

## Hepatoprotective effect of Co-enzyme Q10 in rats treated with Hydrogen Peroxide

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### التأثير الوقائي للأنزيم المساعد Q10 في كبد الجرذان المعاملة بيروكسيد الهيدروجين

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#### المستخلص

اجريت هذه الدراسة لمعرفة دور الـ Co enzyme Q10 من خلال تحسين ومنع الاذى الحاصل نتيجة الاجهاد التأكسدي المستحدث في كبد الجرذان بواسطة جرعة عالية من بيروكسيد الهيدروجين . تم اختيار 24 من ذكور الجرذان المختبرية قسمت عشوائيا الى ثلاثة مجاميع متساوية . المجموعة الاولى عدت مجموعة سيطرة ، والمجموعة الثانية اعطيت 0.75 % بيروكسيد الهيدروجين في ماء الشرب لمدة 30 يوم ، اما المجموعة الثالثة جرعت يوميا بـ Co enzyme Q10 بجرعة 1 ملغم / جرد لمدة 30 يوماً بالاضافة الى بيروكسيد الهيدروجين 0.75 % . تم قياس مستوى الدهون في المصل وانزيمات الكبد ALT ,AST مع دراسة التغيرات النسيجية الحاصلة في الكبد . أظهرت الدراسة تغيير واضح في مستوى الدهون في المجموعة الثالثة التي تم تجريعها بـ CoQ10 المتمثل بأنخفاض معنوي ( $P<0.05$ ) الكوليستيرول الكلي ، الدهون الثلاثية ، البروتين الشحمي واطى الكثافة ، والبروتين الشحمي ذات الكثافة الواطنة جدا مع زيادة في البروتين الشحمي عالي الكثافة . كذلك أظهرت النتائج انخفاض معنوي ( $P<0.05$ ) في تركيز انزيمات الكبد المتمثلة بـ ALT, AST في مصل الحيوانات المعاملة بـ CoQ10 مقارنة مع تركيزها في المجموعة المعاملة بيروكسيد الهيدروجين . أظهرت المقاطع النسيجية بان بيروكسيد الهيدروجين قد احدث افات مرضية مثل تجمع خلايا احادية النواة ، ارتشاح الخلايا الالتهابية ، تغيرات دهنية خفيفة مع تفجى سايتوبلازم الخلايا الكبدية . ومن جهة اخرى التجريع اليومي بـ CoQ10 للمجموعة الثالثة ادى الى اختفاء التغيرات المرضية ، نستنتج من نتائج هذه الدراسة من إمكانية كسح الجذور الحرة ومنع الاذى الناتج عنها باستخدام Co enzyme Q10

الكلمات مفتاحية: الدهون الثلاثية, انزيمات الكبد , بيروكسيد الهيدروجين

#### Abstract

This study was carried out to investigate the role of Co enzyme Q10 in ameliorating the deleterious effect of oxidative stress induced by a high dose of Hydrogen peroxide. Twenty four male rats were divided into three equal groups. One served as control and Group1 treated with 0.75% H<sub>2</sub>O<sub>2</sub> in drinking water for one month, and Group2 administered orally Co Q10 with daily dose 1 mg /rat for 30 days. To assess the effect of H<sub>2</sub>O<sub>2</sub> in drinking water with Co Q10 on the lipid profile, ALT, AST and histological changes were recorded. The present study demonstrated a clear alteration in the lipid profile of G2 and significant ( $P<0.05$ ) decrease in serum TC, TAG, LDL-c and VLDL-c and increase the HDL-c . also the result exhibit significant ( $P<0.05$ ) reduction in serum ALT and AST concentration in animal treated with Co Q10 comparing with the values in G1. Histological section of liver revealed that H<sub>2</sub>O<sub>2</sub> initiate pathological lesion such aggregation mononeuclear cell, infiltration of inflammatory cell, moderate fatty change and cytoplasmic vaculation ,on the other hand, oral administration of Co Q10 completely regressed these lesion. In conclusion, the result of this study clarified the possibility of induction oxidative stress in rats in 30 days provided by 0.75% H<sub>2</sub>O<sub>2</sub>, and ameliorating the oxidative stress effect of H<sub>2</sub>O<sub>2</sub> by administration of Co Q10.

**Key word: Coenzyme q10, ALT, AST, Hydrogen peroxide**

## **Introduction**

The term "free radicals" refers to any chemical species possessing one or more unpaired electron in the outer orbital (1). Radicals are generated at the initiation step, then they react in a series of propagation steps in which the number of free radicals are conserved and termination ensure the destruction of the radicals (2). Free radicals are created as a consequence of adenosine triphosphate (ATP) production by the mitochondria, these are generally reactive oxygen species (ROS) as well as reactive nitrogen species (RNS). Free radicals and oxidants which characterized in their ability to react with / and modify all kinds of macromolecules; play a dual role as both toxic and beneficial compounds, since they can be either harmful or helpful to the body (3). They are produced either from normal cell metabolism or from external sources such as pollution, cigarette smoke, radiation and medication (4). Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) is one of the major forms of ROS is reduced to highly reactive hydroxyl radical (OH $\cdot$ ). Increase reactive species lead to oxidative stress (5), which is associated with oxidation of LDL-c which might be a crucial important step in the initiation and pathogenesis of atherosclerosis and other diseases (4, 6). Co enzyme Q10 is the co-enzyme for mitochondrial enzyme complexes involved in oxidative phosphorylation in the production of ATP (7). This bioenergetics effect of Co q10 is believed to be of fundamental importance, particularly in cell with high metabolic demand such as cardiac myocytes in addition to antioxidants function (8). The objective of this study to determine the protective effect of CO q10 against oxidative stress induced experimentally by H<sub>2</sub>O<sub>2</sub> in male rats depending on measuring lipid profile and liver transaminase enzyme.

## **Materials and methods**

### **Co-enzyme Q10**

Co enzyme Q10 was purchased from Vitane Pharmaceutical company (Karooose company/ Iraq), USA.

### **Experimental design**

Twenty four mature albino rats of the Wister strain (200 – 250 mg) were used in this study. The experimental animals were housed 8 per cage in a room with 12 / 12 h. light / dark cycle at ambient temperature of 25  $\pm$  1 C. The rats were randomly divided into three groups of 8 each. Rats of group1 served as control, fed with standard diet and had free access to water for 30 days. Rats of group2 treated with 0.75 % H<sub>2</sub>O<sub>2</sub> (9) in drinking water for 30 days and finally group 3 treated with 0.75% H<sub>2</sub>O<sub>2</sub> in drinking water and administrated orally with 1 mg/ rat Co enzyme Q10 daily for 30 days(10).

### **Blood sampling**

Blood samples were collected from fasting experimental animals (10-12 h.), Blood was drawn via cardiac puncture technique using disposable medical syringe (5 ml.)

Blood samples were kept into sterilized tubes, held for not more than 2 hours before collecting serum by centrifugation (3000 rpm) for 15 minutes and frozen at -18 C for biochemical testes

### **Biochemical testes**

#### **Serum alanine aminotransferase (ALT)**

Serum ALT activity was enzymatically measured using standard assay (Biomagreb chemical-kit) based on the fact that glutamic transaminase enzyme catalyze the transfer of the amino group of glutamic acid to pyruvic acid in reversible reaction (11).

#### **Serum aspartate aminotransferase (AST)**

Serum AST activity was enzymatically measured using standard assay (Biomagreb chemical-kit) based on the fact that glutamic transaminase enzyme, catalyze the transfer of the amino group of Aspartic acid to 2-Oxoglutarate acid in reversible reaction (11).

#### **Determination of total cholesterol (TC) mg / dl**

Serum TC concentration was enzymatically measured using standard assay (cholesterol kit- Linear chemical) (12).

#### **Determination of serum triacylglycerol (TAG) mg/dl**

Enzymatic estimation of serum triacylglycerol concentration was carried out by using a linear chemical kit(12).

#### **Determination of serum high density lipoprotein–c (HDL-c) concentration (mg/dl)**

Serum HDL-c concentration was measured enzymatically (HDL-c Kit-Linear chemical)(12) .

#### **Determination of serum Low density lipoprotein –c (LDL-c) concentration (mg/dl)**

Serum LDL-c concentration was calculated by Friedewald formula (13).

#### **Determination of serum Very Low density lipoprotein –cholesterol (VLDL-c ) concentration (mg/dl)**

Serum VLDL-c concentration was calculated dividing serum triglyceride by five (13).

### **Histological examination**

For a histological examination, rats were killed by withdrawal of blood from the heart immediately after death; the liver was excised, blotted, opened longitudinally and preserved in 10% natural formalin buffer solution till preparation of the histological section. Several tissues section were prepared and stained with hematoxyline-Eosin

(H&E) stain according to the methods as described by Bancroft and Stevens (1982) method (14).

### Statistical analysis

The statistical analysis of data was performed by using SPSS on the bases of Two Way Analysis Of Variance (ANOVA) depending on the experimental design, at each time specific group differences were determined using less significant differences (LSD)  $P \leq 0.05$  (15).

## Results

### Lipid profile

#### Total cholesterol

The concentration of serum total cholesterol (mg / dl) in all treated groups was explained in table (1). The table showed no significant ( $p > 0.05$ ) differences in the mean of TC concentration between all experimental groups at zero time and 15 days of treatment. The TC concentration increased significantly ( $P < 0.05$ ) in group 1 ( $98.52 \pm 3.2$ ) that treated with  $H_2O_2$  comparing to the all treated groups at the day 30 of experiment .Within the time , significant ( $P < 0.05$ ) increment in the value of TC concentration was observed in group 1 comparing to the mean value at zero and 15 days.

#### Triacylglycerid (TAG)

According to the result demonstrated in the table (2) there were no significant ( $p > 0.05$ ) difference in mean value of TAG concentration between the experimental groups in pretreatment period , while there was a significant ( $P \leq 0.05$ ) increase in the concentration of serum TAG was detected in the day 30 in group 1 ( $72.65 \pm 2.3$ ) treated with  $H_2O_2$  comparing to the control ( $60.80 \pm 1.65$ ) and group2 ( $66.35 \pm 2.15$ ) also there were significant ( $P < 0.05$ ) difference between group1 and group 2 that treated with  $H_2O_2$  plus Coq10 at the end of experiment. Also there were significant increase ( $P < 0.05$ ) in the TAG concentration in group 1 and group 2 when compared with zero time and 15 days of experiment .

#### High density lipoprotein –cholesterol

Table (3) clarified the mean value of HDL-c concentration in treated groups . From the result , there were no significant ( $P > 0.05$ ) deference in the concentration of HDL-c at zero time and 15 days of experiment between all treated groups , while there were significant ( $P < 0.05$ ) decrease in the concentration of HDL-c in group 1 ( $23.4 \pm 1.60$ ) and group2 ( $26.50 \pm 1.06$ ) when they compared with control ( $31.77 \pm 1.59$ ) at the end of experiment (day 30). Also, within the time, there were significant ( $P < 0.05$ ) decrease in HDL-c concentration in group 1 and group 2 comparing to the value in zero time and 15 days of treatment.

#### Low density lipoprotein –cholesterol

The concentration of serum LDL-c (mg/dl) in rats treated with  $H_2O_2$  and Co enzyme Q10 was clarified in table (4). There were no significant ( $P < 0.05$ ) differences in LDL-c concentration between experimental groups in the zero time. after 30 days a

significant ( $P > 0.05$ ) increase in LDL-c concentration were detected in group1 with mean value ( $60.59 \pm 1.14$ ) comparing to control ( $44.83 \pm 0.77$ ) and group2 ( $49.58 \pm 0.27$ ) that treated with Co q10 plus H<sub>2</sub>O<sub>2</sub>. On the other hand, a significant ( $P > 0.05$ ) elevation in the mean value of LDL-c concentration was recorded in group1 as compared with the pretreatment period.

### Very low density lipoprotein–cholesterol

Depending on the result clarified in table (5), there was no significant ( $P < 0.05$ ) differences in mean value of serum VLDL-c concentration at zero time in all experimental groups. However, significant ( $P > 0.05$ ) elevation in serum VLDL-c in group 1 ( $14.53 \pm 0.46$ ) after 30 days of exposure to H<sub>2</sub>O<sub>2</sub> comparing to control ( $12.16 \pm 0.33$ ) and group 2 ( $13.27 \pm 0.43$ ) because oral intubation of Co Q10 caused significant depression in VLDL-c concentration. Within the time, the results also clarified that there was significant ( $P > 0.05$ ) elevation in concentration of VLDL-c of group1 comparing to the zero time.

**Table (1): Effect of CoQ10 on total cholesterol mg / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

Group Time	Control	Group1 (H <sub>2</sub> O <sub>2</sub> )	Group2 (H <sub>2</sub> O <sub>2</sub> )+COQ10
Zero time	$87.25 \pm 2.2$ Aa	$86.35 \pm 1.80$ Aa	$87.89 \pm 2.1$ Aa
15 days	$87.67 \pm 1.9$ Aa	$90.66 \pm 2.6$ Aa	$88.37 \pm 1.76$ Aa
30 days	$88.76 \pm 2.69$ Aa	$98.52 \pm 3.2$ Bb	$89.35 \pm 1.76$ Aa

Capital letter denote a significant differences between groups. Number represent (mean  $\pm$  SE) .

Small letter denote a significant difference within group.

**Table (2): Effect of CoQ10 on triacylglycerid mg / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

Group Time	Control	Group1 (H <sub>2</sub> O <sub>2</sub> )	Group2 (H <sub>2</sub> O <sub>2</sub> )+COQ10
Zero time	$58.37 \pm 1.19$ Aa	$60.25 \pm 1.44$ Aa	$59.80 \pm 0.95$ Aa
15 days	$60.40 \pm 2.16$ Aa	$63.76 \pm 1.84$ Aa	$61.85 \pm 1.7$ Aa
30 days	$60.80 \pm 1.65$ Aa	$72.65 \pm 2.3$ Bb	$66.35 \pm 2.15$ Cb

Capital letter denote significant difference between groups. Number represent (mean  $\pm$  SE) .

Small letter denote a significant differences within group.

**Table (3): Effect of CoQ10 on high density lipoprotein HDL-c mg / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

<b>Group</b> <b>Time</b>	<b>Control</b>	<b>Group1</b> <b>(H<sub>2</sub>O<sub>2</sub>)</b>	<b>Group2</b> <b>( H<sub>2</sub>O<sub>2</sub>)+COQ10</b>
Zero time	31.15 ± 1.95 Aa	30.86 ± 1.15 Aa	30.60 ± 0.95 Aa
15 days	32.95 ± 1.50 Aa	28.20 ± 1.67 Aa	28.80 ± 1.16 Aa
30 days	31.77 ± 1.59 Aa	23.4 ± 1.60 Bb	26.50 ± 1.06 Ca

Capital letter denote significant difference between groups. Number represent (mean ± SE) .

Small letter denote a significant differences within group.

**Table (4): Effect of CoQ10 on low density lipoprotein LDL-c mg / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

<b>Group</b> <b>Time</b>	<b>Control</b>	<b>Group1</b> <b>(H<sub>2</sub>O<sub>2</sub>)</b>	<b>Group2</b> <b>( H<sub>2</sub>O<sub>2</sub>)+COQ10</b>
Zero time	44.43 ± 0.05 Aa	43.44 ± 0.45 Aa	45.33 ± 0.96 Aa
15 days	42.64 ± 0.03 Aa	49.71 ± 0.56 Bb	47.20 ± 0.27 Aa
30 days	44.83 ± 0.77 Aa	60.59 ± 1.14 Bc	49.58 ± 0.27 Cb

Capital letter denote significant difference between groups. Number represent (mean ± SE) .

Small letter denote a significant differences within group.

**Table (5) Effect of CoQ10 on very low density lipoprotein LDL-c mg / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

<b>Group</b> <b>Time</b>	<b>Control</b>	<b>Group1</b> <b>(H<sub>2</sub>O<sub>2</sub>)</b>	<b>Group2</b> <b>( H<sub>2</sub>O<sub>2</sub>)+COQ10</b>
Zero time	11.67 ± 0.24 Aa	12.05 ± 0.29 Aa	11.96 ± 0.19 Aa
15 days	12.08 ± 0.43 Aa	12.75 ± 0.37 Aa	12.37 ± 0.34 Aa
30 days	12.16 ± 0.33 Aa	14.53 ± 0.46 Bb	13.27 ± 0.43 Aa

Capital letter denote significant difference between groups. Number represent (mean ± SE) .

Small letter denote a significant differences within group.

**Liver enzymes****Alanine aminotransferase (ALT) IU/L**

Table (6) demonstrated the mean value of ALT activity in control and treated groups. There was no significant ( $P > 0.05$ ) differences in the mean value of ALT activities between all treated groups in pretreated period. While there were significant ( $p < 0.05$ ) increment in ALT activity in group 1 ( $144.72 \pm 8.11$ ) and group 2 ( $127.4 \pm 8.7$ ) when they compared with control ( $111.77 \pm 9.60$ ) after 30 day from treatment. Within the time, also, there was significant ( $P < 0.05$ ) increased in ALT activity in group1 and group2 comparing to the zero time and 15 days of treatment.

**Aspartate aminotransferase (AST)**

Table (7) illustrates the results of serum AST concentration in male rats throughout the experimental period. At zero time there were no significant ( $P > 0.05$ ) differences in AST concentration between all treated groups, while, the statistical analysis revealed significant increase ( $P < 0.05$ ) in AST concentration of group1 male rats ( $105.70 \pm 7.65$ ) compared with control ( $83.66 \pm 9.6$ ), and group 2 ( $90.75 \pm 6.87$ ). Also, there were significant ( $P < 0.05$ ) increase in AST concentration in group1 treated with 0.75%  $H_2O_2$  comparing with result in zero time and 15 days of treatment.

**Table (6): Effect of CoQ10 on alanine aminotransferase (ALT) IU / dl in albino rats treated with  $H_2O_2$**

Group Time	Control	Group1 ( $H_2O_2$ )	Group2 ( $H_2O_2$ )+COQ10
Zero time	$110.25 \pm 7.15$ Aa	$114.70 \pm 8.5$ Aa	$113.15 \pm 9.34$ Aa
15 days	$112.65 \pm 6.75$ Aa	$120.50 \pm 10.25$ Aa	$115.6 \pm 9.82$ Aa
30 days	$111.77 \pm 9.60$ Aa	$144.72 \pm 8.11$ Bb	$127.4 \pm 8.7$ Cb

Capital letter denote significant difference between groups. Number represent (mean  $\pm$  SE) .

Small letter denote a significant differences within group.

**Table (7): Effect of CoQ10 on aspartate aminotransferase (AST) IU / dl in albino rats treated with H<sub>2</sub>O<sub>2</sub>**

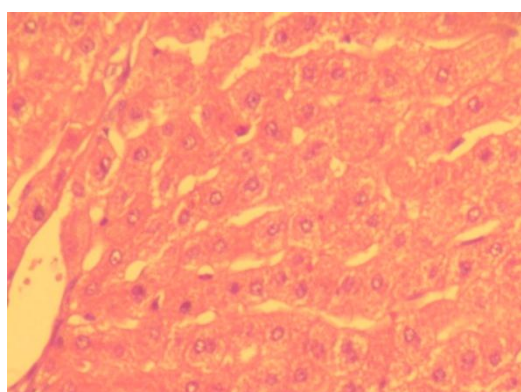
Group Time	Control	Group1 (H <sub>2</sub> O <sub>2</sub> )	Group2 (H <sub>2</sub> O <sub>2</sub> )+COQ10
Zero time	84.65 ± 7.6 Aa	81.36 ± 5.85 Aa	79.85 ± 6.72 Aa
15 days	80.5 ± 5.9 Aa	84.22 ± 8.65 Aa	82.48 ± 5.43 Aa
30 days	83.66 ± 9.6 Aa	105.70 ± 7.65 Bb	90.75 ± 6.87 Aa

Capital letter denote significant difference between groups. Number represent (mean ± SE).

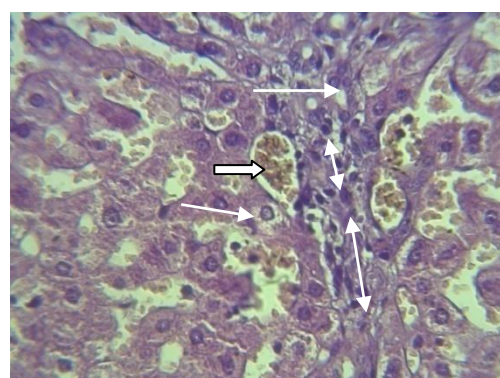
Small letter denote a significant differences within group.

### Histological examination

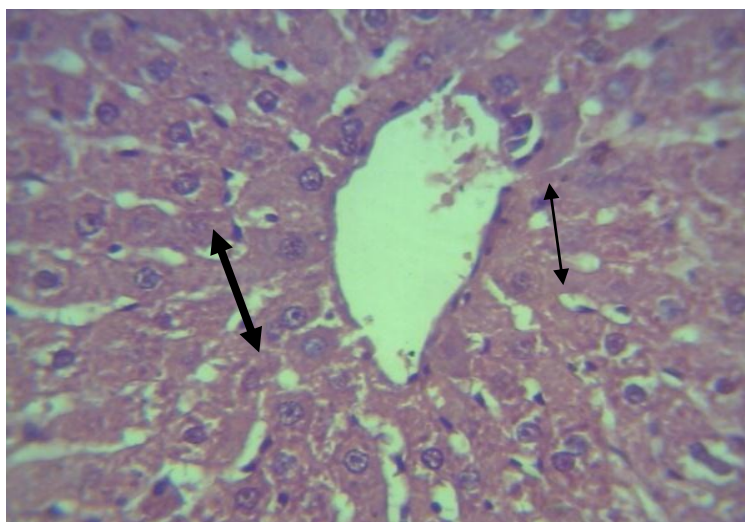
Figure (1) revealed microscopic section in liver of rats of control group. The microscopic examination of the liver in male treated with 0.75% H<sub>2</sub>O<sub>2</sub> in drinking water for 30 days shown hemorrhage and moderate fatty change, aggregation of mononuclear cell around blood vessels and inflammatory cells infiltration mainly macrophage in liver parenchyma, as well as cytoplasmic vacuolization and dilatation of sinusoid ( Fig. 2). While there were no clear pathological lesion and normal architecture of liver parenchyma in rats of group2 that treated with Co enzyme Q10 in addition to H<sub>2</sub>O<sub>2</sub> (Fig.3).



**Figure (1):** histological section of liver in control group, show normal architecture of liver parenchyma (H&E X40)



**Figure (2):** Histological section of liver in group1 animals treated with H<sub>2</sub>O<sub>2</sub>. revealed infiltration of inflammatory cell in liver parenchyma ( ↔), moderate fatty changes and aggregation of mononuclear cell around blood vessels ( →) and congested blood vessels ( ➡) (H&E X40)



**Figure (3): Histological section of liver in group2 animals treated with H<sub>2</sub>O<sub>2</sub> plus Co enzyme Q10 shown no clear pathological lesion only very moderate fatty change ( ←→ ) (H&E X40) .**

## Discussion

### Lipid profile

ROS or free radical in biological system can be formed by prooxidative enzyme system, lipid peroxidation, irradiation, inflammation, smoking and air pollutant (16, 17). The result of this experiment revealed that incidence of lipid profile significantly increased represented by TC, TAG, LDL-c, VLDL-c, in parallel to significant decrease in the level of HDL-c in group treated with H<sub>2</sub>O<sub>2</sub>. This result documented the well-known fact that H<sub>2</sub>O<sub>2</sub> is one of the reactive oxygen species which has a direct effect on the level of plasma TC, TAG and atherogenic lipoprotein. The results of this study are accordance with the results of other worker (18,19,20). Such changes in serum lipid may reflect the suppression of lipid metabolism due to H<sub>2</sub>O<sub>2</sub> induced oxidative stress and there might be a dynamic alteration in the process of absorption and exertion of steroid or there was reduction in bowel bile salts (21,22). Partial deficiency of lipoprotein lipase (the Key enzyme determining the removal rate of TG from plasma) associated with increased output of lipoprotein from the liver may contribute to the elevation of serum TG level in H<sub>2</sub>O<sub>2</sub> treated group (23). Besides, increment of TAG level in animal received H<sub>2</sub>O<sub>2</sub> in the present study may be due to an increase in serum VLDL-c level which acts as a carrier for the TAG in the plasma. (24). From the result of the present study showed that one month of administration rats with Co enzyme q10 was effective in improving serum lipid profile in rate treated H<sub>2</sub>O<sub>2</sub> compared with control level. Co q10 carried in the blood with low density lipoprotein and serve to diminish the oxidation of LDL-c in settings of oxidative stress (25). The relationship between oxidative stress and cholesterol level was confirmed in many studies (26,27). The reduction in the lipid level and increase in HDL-c level may be due to inhibition of LDL-c oxidation and reduce oxidative stress. Moreover, Modi *et al.*, 2006a&b (28, 29) showed that the treatment with Co q10

producing significant decreases in the elevated levels of serum cholesterol, triglycerides, VLDL-c, LDL-c and increased HDL-c level in diabetic treated rats.

### Liver enzyme

Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) enzymes are commonly employed as a biological marker for hepatic and heart injury and muscle damage. Our results demonstrated that H<sub>2</sub>O<sub>2</sub> treated rats (group1) revealed a significant increase in serum ALT and AST. Mechanism of increased activity of enzyme in serum may indicate a leakage of enzyme from damaged cell. Beside, release of liver enzyme from can occur secondary to cellular necrosis with membrane damage (30), because hydrogen peroxide has important roles in oxidative damage and carcinogenesis, since it is stable and diffuse easily through biological membrane. Thus reaching other cellular compartments, further producing cellular injury, especially if it becomes converted to highly reactive OH<sup>•</sup> (31). Also, the results revealed that treatment of rats in group2 H<sub>2</sub>O<sub>2</sub> with Co enzyme Q10 lead to decrease ALT and AST serum concentration. This meaning that CoQ10 protect the membrane of hepatocytes from free radical damage. Previous studies showed the therapeutic effect of CoQ10 on the metabolic stress by inhibition of apoptosis in hepatocytes (32). Moreover, it was revealed that CoQ10 through its antioxidant, anti-inflammatory, and antiapoptotic effect could have a role in improvement of acetaminophen induced toxicity. These effects were assumed to be able to attenuate the cyclooxygenase activity (33). In this study, administration of CoQ10 in H<sub>2</sub>O<sub>2</sub>-induced liver damage in rat models showed its beneficial effects as a hepatoprotective agent.

### Histological examination

Hydrogen peroxide induced the generation of hydroxyl radical in the liver which may be responsible for the induction of oxidative stress (34). Hydrogen peroxide as a stress inducer ROS caused a variety of cell and tissue damage. Exposure of hepatocytes to exogenous oxidants including H<sub>2</sub>O<sub>2</sub> can induce both apoptotic and necrotic cell death (35). There were no clear pathological lesion and normal architecture of liver parenchyma in rats of group2 that treated with Co enzyme Q10 in addition to H<sub>2</sub>O<sub>2</sub> (Fig.3). This meaning that CoQ10 protect the membrane of hepatocytes from free radical damage. Previous studies showed the therapeutic effect of CoQ10 on the metabolic stress by inhibition of apoptosis in hepatocytes (32). Moreover, it was revealed that CoQ10 through its antioxidant, anti-inflammatory and antiapoptotic effect could have a role in improvement of acetaminophen induced toxicity (33).

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