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The Influential Antioxidant Role Of Coenzyme Q10 and Dehydroepiandrosterone against Carbon Tetrachloride Induced Liver Damage In Male Rats

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Abstract: This study evaluated the protective role of exogenous CoQ10 and DHEA and their combination on CCl4-induced hepatotoxicity in adult male rats. Thirty adult male rats 225-250 grams, 12-14 weeks old, were used in this study and randomly divided into five equal groups, 6 animals each as in the following: Control group (G1): 6 male rats received DMSO 0.5ml/ animal/day orally, First treated group (T1): 6 male rats received daily CCl4 1ml/kg (1:1 olive oil, IP), Second treated group (T2): 6 male rats received CCl4 1ml/ kg and after 1 hour injected daily with CoQ10 200 mg/kg IP, Third treated group (T3): 6 male rats received CCl4 1ml/kg and after 1hour injected daily with DHEA 25 mg/kg IP, Fourth treated group (T4): 6 male rats received CCl4 1ml/kg and after 1hour injected daily with a combination of CoQ10 200 mg/kg + DHEA 25 mg/kg IP. The experiment lasted for 28 successive days. The obtained results illustrated that male rats received CCI4 (1ml/kg) caused a significant increase in hepatic enzyme function AST, ALT and ALP, as well as MDA levels, and caused a significant decrease in antioxidant enzyme activity GPx, SOD and CAT levels. In addition, CCl4 also caused various degrees of liver damage, such as dilation and congestion of the central vein with hemorrhage, apparent fatty degeneration and infiltration of inflammatory cells compared to the control group. Whereas, the group treated with CoQ10 200 mg/kg and DHEA 25 mg/kg showed a significant decrease (P< 0.05) in serum AST, ALT and ALP as well as MDA value, and significantly increased in GPx, SOD with the decline in CAT levels compared to the group treated with CCl4 intoxication. It is also observed from the results that the combination of CoQ10 and DHEA caused a highly significant (P < 0.05) decline in AST, ALT and ALP as well as MDA levels, and a significant elevate in GPx, SOD and decline in CAT, and almost return to average level compared to control. As well as, the histopathological examination of the liver revealed that rats treated with CoQ10 and DHEA and their combination had usual central veins and hepatocytes compared to groups treated with CCl4 due to antioxidant, anti-inflammatory and anti-apoptotic properties. It has been concluded that CoQ10 and DHEA have a protective effect against liver damage induced by CCl4 through improving antioxidant enzyme activity in CCl4 treated group leading to a declined MDA level and reduced lipid peroxidation. Thus, CoQ10 and DHEA are potential therapeutic antioxidant agents on hepatotoxicity by suppressing hepatic oxidative stress.

Key words: CoQ10, DHEA, antioxidant, CCl4, hepatic damage, male rat.

Introduction

Coenzyme Q10 (CoQ10) is an endogenous substance that acts as a vital antioxidant proposed for cellular membrane integrity by directly reacting with free radicals or regenerating another antioxidant¹. It is a lipid-soluble, vitamin-like substance required for the proper functioning of many organs and chemical reactions in the body². It has many beneficial effects on human and animal health, including cardiovascular disease, age-related disorders, neuromuscular and neurodegenerative disorders, autoimmune disorders, DNA damage, thyroid disorders, male infertility, cancers, diabetes, fibrosis, apoptosis, and obesity. It is an important redox and proton translocations constituent of the mitochondrial respiratory chain. It plays an essential role in mitochondrial energy production through redox activity in the electron transport chain, transporting electrons between enzymes. Thus, it plays an essential role in cellular bioenergetics and membrane stabilizer and production of ATP in the oxidative respiration process³. (4) demonstrated that CoQ10 has anti-inflammatory properties decreasing the production of pro-inflammatory cytokines such as interleukin (IL) and tumor necrosis factor (TNF- α).

Dehydroepiandrosterone (DHEA) is one of the most abundant endogenous circulating steroid hormones with multi-functional properties; it is produced in the adrenal glands, gonads, and brain, where it functions as a metabolic intermediate in the biosynthesis of androgen and estrogen sex steroids5. It plays a critical endogenous antioxidant and pro-oxidant activity. It can also protect against cell membrane lipid peroxidation (LPO) induced by oxidative damage⁶. DHEA also has anti-inflammatory properties via suppression of pro-inflammatory cytokines secretion like IL and TNF- α and regulating the body's immune response⁷. DHEA and DHEAS are products of cholesterol metabolism, with the first enzymatic reaction occurring in mitochondria and resulting from the action of cytochrome P450⁸. Cholesterol transport across mitochondrial membranes requires the action of steroidogenic acute regulatory protein (STAR) and converts cholesterol to pregnenolone9. This study aimed to evaluate the amelio-

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rative effect of CoQ10 and DHEA and their combination on hepatotoxicity induced by CCl4 in adult male rats.

Materials and methods

Drugs and chemical reagents

Norfloxacin was obtained from Zwijndrecht-Holland, CoQ10 200 mg and DHEA 25mg (Sigma, St. Louis, MO, USA) and administered intraperitoneally. Dimethylsulphoxide (DMSO) was purchased from Merck, Darmstadt, Germany.

Experimental animals

Thirty adult male rats (Rattus norvegicus) weighing 225-250 grams, 12-14 weeks old. The rats were housed in the animal house of Basrah's College of veterinary medicine/university. They were left for 2 weeks for an adaptation previous to the experiment. Each 6 animal was housed in a cage measuring $15 \times 35 \times 50$ cm and kept under an average temperature of 22 - 28 °C. The daily light period was 12 hours using two fluorescent lamps, and the humidity rate was about 50 %. Animals were provided with water and diet ad libitum.

Experimental Design and study strategy

After the acclimatization period, animals were randomly divided into five equal groups, 6 animals each, as in the following: Control group (G1): 6 male rats received DMSO 0.5ml/animal/day orally, First treated group (T1): 6 male rats received daily CCl4 1ml/kg (1:1 olive oil, IP), Second treated group (T2): 6 male rats received CCl4 1ml/kg and after 1hour injected daily with CoQ10 200 mg/kg IP, Third treated group (T3): 6 male rats received CCl4 1ml/kg and after 1hour injected daily with DHEA 25 mg/kg IP, Fourth treated group (T4): 6 male rats received CCl4 1ml/kg and after 1hour injected daily with a combination of CoQ10 200 mg/kg + DHEA 25 mg/kg IP. The experiment lasted for 28 successive days. All animals in the study were sacrificed at the end of the experiments. However, the rats before sacrifice were first weighed and then anesthetized by placing them in a closed beaker containing cotton sucked with chloroform for anesthesia. To take the samples, the abdominal cavity was opened through a midline abdominal incision. Blood samples were collected via cardiac puncture according to the method of (10). Then, blood samples were dropped directly from the heart using a 5 ml disposable syringe. The blood was put in the plane tube until coagulated, then centrifugated (3000 rpm for 15 minutes) to obtain the serum. The serum samples were separated into many Eppendorf tubes to avoid repeated thawing. All tubes were stored at (-4c) until they were analyzed.

Histopathological examination

Immediately were removed liver and kidneys and separated from surrounding tissues and lipids, then weighed with an electronic balance. Sorted liver fragments were collected from all groups and prepared and fixed using 10% formalin for histological examination according to 11 with the aid of the light microscope. The samples were fixated in natural buffered formalin 10% for 24-48 hours. They were put in the rotary microtome and were sliced by the microtome, steel blade into sections 5 micrometers thick. Sections were floated on a water bath (50-550 C) and then transferred into glass slides coated with Mayers albumin as an adhesive substance and left to dry. The histological section of organs was stained with Hematoxylin-Eosin stain and photomicro-

graphs were taken at 40X magnifications.

Statistical analysis

In this study, ANOVA Analysis and LSD tests are used according to (IBM SPSS, version 20) program at ($P \le 0.05$) to find the means for all treatments (IBM SPSS, 2011).

Results

Biochemical assessment

The results in Table 1 demonstrate that male rats who received CCl4 (1ml/kg) caused a significant increase (P< 0.05) in serum AST, ALT and ALP levels compared to the control group. Whereas the groups treated with CoQ10 200 mg/kg and DHEA 25mg/kg showed a significant decrease (P< 0.05) in serum AST, ALT and ALP levels compared to groups treated with CCI4 intoxication, but they were still high significantly (P< 0.05) compared to the control value. It is also clear from Table (1) that combination of CoQ10 and DHEA caused a highly significant declined in AST, ALT and ALP levels and almost returned to their normal level compared with the control value. However, results in Table (2) pointed out that male rats who received CCI4 showed a sharp, significant decrease (P< 0.05) in serum GPx and SOD value compared to the control group. Whereas the groups treated with CoQ10, DHEA, and a combination of CoQ10 and DHEA showed a significant increase (P< 0.05) in serum GPx and SOD levels compared to groups treated with CCl₄ intoxication, and they seem they reached statistically to GPx and SOD normal value compared to the control value.

In contrast, Table (2) also showed that male rats who received CCl_4 showed significant elevation (P< 0.05) in serum CAT value compared to the control group. Whereas the groups treated with CoQ10, DHEA and a combination of CoQ10 and DHEA showed a significant sharp decline (P< 0.05) in serum CAT values compared to groups treated with CCl4. However, they returned statistically to CAT normal value compared to the control value.

Lipid peroxidation assessment

According to the results obtained in Table (2), serum MDA concentration increased significantly (P<0.05) in male rats that received CCl4 compared to the control group. Whereas the group treated with CoQ10, DHEA and a combination of CoQ10 and DHEA showed a significant decrease (P< 0.05) in serum MDA value compared to the group treated with CCl₄, but they still high significantly (P< 0.05) compared with control value.

Histopathological studies

The results in Figure 2 pointed out that the male rats that received a CCl_4 dose (1mg/kg) caused various degrees of liver injury, such as dilation and congestion of the central vein with hemorrhage, evident fatty degeneration and infiltration of inflammatory cells after 28 days of exposure compared to the control group Figure 1. At the same time, the male rats treated with CoQ10, DHEA, and a combination of CoQ10 and DHEA showed usual central vein and hepatocytes compared to groups treated with Ccl4 intoxication (Figure 3, 4, and 5), respectively. It is also observed from Figure (5) that combination of CoQ10 and DHEA showed the best results with usual central vein and hepatocytes compared to control and other treated groups.

Parameters Groups	AST (U/L)	ALT (U/L)	ALP (U/L)
Control	57.21 ± 5.45	26.10 ± 2.75	112.4 ± 3.20
	С	с	d
CCl4 1ml/kg	92.73 ± 3.64	40.14 ± 3.06	163.2 ± 3.20
	а	а	а
CCl4 1ml/kg + CoQ10	73.72 ± 5.42	32.30 ± 3.38	134.1 ± 1.3
200 mg/kg	b	b	b
CCl4 1ml/kg + DHEA	75.74 ± 5.40	35.43 ± 3.37	136.1 ± 1.2
25 mg/kg	b	b	b
CCl ₄ 1ml/kg + Com-	63.76 ± 6.56	27.58 ± 3.39	122.1 ± 1.3
bination CoQ10 200	с	с	с
mg/kg + DHEA25			
mg/kg			
LSD	7.4	3.8	6.2

Table 1. The effect of CCI4 and the protective role of CoQ10, DHEA, and their combination on liver function enzymes of male rats for 28 days of exposure. Mean ± SD.

Parameters	MDA (µm / L)	GPx (µm / L)	SOD (µm / L)	CAT (IU/ml)
Groups				
Control	1.68 ± 0.30	78.4 ± 2.23	28.60 ± 2.20	2.40 ± 0.50
	С	b	b	b
CCl₄ 1ml/kg	10.25 ± 1.20	39.2 ± 1.30	12.34 ± 0.26	4.00 ± 0.30
	а	а	а	a
CCl ₄ 1ml/kg + CoQ10	6.51 ± 0.20	75.2 ± 2.23	28.80 ± 1.10	2.50 ± 0.60
200 mg/kg	b	b	b	b
CCl ₄ 1ml/kg + DHEA	6.55 ± 0.30	73.2 ± 2.25	28.56 ± 1.12	2.43 ± 0.52
25 mg/kg	b	b	b	b
CCl4 1ml/kg +	5.43 ± 0.30	77.2 ± 2.33	30.30 ± 1.40	2.37 ± 0.50
Combination CoQ10	b	b	b	b
200 mg/kg + DHEA25 mg/kg				
LSD	2.25	5.23	1.26	0.43

Small letters mean significant differences between treatments at (P < 0.05) Table 2. The effect of CCl4 and the protective role of CoQ10, DHEA, and their combination on antioxidant enzyme activities of male rats for 28 days of exposure. Mean \pm SD.



Figure 1. Liver of male rats treated with 0.5 DMSO as a control (H&E Stain, 100 X) observe normal central vein (A), and normal hepatocytes (B).



Figure 2. The liver of male rats treated with CCl4 (T1) for 28 days (H&E Stain, 400X) observed dilation and congestion of the central vein (A), evident fatty degeneration (B), and infiltration of inflammatory cells (C).



Figure 3. The liver of male rats treated with 1m/kg CCl4 + 200 mg/kg CoQ10 for 28 days (H&E stain, 100X) observe usual central vein (A), and normal hepatocytes (B).



Figure 4. The liver of male rats treated with 1m/kg CCl4 + 25 mg/kg DHEA for 28 days (H&E stain, 100X) observed normal central vein (A), and normal hepatocytes (B).



Figure 5. Liver of male rats treated with 1mg/kg CCl4 and a combination of 200 mg/kg CoQ10 + 25 mg/kg DHEA for 28 days (H&E Stain, 100X) observe usual central vein (A), and normal hepatocytes (B).

Discussion

It is clear from the results that CCI, intoxication caused a significant increase in serum levels of liver function enzyme AST, ALT and ALP activities in male rats may be clearly due to increased serum levels of MDA in this study, where increased lipid peroxidation led to depression in antioxidant and liver enzymes activity compared to the control group. This pointed to detrimental results of CCl4 on the liver, evidenced by an increase of AST, ALT and ALP, which indicate liver injury. Also, (12) have reported damaged liver after streptozotocin treatment, showing a decrease in serum AST, ALT and ALP activity. The CCI_4 hepatotoxicity may be affected in two ways, firstly by the incidence of inflammatory conditions and secondly by the direct toxic action of CCI, on liver cells. The utilization of CoQ10 significantly decreased levels of these enzymes compared to control and CCI, intoxicated groups. Similar results were reported by (13), who established the role of CoQ10 in hepatotoxicity induced by sodium arsenite in male rats; it also shows that hepatic enzymes are mainly responsive biomarkers directly concerned with existing cellular damage and toxicity due to they are located in the cytoplasm and are released into circulation after cellular damage. It has been known that the increase in AST, ALT and ALP are good indicators of impaired liver function. However, the hepatotoxicity induced by CCI, may be affected in two ways, firstly by the occurrence of inflammatory condition, and secondly by direct toxic action of CCI, on the liver cell through trichloromethyl-peroxyl free radicals leading to induce lipid peroxidation and destruction of Ca2+ homeostasis, finally results in cell death14. Other authors have shown that CoQ10 can elevate the level of AST, ALT and ALP after intoxication; this may be attributed

to CoQ10, which stabilizes hepatocytes' plasma membrane and prevent delivery of AST, ALT and ALP to extracellular fluid¹⁵. In contrast, Co-administration of CoQ10 with CCl, re-establish the AST, ALT and ALP activity in male rats as a sign of protecting the effect CoQ10 against liver injury induced by CCl₄ intoxication. (16) reported that CoQ10 characterized the liver as a target organ by distributing CoQ10 into different rat tissues. This effect may be related to powerful CoQ10 effectiveness in suppressing increased lipid peroxidation and the hepatocyte membrane's destruction in regenerating liver cells. Furthermore, CoQ10 shows signs of defense against hepatotoxicity by lower levels of TBARs and alanine release, leading to decreased hepatic enzyme activities¹⁷. This is agreed with (18), who mentioned that CoQ10 has a prophylactic effect against aflatoxin-B1-induced hepatotoxicity. Prophylactic effects of CoQ10 on metabolic stress by inhibition of apoptosis in hepatocytes¹⁹. However, (20), (21), and (22) mentioned that CoQ10 protects against metabolic stress-induced hepatotoxicity induced by acute acetaminophen, mainly probably through its antioxidant, anti-inflammatory, and anti-apoptosis effects. Moreover, CoQ10 shows the anti-inflammatory and antigenotoxic effect on 1,2-dimethyl hydrazine (DMH) induced leukocytic DNA damage in blood cells by direct inhibition and modulating gene expression of cyclooxygenase-2 activity (COXand inducible nitric oxide synthase (iNOS) in the colonic mucosa of male rats²³. In contrast, present results in at similar Table show that supplementation of DHEA with CCI, reduced serum levels of hepatic enzymes ALT, AST and ALP activities compared to control and CCl4 intoxicated groups. This pointed to a potential protective effect of DHEA against liver injury in adult male rats. While it is stated previously the supplementation with DHEA protects against hepatotoxicity in rats, it may be through its antioxidant, anti-inflammatory,

and anti-apoptosis effects²⁴. Similar results were given by (25). According to (26), the antioxidant role of DHEA may be associated with its active metabolites (DHEA-S), exposing cell membranes more resistant to being attacked by ROS. Moreover, liver tissue characterized the target organ for DHEA on considering circulation of DHEA into various rat tissues as reported previously by (27) after demonstrating copper-induced oxidative lipid peroxidation. These results may be associated with the efficiency of DHEA in suppressing the elevated lipid peroxidation and damage of cell membranes in restored liver cells of rats. The administration of CoQ10 by itself did not lead to a significant decrease in liver damage induced by CCl₄ intoxication. It seems from the above Table that the ameliorating effect of DHEA may be attributed to their antioxidant properties that would reduce lipid peroxidation by protecting cellular GSH content.

The results also clearly show that CCI, caused a significant decrease in the antioxidant enzymes GPx, SOD, and CAT activity in male rats compared to the control group. These results showed that CCl₄ causes clear changes in enzymatic GPx, SOD, and CAT constituents of antioxidants due to increased lipid peroxidation, which leads to depression in antioxidant enzyme activity. These results agree with (28) stated that SOD and CAT antioxidants enzymes act as protection agents from oxidative damage by scavenging ROS. (29) who showed that the effect of CCI, on cellular antioxidant defense system is the second mechanism for CCI induced oxidative stress by changes in antioxidant activities by inhibiting function SH groups in the SOD, CAT and GPx enzymes which generally protect against free radical toxicity. However, SOD is a first line of defense against oxygen free radicals and catalyzes superoxide anion radical (O2⁻⁻) into less toxic H₂O₂ and O₂, whereas CAT reduces H₂O₂ to non-toxic H₂O and O₂. The CCl₄ causes widespread oxidation leading to depletion of GSH, and decreased GSH and GPx activity are led to elevate oxidative damage to DNA, lipids and proteins. Generally, the decline of endogenous antioxidants by exposure to CCI, could be because CCI, has a very high affinity for glutathione. Therefore, exposure to CCI, decreases GSH levels due to either increased use of GSH by cells to act as scavengers of free radicals caused by toxic chemical agents or enhanced utilization of GSH by GPX under oxidative stress which results in increased lipid peroxidation. Also, exposure to CCI, decreases nitric oxide (NO) generation, and inhibition of NO synthesis leads to an apparent decrease in GSH synthesis through the down-regulation of the rate-limiting enzyme³⁰.

On the other hand, CoQ10 supplementation significantly increases endogenous antioxidant enzymes GPX, SOD and CAT, which may be due to its direct free radical scavenging activity and decrease in lipid peroxidation as compared to CCI, intoxicated groups. These results agreed with results obtained by (31), who stated that pretreatment with CoQ10 is related with preserving against isoproterenol induced cardiac hypertrophy in rats heart through decreased myocardial injury by protecting endogenous antioxidant and decreased lipid peroxidation. Whereas (32) concluded that CoQ10 is a powerful antioxidant either directly or indirectly against CCl₄ toxicity by suppressing oxidative stress, scavenging oxygen radicals, and inhibiting lipid peroxidation, thus increasing glutathione, GPX, SOD and CAT activities. The current study results agreed with results obtained by many researchers, such as (33) in their study on CoQ10 in adult males with fructose-induced metabolic syndrome, (34) in adult male albino rats fed on high cholesterol diet in

the cerebellar cortex. Ameliorating effect of CoQ10 on antioxidant enzymes in the present study may be attributed mainly to antioxidant action, which is known to supplement GSH and antioxidant enzyme levels and scavenge lipid peroxides.

The results of CCl₄ caused a significant increase in serum malondialdehyde (MDA) levels. The study results came in agreement with the results of other articles, such as (35),(36) and (37), which studied intraperitoneally administration of CCI, and toxicity effects on lipid peroxidation of male rats. The CCI, metabolism in the liver results in the generation of reactive metabolites like trichloromethyl (CCI3·) and trichloromethyl peroxy (CCI3OO·) radicals which initiate membrane peroxidation of unsaturated fatty acids and causes fatty liver, fibrosis and cell necrosis. (38) reported that the increase in oxidative stress and lipid peroxidation might be attributed to the depletion and reduction in hepatic GSH content, which has an essential and protective role against oxidative stress. Therefore, CCI, begins producing free radicals and induces lipid peroxidation in subcellular membrane structures and accumulation of ROS to inhibit the electron transfer respiratory chain in the mitochondria³⁹. However, (40) concluded that CCl₄-induced oxidative stress might be attributed to CCI,-inducing inflammation in tissue with the production of inflammatory mediators, which stimulates the generation of free radicals in tissue. It arises when hydroxyl radicals like oxygen react with membranes' unsaturated lipids resulting in lipid peroxide radicals (ROO•), lipid hydroperoxide (ROOH) generation, and disintegration generates, such as malondialdehyde41. Thus, increased levels of MDA in our study are a good indicator of oxidative stress and lipid peroxidation caused by CCI, intoxication. Co-administration of CoQ10 with CCl₄ resulted in a significant reduction in the malondialdehyde level. These results indicate that CoQ10 has potent antioxidant activity, as obviously by malondialdehyde reduction. The protective role of CoQ10 against CCI,-induced oxidative stress may be attributed to its potent free radical scavenger activity and inhibit lipid peroxidation or to the regulation of oxidative phosphorylation and prevention of lipid peroxidation. Also, it can normalize endothelial function by combining oxidative phosphorylation in mitochondria and endothelial nitric oxide synthesis activity⁴². Furthermore, (43) and (44) demonstrate that CoQ10 decreased the production of ROS, which changes redox balance in cells toward oxidative stress under inflammatory conditions due to its anti-inflammatory and immuno-modulatory action through suppression release and generation of pro-inflammatory cytokine from the cell and increase of anti-inflammatory cytokine mediators such as TNF- α and IL-10. The results also showed that DHEA supplementation reduced the oxidative stress and lipid peroxidation induced by CCI₄ toxicity. This was detected by potent antioxidant actions by decreasing MDA levels. (45) demonstrate that reduced MDA concentration may be related to the antioxidant activity of DHEA to inhibit definite enzymes occupied in free radicals formation. Moreover, the ameliorating effect of DHEA against oxidative stress may be attributed to antioxidant properties that would reduce lipid peroxidation by protecting cellular GSH content⁴⁶. The antioxidant role of DHEA may be associated with its active metabolites (DHEA-S), exposing cell membranes more resistant to being attacked by ROS. However, DHEA inhibits NADPH level, a substrate essential for NADPH oxidase reaction to generate O-from O• by inhibiting glucose-6-phosphate dehydrogenase (G-6-PDH). (47) demonstrate that DHEA exerts antioxidant and anti-inflammatory role by reducing tissue susceptibility to the oxidation of both lipid and protein and improving endothelial function, which changes redox balance in cells toward oxidative stress under inflammatory condition due to it has anti-inflammatory and immune modulation properties through suppression release and generation of pro-inflammatory cytokine from cell and increase of anti-inflammatory cytokine mediators such as TNF- α and IL- 6 and IL-10.

It is clear from the results that CCI4 toxicity caused various degrees of liver injury in treated male rats, such as dilation and congestion of the central vein, apparent fatty degeneration of hepatocytes, and infiltration of inflammatory cells after 28 days of exposure compared to the control group. These results followed those obtained by many researchers, such as (48,49,50,51,52,53,54), who studied intraperitoneally administration of CCI,-induced liver damage and hepatotoxicity. The metabolism of CCI, in the liver results in the generation of reactive metabolites like trichloromethyl (CCI3·) and trichloromethyl peroxy (CCI3OO·) radicals which initiate membrane peroxidation of unsaturated fatty acids and causes fatty liver fibrosis and cell necrosis⁵⁵. Conversely, supplementation of CoQ10, DHEA and a combination of CoQ10 and DHEA caused reduced changes. It restructured reliability with the standard architecture of the liver, which may be attributed to antioxidant, anti-inflammatory, and anti-apoptotic activities compared to CCI, intoxicated groups. The pretreatment with CoQ10 and DHEA improved of degeneration effect with inhibited inflammatory infiltration and nearly restored them to normal architecture, possibly due to prevented CCI, conversion into its reactive metabolites like trichloromethyl (CCI3·) and trichloromethyl peroxy (CCI3OO·) radicals, reduced oxidative stress with scavenging its free radical, and protected hepatic antioxidant enzymes activities⁵⁶.

Conclusions

The group treated with CoQ10 200 mg/kg and DHEA 25 mg/kg showed a significant decrease (P< 0.05) in serum AST, ALT and ALP as well as MDA value and a significantly increased in GPx, SOD with a decline in CAT levels compared to the group treated with CCl4 intoxication. It is also observed from the results that the combination of CoQ10 and DHEA caused a highly significant (P < 0.05) decline in AST, ALT and ALP as well as MDA levels, and a significant elevate in GPx, SOD and decline in CAT, and almost return to average level compared to control. As well as, the histopathological examination of the liver revealed that rats treated with CoQ10 and DHEA and their combination had normal central veins and hepatocytes compared to groups treated with CCl4 due to antioxidant, anti-inflammatory and anti-apoptotic properties. It has been concluded that CoQ10 and DHEA have a protective effect against liver damage induced by CCl4 through improving antioxidant enzyme activity in CCl4 treated group leading to a declined MDA level and reduced lipid peroxidation. Thus, CoQ10 and DHEA are potential therapeutic antioxidant agents on hepatotoxicity by suppressing hepatic oxidative stress.

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