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Immuno-Haematological Indices Stabilizing Attributes of Co-Enzyme Q10 Supplementation in Thioacetamide Poisoned Wistar Rats

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Abstract

Coenzyme Q10 (CoQ10 or Co_Q10) as a known endogenous compound has been linked to some therapeutic functions, thus, the need for further exploration in more dysfunctional biological scenarios. This present study, thus, evaluated the stabilizing attributes of Co-enzyme Q10 supplementation in thioacetamide (TAA) altered immuno-haematological system in Wistar rats. One hundred and twenty (120) male Wistar rats weighing 250 and 280g were used for the study and were randomly separated into four sub-groups of 30 rats per treatment interval of week 3, 6, 9 and 12. In the individual weeks, the rats were further grouped into six different groups of five rats each. The groups included Group 1-control and received 1ml of normal saline (intraperitoneally—ip), Group 2 received only 200 mg/kg TAA (ip) twice weekly, Group 3 received 5mg/kg Co_Q10, daily per oral (po), Group 4 received 10mg/kg Co_Q10 daily (po), Group 5 received 200 mg/kg TAA (ip) twice weekly and 5mg/kg Co_Q10 (po) daily and Group 6 received 200 mg/kg TAA (ip) twice weekly and 10mg/kg Co_Q10 (po) daily. After weeks 3, 6, 9 and 12 of treatments, blood samples were collected and instantly transferred into well labeled blood sample bottles with anticoagulant. After appropriate laboratory and statistical analyses, the quantitative results were obtained. The result showed that following TAA toxicity, the levels of white blood cells (WBC) were significantly ($P<0.05$) reduced; meanwhile, those of macrophage and tissue necrotic factor alpha (TNFα) were remarkably ($P<0.05$) increased. However, upon the supplementations with Co-Q10 in the respective weeks (3, 6, 9 and 12) of treatment, all the aforementioned deranged values of WBC, macrophages and TNFα were significantly ($P<0.05$) stabilized/normalized (i.e. brought to similar range of the normal untreated rats). Therefore, Co-Q10 supplementation may be of beneficial therapeutic value in particular haematological dysfunctional scenarios.

Keywords*:* Co-Enzyme Q1 Supplementation, Thioacetamide (TAA), Immuno-Haematological Indices.

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INTRODUCTION

For more than a decade now, a critical advancement in biomedical research has been the recognition of altered immune system function in many chronic disease states [1]. Also, in clinical practice, the evaluation of haematological and immunological parameters are frequently utilised to evaluate health and illness conditions [2, 3]. This is so because; the variations in these indices may serve as valuable biomarkers for evaluating the course of the disease or the efficacy of treatment [2-4].

On the other, the isolation of endogenous substances that seem to be natural ligands for drug receptors in humans and animals has attracted a lot of attention for some time now [5, 6]. This was an expected result of the finding that many pharmacological agents bind to sterospecific receptors in order to exert their therapeutic effect [5, 6].

Considering the fact that tissues and cells involved in immune function are highly energy-dependent and as such require an adequate supply of CoQ10 for optimal function, it becomes a substance of great research interest [7, 8]. CoQ10 is a compound that serves as a cofactor in the electron-transport chain and is naturally occurring in the mitochondria of virtually all aerobic organisms [9]. Furthermore, CoQ10 plays a significant role in enhancing both the immune system and other physiologic functions [10]. As an endogenous substance that has been considered to possess significant

therapeutic function by different schools of thought, Coenzyme Q10's supplementation may perhaps exert some beneficial effects on a dysfunctional biological system [11, 12].

Consequently, this present study set out to evaluate the stabilizing attributes of Co-enzyme Q10 supplementation in thioacetamide (TAA) altered immuno-haematological indices in Wistar rats.

MATERIALS AND METHOD

The Study Animals

Adult male Wistar rats weighing between 250 and 280g were used for the study. The animals were procured from the Animal Farm of the Department of Pharmacology, University of Port Harcourt, Nigeria and used for the present study. The study was conducted in same location and the animals were housed in standard wire-gauze covered plastic cages with suitable beddings under the 12hours light/dark cycles at about 25ºC. The animals were randomly separated into four sub-group of 30 rats per treatment interval of weeks 3, 6, 9 and 12. In the individual weeks, the rats were further grouped into six different groups of five rats each.

Treatment Protocol for the Study

The groupings of the animals and their respective treatment protocols were as stated below:
Group 1-control and received 1ml of normal saline (intraperitoneally—ip),
Group 2 received only 200 mg/kg TAA (ip) twice weekly,
Group 3 received 5mg/kg Co_Q10, daily per oral (po),
Group 4 received 10mg/kg Co_Q10 daily (po),
Group 5 received 200 mg/kg TAA (ip) twice weekly and 5mg/kg Co_Q10 (po) daily and
Group 6 received 200 mg/kg TAA (ip) twice weekly and 10mg/kg Co_Q10 (po) daily.

Harvest of Samples from the Study Animals

Immediately after the respective 3, 6, 9 and 12 weeks of treatments, blood samples were harvested from the study animals via cardiac puncture after proper sedation using the animals were anaesthetized under ketamine (70 mg/kg) and xylazine (8 mg/kg) anaesthesia. The obtained blood samples were then immediately transferred into well labeled lithium heparin bottles and presented for the appropriate laboratory investigation.

Determination of Immuno-Haematologic Parameters

The determination of the serum level of tumor necrosis factor-α (TNF-α) was done using the enzyme-linked immunosorbent assay (ELISA) technique [13]. The automated haematology analyzer was used following the guide of the manufacturer to determine the white blood cell count and differentials.

Method of Data Analysis

The quantitative outcomes of the present study were subjected to statistical analyses using analyses of variance and Post Hoc tools of the IBM Statistical Product and Service Solutions (SPSS) 21.0V software. The data were presented as Mean ± Standard error of mean. Differences between means were determined using Analysis of variance (ANOVA) and post-test using LSD multiple comparison test and Dunnett at 95% probability.

Ethical Approval

Ethical approval for the present study was granted by the Research Ethics Committee of the University of Port Harcourt with reference number: UPH/CEREMAD/REC/MM86/045.

RESULTS

The result on Table 1 shows the effects of Coenzyme Q10 on White Blood Cells (WBC) in the TAA poisoned rats. The TAA-only treated rats had significantly ($P<0.05$) depressed level of WBC when compared to those of both test and control groups. It was found that the treatment with the two doses of Co-Q10 (5mg and 10mg) in both the normal and TAA poisoned rats stabilized the WBC level within normal range as there were only marginal differences when their values were compared to that of the control group.

Table 1: Effects of Coenzyme Q10 on WBC (10^9/L) in Thioacetamide (TAA) Poisoned Wistar Rats

Group	Week 3	Week 6	Week 9	Week 12
TAA only	5.06±0.10	4.80±0.07	4.40±0.13	4.06±0.19
Control	5.70±0.07*	6.20±0.07*	6.90±0.28*	7.50±0.16*
Co_Q10 (5mg)	6.80±0.27*	7.00±0.23*	7.30±0.11*	7.60±0.19*
Co_Q10 (10mg)	6.90±0.10*	7.20±0.70*	7.50±0.17*	7.70±0.22*
Co_Q10 (5mg+TAA)	6.400±0.13*	6.60±0.22*	6.70±0.22*	6.90±0.30*
Co_Q10 (10mg+TAA)	6.50±0.17*	6.80±0.28*	7.30±0.10*	7.80±0.13*

Values represent mean ± SEM; n=5. *=significant when compared to that of TAA-only.

Table 2: Effects of Coenzyme Q10 on Neutrophils (%) in Thioacetamide Poisoned Wistar Rats

Group	Week 3	Week 6	Week 9	Week 12
TAA- only	14.00±0.71	9.00±0.07	6.50±0.18	3.50±0.16
Control	15.70±0.64*	17.00±0.73*	19.00±0.50*	22.00±0.39*
Co_Q10 (5mg)	10.00±0.63*	15.00±0.40*	17.00±0.39*	20.00±0.66*

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Group	Week 3	Week 6	Week 9	Week 12
Co_Q10 (10mg)	9.70±0.23*	17.20±0.07*	17.78±1.74*	19.00±1.14*
Co_Q10 (5mg+TAA)	12.00±0.54*	15.00±0.49*	16.00±0.66*	20.00±0.18*
Co_Q10 (10mg+TAA)	11.20±0.26*	14.50±0.17*	17.00±0.36*	21.00±0.71*

Values represent mean ± SEM; n=5. *=significant when compared to that of TAA-only.

Table 3: Effects of Coenzyme Q10 on Macrophages (%) in Thioacetamide Poisoned Wistar Rats

Group	Week 3	Week 6	Week 9	Week 12
TAA- only	11.00±1.00	7.62±0.18	6.40±0.16	4.48±0.12
Control	2.40±0.07*	2.50±0.17*	2.50±0.07*	2.60±0.14*
Co_Q10 (5mg)	2.90±0.57*	2.82±0.14*	2.70±0.29*	2.40±0.07*
Co_Q10 (10mg)	2.60±0.16*	2.41±0.10*	2.60±0.21*	2.40±0.07*
Co_Q10 (5mg+TAA)	8.40±0.13*	6.80±0.25*	5.10±0.07*	3.20±0.07*
Co_Q10 (10mg+TAA)	6.90±0.29*	5.60±0.19*	4.08±0.12*	2.90±0.30*

Values represent mean ± SEM; n=5. *=significant when compared to that of TAA-only.

Table 4: Effects of Coenzyme Q10 on Tumor Necrotic Factor Alpha (TNFα) (pg/ml) in Thioacetamide Poisoned Wistar Rats

Group	Week 3	Week 6	Week 9	Week 12
TAA- only	24.00±0.35	29.00±0.57	33.00±0.65	37.00±0.40
Control	8.40±0.14*	8.30±0.10*	8.40±0.13*	8.50±0.17*
Co_Q10 (5mg)	8.90±0.29*	8.60±0.20*	8.50±0.17*	8.30±0.10*
Co_Q10 (10mg)	8.70±0.24*	8.50±0.18*	8.20±0.07*	8.00±0.13*
Co_Q10 (5mg+TAA)	11.50±0.18*	10.70±0.24*	10.10±0.16*	9.20±0.07*
Co_Q10 (10mg+TAA)	9.20±0.14*	9.10±0.16*	8.80±0.26*	7.70±0.22*

Values represent mean ± SEM; n=5. *=significant when compared to that of TAA-only.

The data on Table 2 displays the effects of Co-Q10 on neutrophil (NEUT) level in TAA poisoned rats.

It was found that the TAA-only treated groups significantly ($P<0.05$) reduced the neutrophil levels when compared to those of the control and Co-Q10 treated groups. In fact, while the decrease was progressive down the treatment weeks for the TAA-only groups while the other groups continuously increased as the weeks progressed.

Table 3 is showing the result on the effects of Co-Q10 on macrophages in TAA poisoned male Wistar rats.

The TAA-only treated group indicated significantly ($P<0.05$) raised macrophage levels when compared to those of the test groups and the control group across all respective treatment durations (weeks 3, 6, 9 and 12). Notably, it was seen that the raised macrophage level which was highest in week 3 of the TAA-only group gradually and progressively decreased down weeks 6, 9 and 12. Again, the Co-Q10 treatment in the TAA poisoned groups indicated dose-dependent decrease in the elevated level of macrophages.

Table 4 represents the effects of Co-Q10 on Tumor Necrotic Factor alpha (TNFα) (pg/ml) in TAA poisoned male Wistar rats.

The TNFα level was seen to be markedly ($P<0.05$) elevated in the TAA-only treated group when compared to those of the control and test groups respectively. And this elevation was also seen to be progressively higher down the treatment durations of weeks 3, 6 9 and 12. Further, the treatment with different doses of Co-Q10 in the TAA poisoned groups had dose—dependent reductions in their raised levels of TNFα.

DISCUSSION

As the search for natural sources of therapeutic agent increases [14], emphasis has been made on the identification of endogenous substances with therapeutic potentials [15, 16]. Such substances, like hair proteomics and secretases and others have been considered to possess significant therapeutic roles [15-17]. Coenzyme Q10's supplementation has also been insinuated to possibly exert some beneficial effects on a dysfunctional biological system [11-18]. Therefore, this present study explored and made some useful findings on the stabilizing attributes of Co-enzyme Q10 supplementation in thioacetamide (TAA) altered immuno-haematological system in Wistar rats and discussed them in the following paragraphs.

In this study, it was observed that administration of thioacetamide resulted in a remarkable decreases in WBC count and percentage of neutrophils, lymphocytes, monocytes, and considerable increase in macrophage and TNFα levels. These results are in line with some earlier reports [19, 20], that reported that TAA administration caused a decrease in red blood cells (RBC), hemoglobin (Hb), and hematocrit levels, while simultaneously leading to a significant increase in white blood cells (WBC) amongst others.

The effect of TAA as seen in the result of the present study was expected as it is known to elicit oxidative stress via lipid peroxidation on cellular membrane [21]. The foregoing attribute of TAA informed its choice by the present study in order to exert experimental model of a dysfunctional immuno-haematological system prior to the supplementation with Co-Q10.

Of course, low white blood cell count, may indicate immunosuppression or a lowered level of immunity that could be due to a number of conditions like cancer or its therapy [22, 23]. Thus the elevation of the TAA—depressed levels of WBC and neutrophils is an indication of the fact Co-Q10 may be acting via yet to be understood multiple mechanisms. It is established that to increase corpuscular volume including WBC, involve diet, medications, and supplementing vitamins [24]. The finding of the present study therefore portends that Co-Q10 supplementation may be of huge therapeutic value in especially haematological dysfunctional states.

The fascinating stabilization effects on the TAA elevated macrophage and TNFα levels following Co-Q10 treatment may be an indication that it could possess the potential to counteract the possible actions of the active oxygen species, collagenases, proteases, etc., [25], which are responsible for tissue necrosis. This possible exertion of anti-apoptotic and anti-inflammatory activities of Co-Q10 has also been suggested to be via redox-dependent mechanisms [26]. It could perhaps be a very promising anti-inflammatory agent for numerous necrotic models.

CONCLUSIONS

The marked reduction in WBC level and raised levels of macrophage and TNFα following TAA-poisoning in the study animals were stabilized/normalized by the supplementation with different doses of Co-Q10 (5mg/kg and 10 mg/kg) in a dose—dependent manner. The finding of the present study may be an indication that Co-Q10 as an endogenous ligand followed the "drug-receptor mechanism". It is suggestive that Co-Q10 supplementation may be of major therapeutic value in particularly haematological dysfunctional scenarios. Considering the beneficial outcome of the present study, clinical trials of Co-Q10 supplementation in similar disease models is recommended.

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