

ORIGINAL ARTICLE

Role of Co-Enzyme Q10 in the improvement of diet-induced hypercholesterolemia in an animal model: Laboratory-based experimental study.

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ABSTRACT... Objective: To create a model by inducing hypercholesterolemia in rabbits by feeding them with a high-cholesterol diet in order to perform the lipid profile for alterations in the serum levels of LDL and total cholesterol in the blood and to observe the role of coenzyme Q10 in these Animals. **Study Design:** Experimental study. **Setting:** Animal House of National Institute of Health Islamabad, Pakistan. **Period:** Jan 2023 - Nov 2023. **Methods:** This study was conducted on thirty-six adult healthy rabbits. Increased blood cholesterol level was developed in experimental animals by giving them high-cholesterol diet for 120 days, the very next day Coenzyme Q10 was given to rabbits for 30 days. Base line levels of serum cholesterol, triglycerides, very low density lipoprotein, Low density lipoprotein, and High density lipoprotein were measured. After 24 hours of the last test dose Lipid markers were tested. One-way ANOVA followed by post hoc Tukey test were applied for calculating mean and standard deviations. **Results:** High cholesterol diet-fed rabbits showed a significant increase in cholesterol level after 120 days with respect to day zero, the serum total cholesterol level decreased after giving CoQ10 for the next 30 days. Similarly, serum low-density lipoprotein levels showed a significant increase following 120 days of intake of a high-cholesterol diet. However, this increase is followed by a decrease in levels when treated with CoQ10 for 30 days. **Conclusion:** A High cholesterol diet produces hyperlipidemia in animal models. CoQ10 can be effectively used for lowering the serum levels of cholesterol and low-density lipoprotein, which may be beneficial in correcting dyslipidemia in patients with cardiovascular diseases.

Key words: Coenzyme Q10, Cholesterol, Hypercholesterolemia, Low-Density Lipoprotein, Rabbits.

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INTRODUCTION

No one disagrees that lipids are essential biomolecules that constitute a balanced, healthy diet. Low density lipoprotein is a specialized transporter which carries cholesterol throughout the body to maintain normal and healthy body functions.¹ Cholesterol is a soft and waxy constituent found among the lipids (fats) in circulation and all parts of the body's cells. Cholesterol is an essential component for our body and plays an integral role in our health, as it forms cell membranes, various hormones and many tissues throughout the body.² High levels of low density lipoprotein leads to accumulation of cholesterol in the arterial walls increasing fatal cardiovascular abnormalities.³

Those who are on a high cholesterol diet, regular monitoring of lipid profile is required, to have a check on plasma lipid biochemistry. CoQ10 is a

fat-soluble, vitamin-like enzyme. It is synthesized in all the tissues of the body, especially the liver. Nowadays CoQ10 is recommended as a supplement to be prescribed as adjunct with the traditional treatment of cardiovascular diseases.³ The food rich in Coenzyme Q10 include spinach, broccoli, soybeans, fish, meat, poultry products and nuts.⁴ Different formulations of Coenzyme Q10 are available, these include injections, tablets, gel, and capsules. Co enzyme Q10 is hydrophobic in nature with a large molecular weight. Absorption is slow but increases when taken with a fatty meal. Solubilized formulations increases its absorption and time to reach maximum concentration is approx. 6 hrs.⁵ Tissues like heart and brain mitochondria takes up Coenzyme Q10. It also undergoes enterohepatic circulation.⁶ Coenzyme Q10 is incorporated into the mitochondria of tissues with high metabolic rates like heart, kidney, liver and skeletal muscles.

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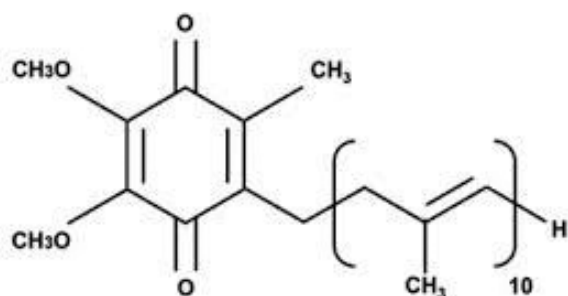
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CoQ10 during electron transport mechanism produces energy in the form of ATP necessary to maintain essential metabolic functions like taking up and proper utilization of nutrients for the synthesis of new proteins and discarding waste materials.⁷ The proposed experimental animal study aims to explore the effect of Coenzyme Q10 on lipid profile and observe its hypolipidemic efficacy in various lipid parameters.

FIGURE-1

Chemical structure of CoQ10.⁸



Structure of CoQ10

METHODS

The study was conducted and reported according to the ARRIVE guidelines (version 2.0). After approval from the ethical committee of the Institution Review Board (IRB) of Akhtar Saeed Medical College Rawalpindi vide letter no: 18-10/22, dated: 22nd November 2022, This research study was carried out from January 2023 till November 2023 in the animal house of the National Institute of Health Islamabad, Pakistan.

Thirty-six adult healthy rabbits (*Oryctolagus Cuniculus*) belonging to both genders, non pregnant female Rabbits with weight between 1.5 to 2.0 kg were purchased from the local market. After evaluating the serum lipid profile from the Chemical Pathology Lab of Army Medical College Rawalpindi Islamabad. Those with normal lipid profile were selected and kept in the animal house of NIH Islamabad for one week to get acclimatized under standard laboratory environment. Room temperature was maintained at 24 °C humidity at 70%. 12 hours dark and light cycle was maintained, Free access to diet and water ad libitum was available throughout the study

The diet formula for animals used in the study was according to the guidelines for the care of laboratory animals, NIH, Islamabad, and comprised Table-I.

TABLE-I

DIET formula used per rabbit in the study per day

whole gram	30 grams
Wheat bran	30 grams
Green fodder	100 grams
Seasonal fruits(cucumber, carrot, apples)	100 grams
Cholesterol powder	1 gram

After one week of acclimatization the rabbits (n=36) were given high cholesterol diet (1g/day) mixed with normal diet for 120 days. Then they were fed on cholesterol free diet and small pellets containing coenzyme Q10 (10mg/kg) mixed in whole gram and wheat bran once daily for 30 days.

Blood samples were taken on day zero the start of giving high cholesterol diet and on day 120 and 150 after the completion of study.

After 8-10 hours of fast of all the experimental animals, 4 ml of blood was drawn from the marginal ear vein of each rabbit and within 45 minutes transferred to Chemical Pathology lab Army Medical College Rawalpindi. Blood samples containing tubes were centrifuged for 10 minutes at the rate of 4500 rounds per minutes. Serum was separated via an automatic micropipette. chemistry auto analyzer was used for estimation of serum cholesterol levels.

Serum LDL was calculated by using the standard Friedewald formula (mmol/L) -

$$\text{LDL-C (mmol/L)} = \text{TC} - \text{HDL} - (\text{TG}/2.2)$$

RESULTS

This study with the cholesterol powder mixed diet was carried out for a total period of five month out of which four months to establish the efficacy of a high cholesterol diet followed by a period of one month with coenzyme Q 10 to observe the antihyperlipidemic effects.

The levels of serum cholesterol on the day 120 was significantly increased as compared to the levels recorded on the day zero, i.e., 4.058 mmol/L and 1.63 mmol/L respectively. Similarly, in contrast

among serum cholesterol recorded on day 120 (Hyperlipidemic rabbits) and day 150 (after taking coenzyme Q10), the levels dropped, but the decrease was not significant, i.e., 4.058 mmol/L and 3.048 mmol/L respectively.

Serum LDL levels recorded on day zero, day 120 and day 150 showed significant difference in values as 1.638 mmol/L 3.357mmol/L and 1.807 mmol/L, respectively. Serum LDL levels increased after taking a high cholesterol diet for 120 days, but the levels declined significantly after taking coenzyme Q10 for another 30 days. (Table-II).

TABLE-II			
Effect of coenzyme Q10 (10mg/Kg) on serum lipid profile in hyperlipidemic rabbits (n=36)			
TEST	Day 0	Day 120	Day 150
Serum Cholesterol mmol/L	1.633	4.058	3.048
	0.59	1.6	1.25
Serum Triglyceride mmol/L	0.433	0.98	1.227
	0.23	0.31	0.5
Serum VLDL mmol/L	0.227	0.372	0.507
	0.1	0.15	0.2
Serum LDL mmol/L	1.638	3.357	1.807
	0.33	1.2	0.75
Serum HDL mmol/L	0.358	0.737	0.683
	0.14	0.3	0.28

DISCUSSION

In our study, we decided to use cholesterol powder in diet, as per formula given in table 1, to produce hyperlipidemia to be treated with CoQ10.⁹ The reason was that we first tried sugar (for sucrose), honey (for fructose) and ghee, egg yolk and peanuts (for fats) for four weeks, but there was no significant increase in the levels of the biomarkers of lipids in rabbits.^{10-11,12}

Cholesterol powder (1g/day) mixed diet was given to all the rabbit for 120 days. Gasparova Z et.al 2023 In their study induced hyperlipidemia in experimental white rabbits in 60 days by giving them high cholesterol diet.¹³ In our study, it took 120 days for hyperlipidemia to develop this may due to difference in the species of rabbits. Fasting blood sample for lipid profile were taken on day zero the

beginning of experimental study and after 120 days before giving coenzyme Q10. It showed marked elevation of serum cholesterol and serum LDL in all the animals.

CoQ10, a provitamin, is a safe and highly tolerable drug, experimental studies showed that a high dose of Coenzyme Q10 (1200 mg/kg) body weight is tolerable.¹⁴ In our study we gave CoQ10 in a dose of 10 mg/kg for a period of 30 days. Fasting blood samples of all experimental animals were collected after giving CoQ10 for one month to compare the levels of serum LDL and serum total cholesterol with the lipid biomarkers taken on day zero and day 120, as elevated levels can lead to cardiovascular complications. In one study Cao X et.al 2022 concluded that elevated levels of serum cholesterol and Low density lipoprotein increases the risk of developing cardiovascular diseases so it is important to monitor their levels.¹⁵

When we compared the results after treatment with CoQ10 in hyperlipidemic rabbits there was reduction in the serum cholesterol level but the decrease was not significant. However, there was a significant reduction in serum LDL with CoQ10, as shown in Table-II. Hashim QA et.al.2025 in their study using rats as an experimental model suggested that CoQ10 has the potential to lower serum total cholesterol and serum triglycerides level.¹⁶ Our results are also consistent with the inference of Tsai I et.al 2022 who suggested from his study that CoQ10 has the potential to significantly lower plasma lipid biochemistry levels.¹⁷

Coenzyme Q10 decreases cholesterol and triglycerides levels in the aorta of those taking high fat diets. Mortensen MB. et.al 2023 from their research said there is reduction in the size of aortic and coronary artery plaque after taking CoQ10 in high-fat diet-induced rabbits.¹⁸

Coenzyme Q10 acts as antioxidant by eradicating harmful free radicals responsible of causing damage to cell membranes.¹⁹ Jia W et.al 2022 suggested that Coenzyme Q10 act as an antioxidant by regenerating vitamin E and vitamin C preventing further oxidation. They said that once an antioxidant is utilized in stabilizing free radical it is to be

regenerated so it can produce its antioxidant action.²⁰ Ardekani A et.al 2023 said that by transferring electrons to oxidized vitamin E and C, CoQ10 is converted to reduced form and regenerates their antioxidant potential thus protecting Cell DNA and mitochondrial DNA from oxidative stress.²¹

Our study showed the beneficial effect of CoQ10 in lowering serum LDL and cholesterol levels. Dunning BJ et.al 2023 concluded from his study that CoQ10 decreases the oxidation of LDL and cholesterol leading to reduction in the development of atherosclerosis cardiovascular diseases.²²

Thus we can say that administration of CoQ10 lowers serum Cholesterol and LDL levels in rabbits with hypercholesterolemia induced by a high cholesterol diet. As we conducted the study in our animal model, we observed remarkable reduction in serum LDL and total cholesterol levels. However, serum VLDL and serum triglyceride levels were elevated with Co-enzyme Q10. Additionally, serum HDL levels were also reduced instead of getting raised. These findings present a limitation of our study. Therefore, further research is recommended to specifically investigate the effects of Coenzyme Q10 (CoQ10) on hypertriglyceridemia.

CONCLUSION

Feeding rabbits with a diet containing 1g of cholesterol per day leads to the induction of hyperlipidemia and deranged lipid levels of serum LDL and total cholesterol in the blood. These elevated levels may increase the risk of developing cardiovascular disorders. CoQ10 10mg/kg in diet reduced the high lipid profile and is considered as a lipid lowering drug.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Sabeen Shakir: Design analysis, drafting.
2	Sana Rasheed Chaudhry: Data analysis.
3	Zunnera Rashid: Interpretation of data.
4	Erum Rashid: Study design.
5	Ayesha Fazal: Data analysis.
6	Farzana Munir: Data collection.