug 1;47(4):1109-16.

[19] Sainio-Pöllänen S, Erkkilä S, Alanko S, Hänninen A, Pöllänen P, Simell O. (1998).The role of Fas ligand in the development of insulitis in nonobese diabetic mice. Pancreas. Mar 1;16(2):154-9.

[20] Park GB, Kim YS, Lee HK, Cho DH, Kim D, Hur DY. (2013). CD80 (B7. 1) and CD86 (B7. 2) induce EBV-transformed B cell apoptosis through the Fas/FasL pathway. International journal of oncology. Nov 1;43(5):1531-40.

[21] Jafar N, Edriss H, Nugent K. (2016). The effect of short-term hyperglycemia on the innate immune

system. The American journal of the medical sciences. Feb 1;351(2):201-11.

[22] Abu-Ashour W, Twells LK, Valcour JE, Gamble JM.(2018). Diabetes and the occurrence of infection in primary care: a matched cohort study. BMC infectious diseases. Dec;18:1-8.

[23] Hussain A, Bhowmink B, Moreira NC. (2020) COVID-19 and diabetes: Knowledge in progress. diabetes research and clinical practice. April;(162):108142.

[24] Novoselova EG, Glushkova OV, Lunin SM, Khrenov MO, Parfenyuk SB, Novoselova TV, Sharapov MG, Novoselov VI, Fesenko EE. (2020). Peroxiredoxin 6 attenuates alloxan-induced type 1 diabetes mellitus in mice and cytokine-induced cytotoxicity in RIN-m5F beta cells. Journal of Diabetes Research. Aug 25;2020.

[25] Manna P, Sil PC. (2012). Arjunolic acid: beneficial role in type 1 diabetes and its associated organ pathophysiology. Free Radical Research. Jul 1;46(7):815-30.

[26] Kumar R, Kumari A, Singh JK, Nath A, Ali M, Sinha S, Kumar A. (2013).Protective effect of zingiber officinale on spleen of diabetic guinea pig. International Journal of Pharmaceutical Science Invention. Mar;2(3):32-7.

[27] Wojnar W, Zych M, Kaczmarczyk-Sedlak I. (2018). Antioxidative effect of flavonoid naringenin in the lenses of type 1 diabetic rats. Biomedicine & Pharmacotherapy. Dec 1; 108: 974-84.

[28] Czerwińska ME, Gąsińska E, Leśniak A, Krawczyk P, Kiss AK, Naruszewicz M, Bujalska-Zadrożny M. (2018). Inhibitory effect of Ligustrum vulgare leaf extract on the development of neuropathic pain in a streptozotocin-induced rat model of diabetes. Phytomedicine. Oct 1; 49: 75-82.

[29] Tsuneki H, Sekizaki N, Suzuki T, Kobayashi S, Wada T, Okamoto T, Kimura I, Sasaoka T. (2007). Coenzyme Q10 prevents high glucose-induced oxidative stress in human umbilical vein endothelial cells. European Journal of Pharmacology. Jul 2;566(1-3):1-10.

تقييم دور الإنزيم المساعد Q10 على انسجة الطحال في الفئران المصابة بالسكري تجريبيا

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الخلاصة:

يعتبر مرض السكري حالة طبية واسعة الانتشار تصيب الأفراد في العراق والعالم. يعطل هذا المرض عملية التمثيل الغذائي للبروتينات والكربوهيدرات والدهون، مما يؤثر على فسيولوجيا الخلايا في جميع أنحاء الجسم. ونتيجة لذلك، يمكن أن يؤدي مرض السكري إلى مضاعفات صحية خطيرة. ان الهدف من البحث هو دراسة تأثير مرض السكري على الطحال والدور المحتمل لعلاج الإنزيم المساعد Q10. شملت الدراسة 20 فأراً تم تقسيمهم إلى أربع مجموعات متكافئة (5 لكل مجموعة)، كانت المجموعة الضابطة هي المجموعة الأولى، وكانت CoQ10 هي المجموعة الثانية التي أعطيت فيها الحيوانات الإنزيم المساعد Q10 بجرعة 10 ملجم/كجم، المجموعة الثالثة. كانت مجموعة الجرذان المصابة بداء السكري والتي تم حقنها عن طريق الوريد بجرعة 42 ملغم/كغم من الألوكسان، وكانت الجرذان المعالجة هي المجموعة الرابعة التي تلقت فيها الجرذان الألوكسان مع الإنزيم المساعد Q10. واستمر العلاج يوميا لمدة شهرين. كشفت الدراسة أن إعطاء الألوكسان أدى إلى زيادة ذات دلالة إحصائية ($P \leq 0.05$) في مستويات السكر في الدم الصائم (FBS) في المصل. بالإضافة إلى ذلك، أدى علاج الجرذان بالألوكسان إلى حدوث تغيرات نسيجية مرضية في الطحال، بما في ذلك تغيرات دهنية شديدة، وضمور اللب الأبيض مع احتقان شديد للب الأحمر. ومع ذلك، أدى الاستخدام المتزامن للإنزيم المساعد Q10 مع الحيوانات المصابة بداء السكري إلى انخفاض كبير ($P \leq 0.05$) في مستويات الجلوكوز في الدم واستعادة السلامة النسيجية للطحال. يوفر CoQ10 تأثيرًا وقائيًا ضد مرض السكري الناجم عن الألوكسان وتلف الطحال في الفئران. قد تحمل هذه النتائج آثارًا كبيرة على تطوير خيارات علاجية جديدة لمرض السكري والحالات المرتبطة به.