# Efficiency of some Antioxidants in Reducing Cardio-Metabolic Risks in Obese Rats

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**Abstract:** This investigation focuses on the relationship between the obesity and cardiovascular diseases (CVD) and the possible amelioration effects of taurine or quercetin and their mixture on cardio-metabolic risks in obese rats. In a preliminary trial, the changes in selected biochemical blood variables which are thought to represent risk factors coincident with obesity were compared between a group of normal control male albino rats and other group suffered from obesity induced by feeding rats on fatty diet (fat 50 % diet). Also, in this study, the effects of two antioxidant nutrients on the same variables were tested and followed in order to show to what extent, these nutrients are valid to control the levels of these variables without any deleterious effects after treatment. Taurine or quercetin was daily received orally for two and four weeks in two groups of obese rats in the following doses 50 mg taurine /100g b.wt/day and 25 mg quercetin /kg b.wt/day, respectively. Another group of obese rats was getting a combination of previous mentioned nutrients. While, an obese rats group was left without any treatment and called as recovery group. All these groups were compaired with healthy rats group (Normal control rats group). Fasting blood samples were drawn at 2 & 4 weeks after the terminal of the treatments. In the first experiment, the obtained results revealed that induced obesity caused significant ($p<0.001$) increase of serum cholesterol, triglycerides, low density lipoprotein-cholesterol (LDL-Ch), aspartate aminotransferase (AST), creatin kinase (CK), lactate dehydrogenase (LDH), resistin, endothelin-1, asymmetric dimethyl arginine (ADMA) and tumor necrosis factor-α (TNF- α) as compared with their relevant level in normal control rats group. On the other hand, induced obesity in rats caused significant ($p<0.001$) decrease the levels of serum total triiodothyronine (T3) and of total nitric oxide (TNO). No remarkable changes were occurred in the concentrations of serum high density lipoprotein-cholesterol (HDL-Ch) and total thyroxin (T4). In the second experiment, the authors studied the beneficial treatment of obese rats with taurine or quercetin and their mixture for 2 & 4 weeks. A marked correction was occurred in all previous parameters depending on the time of treatment. The best amelioration was occurred in the obese rats group which received the both antioxidants at the last interval (4 weeks). The underlining mechanisms were discussed according to available references.
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## 1. Introduction

Obesity is becoming a global epidemic ***(WHO, 2000 and Eckel et al., 2004)***. The epidemic of obesity is occurring on genetic backgrounds that have not changed, but it is nonetheless clear that genetics plays an important role in the development of obesity ***(Snyder et al., 2004).*** In the past 10 years, obesity dramatically has occurred in both children and adults among the World population (***Engeland et al., 2003).*** Obesity is a major risk factor for cardiovascular diseases, but the mechanisms for increased cardiovascular risk in obesity are still unclear ***(Heibashy, 2000; Heibashy & Abdel-Moniem, 2005 and Zhao et al., 2006)***. The inflammation and the increase of oxidative stress are two potential mechanisms proposed to play a major role in the morbidity associated with obesity. Studies that investigate these mechanisms rely on biomarkers, but validated biomarkers for obesity-related cardiovascular outcomes are lacking ***(Heibashy et al., 2010 and Wang et al., 2010).***

Moreover, obesity is associated with abnormal endothelial function ***(Arcaro et al., 1999)***. It is often inferred that the reduction in endothelial function is the result of a decrease in nitric oxide (NO). Decreased NO in obesity may be related to an increase in oxidative stress or may result from proinflammatory cytokines ***(Lee, 2001).***

Resistin, which is one of the most recently identified adipokines, has been proposed to be an inflammatory marker for atherosclerosis. Recent investigations in humans have shown there is higher serum resistin levels in obese subjects as compared to lean subjects. These higher levels were also positively correlated with changes in the BMI and the visceral fat area (***McTernan et al., 2004 and Li et al., 2009)***. ***Lee et al. (2006)*** found higher circulating resistin levels in obese mice when compared to their lean counterparts. Additional studies have reported significant reductions in circulating resistin levels following moderate weight loss (***Haseeb et al., 2009)*** and postgastric bypass (***Asano et al., 2010)***.

Asymmetric dimethyl arginine (ADMA) is an endogenous competitive inhibitor of nitric oxide synthase (NOs) activity. This modified amino acid is derived from proteins that have been posttranslationally methylated and subsequently hydrolyzed ***(Kielstein et al., 1999).***

Taurine, 2-aminoethanesulphonic acid is an essential amino acid. It is widely distributed in mammalian cells and tissues and has many biological and physiological functions ***(Huxtable, 1992; Mochizuki et al., 1998 and Schrader, 2009).*** Among them, taurine has been shown to influence serum lipid levels by changing lipid metabolism in the liver ***(Murakami et al., 1999 & 2002).*** Taurine showed significant hypocholesterolmic effect on rats probably by enhancing the catabolism of cholesterol and reducing the absorption of dietary cholesterol. Also, addition of taurine to high cholesterol diet produced a significant reduction not only in total serum cholesterol and triglyceride levels but also in total liver cholesterol, lipid and triglyceride contets ***(Gandhi et al., 1992).*** Besides its effects on lipid metabolism, taurine plays a crucial role in the production of bile acid conjugates, which are formed from cholesterol in the hepatic cells. These

conjugates are considered the degrading metabolism of cholesterol and play an important role of fat digestion and absorption from the intestine ***(Chensney, 1985).***

Furthermore, taurine was reported to have beneficial effects in various physiological and pathological conditions ***(Chiba et al., 2002*** and ***Ozturk et al., 2003)*** by mainly diminishing production of reactive oxygen species (ROS). It also can prevent DNA damage at physiological concentrations ***(Messina & Dawson, 2000).*** Taurine has also hepatoprotective effects such as inhibition of extracellular matrix accumulation in experimental liver fibrosis ***(Chen & Zhang, 1999 and Balkan et al., 2001)*** and improvement of liver function tests in fatty liver disease of children ***(Obinata et al., 1996).***

Quercetin is considered to be a strong antioxidant due to its ability to scavenge free radicals and bind transition metal ions. These properties of quercetin allow it to inhibit lipid peroxidation **(*Sakanashi et al., 2008*).** Lipid peroxidation is the process by which unsaturated fatty acids are converted to free radicals *via* the abstraction of hydrogen **(*Young & McEneny, 2001*)**. Quercetin can also reduce inflammation by scavenging free radicals. Free radicals can activate transcription factors that generate pro-inflammatory cytokines which are often found elevated in patients that suffer from chronic inflammatory diseases ***(Boots et al., 2008).***

A number of experimental and *in vitro* studies have reported that quercetin possesses several other beneficial activities, including hypolipidemic ***(Kamada et al., 2005; Odbayar et al., 2006 and Lee et al., 2011)***, antihypertensive ***(Duarte et al., 2001 and Egert et al., 2009)***, anti-inflammatory ***(Manjeet & Ghosh, 1999 and Nair et al., 2006)***, and antithrombotic actions ***(Hubbard et al., 2003)***. Quercetin also inhibits the *ex vivo* resistance of low-density lipoprotein (LDL) to oxidation and resistance to DNA strand breakage induced by hydrogen peroxide in human lymphocytes ***(Duthie et al., 1997 and Noroozi et al., 1998)***.

This study focuses on the relationship between the obesity and cardiovascular diseases (CVD) and the possible amelioration effects of taurine or quercetin and their mixture on cardiac function, thyroid function and lipid profile tests. The underlying mechanisms were discussed according to available published researches.

## 2. Material & Methods

**Animals:-**

Sixty adult male albino rats *(Ob/Ob)* with age's 12±1 weeks old and their weight 200±10g were employed in this study. They were housed in a well ventilated vivarum of Biochemistry & Nutrition Department, Women's Collage, Ain Shams University. The animals were caged in wire bottom galvanized metal wall boxes under controlled environmental and nutritional conditions (25°C and 55-60 % relative humidity). The animals fed on a standard diet according to National Research Council *(NRC, 1977)* and fresh tap water was *ad libitum.*

This study was included two experiments carried out as the following: In the first experiment, the rats were randomly divided into two main groups according to the type of diet. In the first group, fifteen rats were fed on a standard rodent ration (basal diet) only and served as control. While, the second group, forty five rats were fed on fat 50 % diet as described by *Moraes et al. (2009)*. After 4 weeks, five rats from each previous group were taken to estimate the alteration in the lipid picture, cardiac function and hormonal profile.

In the second experiment (Form the beginning of the 5$^{th}$ week), the remaining of normal diet rats group (10 rats) was served as normal control animals group (group No. 1) while, the remaining forty obese rats were not further fed on high fat diet and divided into 4 equal groups:

**Table (1): Composition of the normal and fat diets**

| Nutrient | Standard normal diet | Fat 50 % diet |
|---|---|---|
| Starch | 51.55 % | 9.55 % |
| Soya bean | 18.15 % | 18.15 % |
| Sucrose | 17.93 % | 10.13 % |
| Corn oil | 5.15 % | 5.15 % |
| Cellulose | 5.15 % | 5.15 % |
| Vitamin & mineral mixture* | 2.07 % | 2.07 % |
| Lard | zero % | 50.00 % |

*Vitamin & mineral mix containing (g/kg): thiamin HCl 0.6, riboflavin 0.6, pyridoxine HCl 0.7, niacin 3, calcium pantothenate 1.6, folic acid 0.2, biotin 0.02, vitamin B12 (0.1% trituration in mannitol) 1, dry vitamin A palmitate (500,000 U/g) 0.8, dry vitamin E acetate (500 U/g) 10, vitamin D3 trituration (4,000,000 U/g), 0.25, manadione sodium bisulfite complex 0.15, calcium phosphate diabasic 500, sodium chloride 74, potassium citrate 220, potassium sulfate 52, magnesium oxide 24, mangnous carbonate 3.5, ferric citrate 6, zinc carbonate 1.6, cupric carbonate 0.3, potassium iodate 0.01, sodium selenite 0.01, chrominium potassium sulfate 0.55.

Group (No. 2): Ten obese animals were served as obese recovery group.

Group (No. 3): Ten obese animals were received orally by the aid of gastric tube 50 mg taurine (Sigma Chem. Co., St. Louis, Mo., USA)/ 100g b.wt/day for four weeks according to *Byung et al. (2001)* and served as taurine group (T group).

Group (No. 4): Another ten obese rats were treated orally with quercetin at a dose of 25 mg / kg body weight for four weeks by the aid of gastric tube according to *Bieger et al. (2008)* and served as quercetin group (Q group).

Group (No. 5): The last ten obese animals were treated with a mixture of both antioxidants (the same doses and the same time) and served as mixture group (T+Q group).

At the end of each experimental period, ten rats from each above group were overnight fasted and killed by decapitation. Blood was collected in dry clean test tube for the determination of serum lipid profile [cholesterol,

triglycerides, high density lipoprotein-cholesterol (HDL-Ch) and low density lipoprotein-cholesterol (LDL-Ch)], thyroid hormonal profile [total triiodothyronine ($T_3$), total thyroxin ($T_4$)], cardiac profile [aspartate aminotransferase (AST), creatine kinase (CK) and lactate dehydrogenase (LDH) activities and the levels of total nitric oxide (TNO), endothelin-1 and asymmetric dimethyl arginine (ADMA)]. Moreover, the levels of serum resistin and tumor necrosis factor-α (TNF- α) were estimated.

**Estimation of serum lipid profile:**

Serum total cholesterol *(Watson, 1960),* triglycerides *(Fossati et al., 1982)* and HDL-cholesterol *(Freidewald et al., 1972)* were estimated enzymatically using a commercial kits from Randox, Ltd., Co. (UK). LDL-cholesterol was calculated as per *Freidewald's* equation.

*LDL-Chol. = Total Chol. – [TG/5 – HDL- Chol.].*

**Estimation of serum hormonal profile:**

Serum total triiodothyronine ($T_3$) and total thyroxin ($T_4$) levels were estimated by a radioimmunoassay method kit using solid phase component system according to *Ekins (1978)* and *Chopra et al. (1972).* The kits were purchased from Diagnostic Product Corporation (DPC) USA.

The concentration of serum resistin was assayed by ELISA (Sandwich Immunoassay Technique) using commercial kits (IBL-Hamburg, Co. Germany) according to *Thorell (1973)*.

**Determination of serum cardiac profile:**

Serum activities of lactate dehydrogenase (LDH), creatine kinase (CK) and aspartate aminotransferase (AST) were measured kinetically according to the method of *Reitman and Frankel (1957)*, *Szasz et al. (1977)* and *Weisshaar et al. (1975)* respectively. The kinetically commercial kits were purchased from Sclavo Bio-diagnostic Co. (Italy).

Serum rat asymmetric dimethyl arginine (rat-ADMA) was estimated using commercial ELISA kit and purchased from American Laboratory Products Company (Alpco Diagnostics, USA) according to the method of *Böger et al. (1998).*

Moreover, the concentrations of serum rat endothelin-1 *(Wakisaka et al., 1996)* and total nitric oxide *(Green et al., 1982)* were assayed by ELISA (Sandwich Immunoassay Technique) using commercial kits (IBL-Hamburg, Co. Germany).

**Estimation of serum rat-tumor necrosis factor-α (rat TNF-α) level:**

The level of rat-tumor necrosis factor-α (*Beutler et al., 1985)* was assayed by ELISA (Sandwich Immunoassay Technique) using commercial kits (IBL-Hamburg, Co. Germany).

**Statistic analysis:-**

Student "t" test was used to test the difference in parameters tested herein between experimentally obese rats and normal control animal in the preliminary experiment according to *Milton et al. (1986).* While, the comparison between the effects of different antioxidant nutrients on biochemical parameters recorded herein were statistically analyzed using analysis of variance (ANOVA) followed by Duncan's multiple range tests as described by *Duncan (1955) and Snedecor & Cochran (1982).*

**3. Results**

In the first experimental, the obtained data in table (2) clarified a significant ($P<0.001$) elevation in serum cholesterol, triglycerides and low density lipoprotein (LDL) levels in obese rats. The mean values recorded 105.616 ± 1.349, 141.728 ± 1.478 and 61.431 ± 0.694 mg/dL for cholesterol, triglycerides and low density lipoprotein in obese rats regarding to 54.586 ± 0.725, 64.376 ± 0.821 and 26.190 ± 0.457mg/dL in normal control rats respectively. A numerical change but not significant was occurred in high density lipoprotein (HDL) in control rats group as compared to their corresponding results in obese rats group (Table 2).

On detecting serum total triiodothyronine ($T_3$) level using the data tabulated in table (2). It is recognized that rats fed on fat 50 % diet revealed a significant ($P<0.001$) decrease in $T_3$ level as compared to the corresponding normal control rats. While, no remarkable a change was occurred in the level of serum total thyroxin ($T_4$) in both normal control rats and obese rats group. Moreover, a significant ($P<0.001$) elevation in the serum resistin level was noted in obese rats group as a result of feeding the animals on 50 % fat in diet (Table 2).

Table (2): Comparison between normal and obese rats in some blood variables related to cardio-metabolic risks.

| Variable \ Treatment | Normal rats (N=5 rats) | Obese rats (N=5 rats) |
|---|---|---|
| Total cholesterol (mg / dL) | 54.586 ± 0.725 | 105.616 ± 1.349* |
| Triglycerides (mg /dl) | 64.376 ± 0.821 | 141.728 ± 1.478* |
| HDL- cholesterol (mg /dl) | 15.521 ± 0.325 | 15.839 ± 0.381 |
| LDL- cholesterol (mg /dl) | 26.190 ± 0.457 | 61.431 ± 0.694* |
| Total triiodothyronine (ng/ml) | 88.719 ± 0.857 | 64.251 ± 0.582* |
| Total thyroxin (µg/dL) | 4.145 ± 0.009 | 4.129 ± 0.008 |
| Resistin (ng/ml) | 3.268 ± 0.042 | 5.239 ± 0.056* |

| | | |
|---|---|---|
| Lactate dehydrogenase (U / L) | 227.219 ± 2.297 | 368.481 ± 3.182* |
| Creatin phosphokinase (U / L) | 93.745 ± 0.901 | 166.329 ± 1.411* |
| Aspatate aminotransferase (U /L) | 123.368 ± 1.562 | 185.487 ± 2.096* |
| Total nitric oxide (µmol / L) | 52.171 ± 0.658 | 27.937 ± 0.492* |
| Endothelin-1 (pg / ml) | 0.391 ± 0.004 | 0.884 ± 0.009* |
| ADMA (µmol/L) | 1.119 ± 0.029 | 2.347± 0.082* |
| TNF-α (pg/ml) | 5.184 ± 0.013 | 9.386 ± 0.035* |

- Values are expressed as means ± S.E. - N = number of rats in the group.
- * Significant at p< 0.001 between the groups in the same rows.

The activities of all estimated serum cardiac enzymes [aspartate aminotransferase (AST), creatine kinase (CK) and lactate dehydrogenase (LDH)] were significantly (P<0.001) elevated in obese animals group (Table 1). Also, the levels of endothelin-1, asymmetric dimethyl arginine (ADMA) and tumor necrosis factor-α (TNF-α) were significantly (P<0.001) increased in obese rats group (Table 2). In relation to the control rats, a significant (P<0.001) decrease in the serum level of total nitric oxide (TNO) was reported in obese rats group (Table 2).

In the experimental two, a significant (P<0.05) depletion was occurred in the levels of serum cholesterol, triglycerides and low density lipoprotein (LDL) levels in obese rats after treatment with taurine (50mg/100g b.wt/day) or quercetin (25mg/kg b. wt/day) for four weeks (Table 3). The maximum correction effect was reported in the obese rats which treated with both antioxidants dependent on the time of treatment (2 & 4 weeks).

Table (3):- Effects of giving taurine or quercetin and their mixture on serum lipid profile level of obese rats.

| Groups / Parameters | | Control | Recovery Obese group | Obese + T group | Obese + Q group | Obese + T + Q group |
|---|---|---|---|---|---|---|
| Total cholesterol (mg / dL) | 2 weeks n = 5 | $54.702\pm0.613^{A}{}_{a}$ | $101.719\pm1.266^{B}{}_{a}$ | $83.467\pm1.019^{C}{}_{a}$ | $91.762\pm1.132^{D}{}_{a}$ | $72.216\pm0.829^{E}{}_{a}$ |
| | 4 weeks n = 5 | $55.086\pm0.714^{A}{}_{a}$ | $94.942\pm1.327^{B}{}_{b}$ | $72.109\pm0.902^{C}{}_{b}$ | $80.933\pm1.107^{D}{}_{b}$ | $64.538\pm0.181^{E}{}_{b}$ |
| Triglycerides (mg / dL) | 2 weeks n = 5 | $64.682\pm0.834^{A}{}_{a}$ | $121.859\pm1.311^{B}{}_{a}$ | $99.473\pm1.009^{C}{}_{a}$ | $111.683\pm1.113^{D}{}_{a}$ | $89.227\pm0.909^{E}{}_{a}$ |
| | 4 weeks n = 5 | $65.041\pm0.851^{A}{}_{a}$ | $109.863\pm1.282^{B}{}_{b}$ | $85.209\pm0.928^{C}{}_{b}$ | $96.301\pm1.029^{D}{}_{b}$ | $74.016\pm0.882^{E}{}_{b}$ |
| HDL Cholesterol (mg / dL) | 2 weeks n = 5 | $15.619\pm0.342^{A}{}_{a}$ | $15.391\pm0.374^{A}{}_{a}$ | $15.724\pm0.562^{A}{}_{a}$ | $15.707\pm0.571^{A}{}_{a}$ | $15.519\pm0.561^{A}{}_{a}$ |
| | 4 weeks n = 5 | $15.532\pm0.351^{A}{}_{a}$ | $15.417\pm0.365^{A}{}_{a}$ | $15.613\pm0.456^{A}{}_{a}$ | $15.628\pm0.566^{A}{}_{a}$ | $15.748\pm0.559^{A}{}_{a}$ |
| LDL Cholesterol (mg / dL) | 2 weeks n = 5 | $26.147\pm0.455^{A}{}_{a}$ | $61.196\pm0.628^{B}{}_{a}$ | $47.848\pm0.525^{C}{}_{a}$ | $53.718\pm0.551^{D}{}_{a}$ | $33.412\pm0.417^{E}{}_{a}$ |
| | 4 weeks n = 5 | $26.546\pm0.459^{A}{}_{a}$ | $57.522\pm0.589^{B}{}_{b}$ | $39.454\pm0.481^{C}{}_{b}$ | $46.045\pm0.541^{D}{}_{b}$ | $33.987\pm0.854^{E}{}_{a}$ |

- Values are expressed as means ± S.E. - N = number of rats in the group.
- A, B, C, D, E = means bearing different superscripts within the same row are differ significantly (P<0.05).
- a, b = means bearing different subscripts within the same column are differ significantly (P<0.05).

From table (4), a considerable improvement was occurred in the serum total triiodothyronine (T3), total thyroxin ($T_4$) and resistin levels of obese rats which treated with 50mg taurine/100g b.wt/day or 25mg quercetin /kg b. wt/day dependent on the time of treatment (2 & 4 weeks). Due to the synergistic effects of both antioxidants (taurine & quercetin), the best amelioration results was obtained in the obese rats group which treated with both of them and depending on the time of supplementation (Table 4).

**Table (4):- Effects of giving taurine or quercetin and their mixture on serum hormonal profile concentration of obese rats.**

| **Groups / Parameters** | | **Control** | **Recovery Obese group** | **Obese + T group** | **Obese + Q group** | **Obese + T + Q group** |
|---|---|---|---|---|---|---|
| **$T_3$ (ng/ml)** | **2 weeks n = 5** | $88.692\pm0.863^{A}{}_{a}$ | $67.719\pm0.586^{B}{}_{a}$ | $72.167\pm0.609^{C}{}_{a}$ | $71.862\pm0.593^{C}{}_{a}$ | $78.216\pm0.729^{D}{}_{a}$ |
| | **4 weeks n = 5** | $88.726\pm0.904^{A}{}_{a}$ | $73.042\pm0.667^{b}{}_{a}$ | $81.109\pm0.702^{C}{}_{b}$ | $77.608\pm0.681^{D}{}_{b}$ | $88.138\pm0.881^{A}{}_{b}$ |
| **$T_4$ (µg/dL)** | **2 weeks n = 5** | $4.169\pm0.009^{A}{}_{a}$ | $4.161\pm0.011^{A}{}_{a}$ | $4.166\pm0.009^{A}{}_{a}$ | $4.163\pm0.010^{A}{}_{a}$ | $4.167\pm0.009^{A}{}_{a}$ |
| | **4 weeks n = 5** | $4.165\pm0.008^{A}{}_{a}$ | $4.163\pm0.011^{A}{}_{a}$ | $4.169\pm0.008^{A}{}_{a}$ | $4.164\pm0.009^{A}{}_{a}$ | $4.166\pm0.008^{A}{}_{a}$ |
| **Resistin (ng/ml)** | **2 weeks n = 5** | $3.269\pm0.043^{A}{}_{a}$ | $4.991\pm0.064^{B}{}_{a}$ | $4.164\pm0.062^{C}{}_{a}$ | $4.207\pm0.071^{C}{}_{a}$ | $3.579\pm0.064^{D}{}_{a}$ |
| | **4 weeks n = 5** | $3.262\pm0.042^{A}{}_{a}$ | $4.417\pm0.069^{B}{}_{b}$ | $3.713\pm0.056^{C}{}_{b}$ | $3.828\pm0.066^{C}{}_{b}$ | $3.258\pm0.044^{A}{}_{b}$ |

- Values are expressed as means ± S.E. - N = number of rats in the group.
- A, B, C, D, E = means bearing different superscripts within the same row are differ significantly (P<0.05).
- a, b = means bearing different subscripts within the same column are differ significantly (P<0.05).

A significant (P<0.05) recovery occurred in the serum aspartate aminotransferase (AST), creatine kinase (CK) and lactate dehydrogenase (LDH) activities of obese rats which were treated with 50mg taurine/100g b.wt/day or 25mg quercetin /kg b. wt/day dependent on the time of treatment (2 & 4 weeks). This correction was reported in table (5). The best correction in these parameters was noted in the obese rats group which treated with both antioxidants (taurine and quercetin) and also dependent on the time of treatment.

**Table (5):- Effects of giving taurine or quercetin and their mixture on serum cardiac enzymes profile activity of obese rats.**

| Groups / Parameters | | Control | Recovery Obese group | Obese + T group | Obese + Q group | Obese + T + Q group |
|---|---|---|---|---|---|---|
| LDH (U / L) | 2 weeks n = 5 | $227.402\pm2.213^{A}_{a}$ | $336.719\pm2.896^{B}_{a}$ | $288.467\pm2.529^{C}_{a}$ | $291.762\pm2.612^{C}_{a}$ | $267.216\pm2.249^{D}_{a}$ |
| | 4 weeks n = 5 | $229.386\pm2.228^{A}_{a}$ | $308.942\pm2.747^{B}_{b}$ | $249.109\pm2.242^{C}_{b}$ | $253.933\pm2.250^{C}_{b}$ | $226.538\pm0.221^{A}_{b}$ |
| CK (U / L) dL) | 2 weeks n = 5 | $93.772\pm0.921^{A}_{a}$ | $157.859\pm1.361^{B}_{a}$ | $143.473\pm1.229^{C}_{a}$ | $146.683\pm1.237^{C}_{a}$ | $129.227\pm1.109^{D}_{a}$ |
| | 4 weeks n = 5 | $94.081\pm0.928^{A}_{a}$ | $146.163\pm1.248^{B}_{b}$ | $127.209\pm1.118^{C}_{b}$ | $130.001\pm1.216^{C}_{b}$ | $106.016\pm0.937^{D}_{b}$ |
| AST (U / L) | 2 weeks n = 5 | $125.719\pm1.573^{A}_{a}$ | $178.391\pm1.874^{B}_{a}$ | $165.824\pm1.662^{C}_{a}$ | $166.007\pm1.671^{C}_{a}$ | $145.519\pm1.564^{D}_{a}$ |
| | 4 weeks n = 5 | $126.732\pm1.612^{A}_{a}$ | $166.417\pm1.771^{B}_{b}$ | $145.113\pm1.456^{C}_{b}$ | $147.628\pm1.463^{C}_{b}$ | $124.748\pm1.557^{D}_{b}$ |

- Values are expressed as means ± S.E. - N = number of rats in the group.
- A, B, C, D = means bearing different superscripts within the same row are differ significantly (P<0.05).
- a, b = means bearing different subscripts within the same column are differ significantly (P<0.05).

**Table (6):- Effects of giving taurine or quercetin and their mixture on serum TNO, Endothelin-1, ADMA and TNF-α levels of obese rats.**

| Groups / Parameters | | Control | Recovery Obese group | Obese + T group | Obese + Q group | Obese + T + Q group |
|---|---|---|---|---|---|---|
| TNO (µmol / L) | 2 weeks n = 5 | $52.169\pm0.652^{A}_{a}$ | $30.719\pm0.456^{B}_{a}$ | $35.867\pm0.489^{C}_{a}$ | $39.162\pm0.532^{D}_{a}$ | $42.916\pm0.629^{E}_{a}$ |
| | 4 weeks n = 5 | $52.166\pm0.654^{A}_{a}$ | $34.942\pm0.477^{B}_{b}$ | $41.109\pm0.602^{C}_{b}$ | $44.733\pm0.630^{D}_{b}$ | $47.538\pm0.581^{E}_{b}$ |
| Endothelin-1 (pg/ ml) | 2 weeks n = 5 | $0.392\pm0.004^{A}_{a}$ | $0.859\pm0.011^{B}_{a}$ | $0.773\pm0.009^{C}_{a}$ | $0.623\pm0.010^{D}_{a}$ | $0.527\pm0.009^{E}_{a}$ |
| | 4 weeks n = 5 | $0.391\pm0.004^{A}_{a}$ | $0.803\pm0.011^{B}_{b}$ | $0.589\pm0.008^{C}_{b}$ | $0.491\pm0.009^{D}_{b}$ | $0.396\pm0.007^{A}_{b}$ |
| ADMA (µmol/L) | 2 weeks n = 5 | $1.125\pm0.031^{A}_{a}$ | $2.191\pm0.074^{B}_{a}$ | $1.824\pm0.062^{C}_{a}$ | $1.647\pm0.051^{D}_{a}$ | $1.519\pm0.042^{E}_{a}$ |
| | 4 weeks n = 5 | $1.132\pm0.032^{A}_{a}$ | $1.817\pm0.065^{B}_{b}$ | $1.513\pm0.056^{C}_{b}$ | $1.328\pm0.066^{D}_{b}$ | $1.138\pm0.034^{A}_{b}$ |
| TNF-α (pg/ml) | 2 weeks n = 5 | $5.192\pm0.014^{A}_{a}$ | $8.502\pm0.032^{B}_{a}$ | $7.794\pm0.028^{C}_{a}$ | $7.801\pm0.029^{C}_{a}$ | $7.046\pm0.028^{D}_{a}$ |
| | 4 weeks n = 5 | $5.194\pm0.015^{A}_{a}$ | $7.719\pm0.029^{B}_{b}$ | $6.533\pm0.023^{C}_{b}$ | $6.561\pm0.025^{C}_{b}$ | $5.539\pm0.019^{D}_{b}$ |

- Values are expressed as means ± S.E. - N = number of rats in the group.
- A, B, C, D, E = means bearing different superscripts within the same row are differ significantly (P<0.05).
- a, b = means bearing different subscripts within the same column are differ significantly (P<0.05).

After the obese rats treated with 50mg taurine/100g b.wt/day or 25mg quercetin /kg b. wt/day for 2 & 4 weeks, the data recorded a significant (P<0.05) increase in the serum level of total nitric oxide (TNO) dependent on duration of treatment (Table 6). The maximum elevation was occurred the serum level of total nitric oxide (TNO) in obese rats group which received both antioxidants (Table 6). This correction was not reached to their corresponding values in the normal control rats group.

A remarkable correction was reported in the serum levels of endothelin-1, asymmetric dimethyl arginine (ADMA) and tumor necrosis factor-α (TNF-α) after the obese rats treated with 50mg taurine/100g b.wt/day or 25mg quercetin /kg b. wt/day for 2 & 4 weeks (Table 6). These significant (P<0.05) corrections were pronounced in the obese rats group which treated with both antioxidants (taurine and quercetin). This correction in the serum levels of endothelin-1 was reached to the control rats group while, the corrections in the serum levels of asymmetric dimethyl arginine (ADMA) and tumor necrosis factor-α (TNF-α) were still not reached to their corresponding in the control animals group (Table 6).

## 4. Discussion

Obesity is the most common nutritional disorder in the World Population. Obesity is associated with an increased mortality and morbidity of cardiovascular disease (CVD). Obesity is primarily considered to be a disorder of energy balance and it has recently been suggested that some forms of obesity are associated with chronic low-grade inflammation *(Sowers, 2003)*.

In the current study, it has been found that all major classes of serum lipid and lipoprotein pattern were significantly increased in fat-fed rats over those of the controls (Table 2). The obtained data are in agreement with the studies of *Adamopoulos et al. (1996) and Heibashy & El-Nahrawy (2010).* A significant rise in plasme cholesterol was recorded by feeding high fat and cholesterol diet in pig *(Pond et al., 1986).* The present results suggest that the amount of dietary fat can influence serum lipid levels in animals. However, diets rich in fat can be artherogenic by causing increases in cholesterol, triglycerides and total lipid concentrations through a possible development of insulin resistance *(Adamopoulos et al., 1996).* The other possible pathway may be relevant to changes in lipoprotein composition, transport and /or turnover which has been suggested by *Steinberg (1997)* is that exogenous cholesterol influences the lipoprotein profile by regulating the proportion of VLDL, HDL and LDL secreted by the liver.

Liver triglyceride metabolism *in vivo* is altered by hormonal, neural and nutrient signals that regulate metabolic pathways involved in the synthesis, degradation and /or secretion of triglyceride. Leptin has been shown to have a strong influence on fatty acid metabolism and on the endocrine axis *(Meier & Gressner, 2004).* Leptin has also been administrated its profound effects on fatty acid metabolism, resulting in an increase in the capacity to oxidized free acid and lowering triacylglycerol stores *(Duck, 2005).* The effect of leptin on liver triglycerides is dependant on the activation of PI3 kinase and IRS-1 tyrosine phosphorylation and also increased the serum phosphorylation of AKT, a major metabolic target of PI3 kinase activity *(Kim et al., 2000 and Trevaskis et al., 2009).* Increase uptakes of triglycerides into peripheral tissues or decreased synthesis/ export from liver resulted in decreased circulating concentration. The obtained data in table (2) are in harmony with *Adamopoulos et al. (1996); Kim et al. (2000) and Duck (2005)* and confirmed by *Trevaskis et al. (2009).*

In the current study, the reciprocal relationship between the concentrations of thyroid hormones ($T_3$ and $T_4$) in serum and hyperlipidemia (induced by feeding fat) is evident and depends on the percent of fat content (Table 2). These results seemed to be in complete accordance with earlier studies made by *Long et al. (1953) and Deuel (1955).* They observed that thyroid activity has an adverse effect on all plasma lipids. Furthermore, the depletion in serum $T_3$ level with no a remarkable changes in serum $T_4$ level of obese rats may be due to the disturbance in the hypothalamic-pituitary-thyroid axis (HPTA), the increment in the conversion of $T_3$ to $T_4$ or/and the elevation in the formation of reverse $T_3$ ($rT_3$) concentration.

Obesity is associated with numerous comorbidities such as cardiovascular diseases (CVD), type 2 diabetes, hypertension, certain cancers and metabolic syndrome (MetS). In fact, obesity is an independent risk factor for CVD *(Poirier & Eckel, 2000 & 2002)* and CVD risks have been documented in obese children *(Ogden et al., 2002* and *Engeland et al., 2003).* They reported that obesity is a major risk factor in the development of the metabolic syndrome and cardiovascular diseases, and seems to be directly related to heart failure independently of other risk factors. Indeed, a direct relationship between increased body mass index and increased risk for heart failure has been demonstrated. Several potential mechanisms are under discussion to explain this correlation, including hemodynamic changes with cardiac overload and left ventricular remodeling, and lipid accumulation into the myocardium, leading to lipoapoptosis in cardiomyocytes. These mechanisms, however, do not fully explain the development of heart dysfunction in obese individuals. Adipocytes are known to produce and release a wide variety of bioactive molecules into the blood-stream. On the basis of these data, the authors have recently demonstrated that mature human adipocytes release substances (such as resistin) that strongly and acutely suppress the contraction of cardiomyocytes by attenuating intracellular $Ca^{2+}$ concentrations.

The obtained data in table (2), there was a significant ($p<0.05$) elevation in the levels of cardiac profile (AST, CK and LDH) activities after rats fed on high fat diet. A significant decrease in the total nitric oxide concentration was observed with a significant elevation in the levels of resistin, endothelin-1, ADMA and TNF-α in obese rats. These results may be due to the excessive myocardial infraction as a result of free radical production, epigenetic gene alteration, inhibition in the activity of total nitric synathase (NOs), increase the level of serum endothelin-1 accompanied with elevation in serum ADMA level and appearance of hypertension and metabolic syndrome (MetS). These results are in parallel with those obtained by *Mach (2005); Kawanami et al. (2006) and McCormick et al. (2007).*

Also, obesity is characterized by adipose tissue overproduction of proinflammatory cytokines such as TNF-α and decrease in the total nitric oxide level due to metabolic disorders nitric oxide synthase (NOS) expression in fat or muscle is induced by proinflammatory cytokines *(Galisteo et al., 2005).*

Moreover, different mechanisms are implicated in the link between obesity and cardiovascular diseases (CVD). For example, the fetal origin of metabolic risk (*Ogden et al., 2002 and Engeland et al., 2003)* and epigenetic gene regulation (*Poirier et al., 2002 and Ansell, 2007*) are potential causes of increased CVD risk in obesity. These studies focused on two other mechanisms of current interest inflammation and increased oxidative stress. Both can play a role in promoting CVD, such as increased endothelial dysfunction, an early predictor of cardiovascular injury in obese individuals *(De-Clercq et al., 2008).* Notably, both mechanisms are associated with the accumulation of fat that occurs in obesity.

ADMA appears to be the most important endogenous inhibitor and therefore the modulator of NOS activity. Since, the discovery of ADMA in 1992, clinical and experimental studies have shown that elevation of plasma ADMA level correlates with endothelial vasodilator dysfunction, and that ADMA is not only a marker of endothelial dysfunction but, also is a potential novel cardiovascular risk factor *(Böger et al., 1998; Miyazaki et al., 1999; Valkonen et al., 2001 and Zoccali, 2006).*

Plasma levels of ADMA are elevated in hypertension and in patients with occlusive vascular disease or hypercholesterolemia. The elevation of ADMA is

associated with reduced NO production and impaired endothelium-dependent vasodilation *(Böger et al., 1998).*

The inhibition of NOS by ADMA increases endothelial oxidative stress and up regulates the expression of redox-sensitive genes that encode for endothelial adhesion molecules, comparable to that observed in early atherogenesis. ADMA may therefore act as an endogenous proatherogenic molecule. In humans, hypercholesterolemia, peripheral vascular disease, and hypertension are associated with elevated ADMA levels. In hypercholesterolemic man *(Lundman et al., 2001)* and rats *(Heibashy & Abdel Moniem, 2005)* an elevation in the ADMA concentration is related to impaired endothelium-dependent vasodilation, a feature that is indicative of increased cardiovascular risk.

Resistin, which is one of the most recently identified adipokines, has been proposed to be an inflammatory marker for atherosclerosis. However, investigations in humans suggest that resistin is expressed in adipocytes with monocytes and macrophages *(Kunnari et al., 2009 and Manduteanu et al., 2010).* Supporting this possible inflammatory role in humans is results that show recombinant resistin activate human endothelial cells, as measured by an increased expression of endothelin-1 and various adhesion molecules and chemokines.

Moreover, *Calabro et al. (2004)* has shown that resistin can promote human coronary artery smooth muscle cell proliferation by activation of the extracellular signal-regulated kinase 1/2 (ERK) and phosphatidylinositol 3-kinase (PI3 K) pathways. Taken together, these findings suggest a possible mechanistic link between resistin and cardiovascular disease *via* proinflammatory pathways.

In addition, recent investigations in humans have shown there is higher serum resistin levels in obese subjects as compared to lean subjects. These higher levels were also positively correlated with changes in the BMI and the visceral fat area (*McTernan et al., 2004and Li et al., 2009). Lee et al. (2005)* found higher circulating resistin levels in obese mice when compared to their lean counterparts. Additional studies have reported significant reductions in circulating resistin levels following moderate weight loss (*Haseeb et al., 2009)* and postgastric bypass (*Asano et al., 2010)*.

Beginning with the observation that TNF-α could inhibit contractility of isolated hamster papillary muscles in a concentration-dependent and reversible manner, a series of *in vivo* and *in vitro* basic science studies were performed, which paralleled the clinical studies assessing TNF-α levels in patients with congestive heart failure *(Finkel et al., 1992).* First, it was demonstrated that the negative inotropic effects of TNF alpha are virtually immediate *(Eichenholz et al., 1992 and Yokoyama et al., 1993)* and appear to be completely reversible upon removal of the cytokine. How-ever, not only does TNF alpha have immediate negative inotropic properties, but it can recapitulate the cellular and biochemical abnormalities that characterize the failing human heart. For example, IL-1beta induces a down regulation of the expression of sarcoplasmic reticulum $Ca^{2+}ATP_{ase}$ (SERCA) and phospholamban at both the mRNA and protein level in neonatal myocytes, which is associated with a depression and prolongation of the $Ca^{2+}$ transient, effects that may be initiated by TNF-α. In addition, TNF-α effectively uncouples the beta-adrenergic receptors from adenylyl cyclase *via* an effect on the G inhibitory protein. Furthermore, TNF-α activates metalloproteinases and inhibits the expression of inhibitors of metalloproteinases *in vivo* effects that would be expected to activate extracellular matrix remodeling. Although initial studies suggested that the negative inotropic properties of TNF-α were attributable to the ability of cytokines to induce nitric oxide synthase, subsequent investigations demonstrated that the induction of inducible nitric oxide synthase could not in and of itself induce contractile dysfunction in cardiac myocytes and that alterations in calcium homeostasis played an important role *(Bryant et al., 1997)*. Tumor necrosis factor alpha also provokes a hypertrophic growth response in cardiac myocytes, which may be an adaptive response to hemodynamic or environmental stress *(Odeh et al., 2006).* Furthermore, a recent study suggested that the immediate negative inotropic effects of TNF-α may be mediated by sphingosine (*Panagopoulou et al., 2008 and Walker & McEntegart, 2011*). Finally, chronic infusion of TNF-α produces a reversible dilated cardiomyopathy in a rat model without evidence of inflammatory infiltrate or myocyte necrosis *(Bozkurt et al., 1998).*

Moreover, it has been demonstrated that TNF-α shows cardio depressive properties *(Finkel et al., 1992).* Furthermore, TNF-α has been shown to be independent predictors of mortality in heart failure *(Deswal et al., 2001).* Therefore, the current study speculated that the association of elevated TNF-α as proinflammatory cytokines with odesity might put the rats at higher risk for the progression of symptomatic cardiomyopathy.

So, TNF-α is capable of modulating cardiovascular function by various mechanisms. It is now known that virtually every nucleated cell type in the myocardium, including the cardiac myocyte, is able to secrete proinflammatory cytokines in response to various myocardial damage or stressors. The expression of these cytokines can occur in absence of systemic immune activation *(Dinh et al., 2009).*

Although, modern drugs are effective in preventing cardiovascular disorders, their use is often limited because of their side effects. However, the incidence of coronary syndrome and other cardiovascular complications increases as a result of obesity. Premature ventricular contractions causing arrhythmia and sudden death also frequently occur in obese people. Sudden cardiac death, associated with sympathetic activation, in obesity is frequently associated with hyperlipidemia connected with increased plasma FFA levels. *Heibashy (2000)* examined the effect of taurine on serum lipid disturbance in high-cholesterol-induced obese rats. Also, *Heibashy & Abdel-Moniem (2005)* reported the cardioprotective effect of taurine on hypertensive rats. The last authors noted a significant amelioration in both lipid and cardiac profiles after the rats treated with taurine dependent on the time of administration.

Similar results were obtained in the current work (Table 3). These data may be attributed to the hypolipidemic effect of taurine which was partly due to the inhibition of cholesterol absorption in the intestine. Besides this action, cholesterol elimination from the body is postulated as an important factor by which taurine reduces tissue and serum cholesterol levels by increasing the conversion of

cholesterol to bile acid via enhancement of 7∝-hydroxylase, a rate limiting enzyme of hepatic cholesterol catabolism and its conjugation to bile acid lately. Furthermore, it has been suggested that taurine may be responsible for the increase of HDL-cholesterol synthesis in the liver and / or the modification / or of balance of each of the serum lipoprotein fraction containig cholesterol *(Mochizuki. et al., 1998).* Moreover, it is likely possible that chronic administration of taurine may be responsible also for hypocholesterolemia by an enhancement of LDL receptor binding in the liver *(Kamata et al., 1996).* In conclusion, the above mentioned findings show that taurine has a hypocholesterolemic action (Table 3) in exogenous hypercholesterolemia (induced by high fat diet).

High cholesterol-fed rats treated with taurine (15 g/kg/day) for five weeks showed a 37% reduction in plasma LDL, a 32% reduction in total cholesterol and a 43% reduction in triglyceride (TG) levels when compared with control rats fed the same diet without taurine *(Park & Lee, 1998).* Furthermore, rats fed a high taurine diet, in comparison with rats fed a cholesterol-free diet, showed a significant decrease in plasma concentrations of LDL, total cholesterol and TG. In addition, a 43% reduction in hepatic TG and a 77% elevation in free fatty acids in the liver were observed *(Murakami et al., 1999).* In mice, taurine has been shown to lower serum LDL and very low-density lipoproteins by 44%, while elevating high-density lipoprotein concentrations by 25%; taurine also decreased the concentration of cholesterol in the liver by 19% *(Murakami et al., 1999).* It was indicated that the ability of taurine to lower cholesterol may be due to its effect on the conversion of cholesterol to bile acids *(Murakami et al., 1999).* A 31% decrease in aortic lesions in Watanabe heritable hyperlipidemic rabbits given 0.3% taurine in drinking water for 24 weeks has also been reported *(Murakami et al., 2002).* Clinically, taurine treatment (3 g/day) has been demonstrated to improve lipid metabolism and reduce body weight in overweight subjects, as well as reduce TG levels and the atherogenic index *(Zhang et al., 2004).* In another clinical study *(Mizushima et al., 1996),* taurine supplementation (6 g/day) in healthy young men consuming a high-fat diet significantly reduced serum total cholesterol and LDL levels. It should be noted that because taurine has an antioxidant effect, it may also reduce the oxidation of LDL *(Murakami et al., 2002 and Boucknooghe et al., 2006)* and thereby attenuate the process of atherosclerosis.

The potential health benefits of taurine in cardiovascular disease are rapidly emerging. Although more research needs to be performed, numerous experimental and several clinical studies demonstrated that taurine helps the cardiovascular system through a variety of mechanisms including an improved lipid profile, modulation of ($Ca^{2+}$ ion), antioxidant effects and antagonism of angiotensin II action. Because oxidative stress is known to cause intracellular $Ca^{2+}$ overload *(Dhalla et al., 2000),* it is likely that the modulation of $Ca^{2+}$ ion by taurine may be mediated through its antioxidant effects. Furthermore, because angiotensin II generates reactive oxygen species *(Guo et al., 2005),* it can be argued that the antagonism of angiotensin II actions by taurine may also be a consequence of its antioxidant effects. A recent report *(Ulrich-Merzenich et al., 2007)* demonstrated that taurine can prevent endothelial cell dysfunction induced by high glucose and oxidized LDL. Thus, this action of taurine could be an important mechanism for providing

Moreover, it should be mentioned that lysophosphatidic acid (LPA) is a major lipid extracted from human atherosclerotic plaques *(Kaneyuki et al., 2007).* Due to its ability to increase $Ca^{2+}$ ion and increase proliferation and migration of vascular smooth muscle cells *(Xu et al., 2003; Ninio, 2005 and Damirin et al., 2007),* LPA is considered to have an important role in the development of atherosclerosis. While, taurine has been shown to inhibit rat vascular smooth muscle cell proliferation *(Zhang et al., 1999).*

*Zhang et al. (1999); Ninio (2005) and Damirin et al. (2007)* have also revealed that taurine causes concentration-dependent inhibition of the LPA-induced increase in $Ca^{2+}$ ion in cultured vascular smooth muscle cells (unpublished data). This finding could serve as a mechanism for the reported antiatherosclerotic effects of taurine. In addition, taurine may attenuate the progression of atherosclerosis due to its ability to lower serum lipids and reduce the oxidation of LDL, as well as decrease the risk of arterial thrombus formation by decreasing platelet aggregation.

Quercetin is a common flavonoid found in many fresh fruits and vegetables. Quercetin is highly concentrated in apples, onions (especially red onions), and green tea. So, quercetin possesses unique antioxidant activity. It protects the body against reactive oxygen species. Body cells and tissues are continuously threatened by the damage caused by free radicals and reactive oxygen species, which are produced during normal oxygen metabolism or are induced by exogenous damage *(Halliwell, 1995).* The mechanisms and the sequence of events by which free radicals interfere with cellular functions are not fully understood, but one of the most important events seems to be lipid peroxidation, which results in cellular membrane damage. This cellular damage causes a shift in the net charge of the cell, changing the osmotic pressure, leading to swelling and eventually cell death. Free radicals can attract various inflammatory mediators, contributing to a general inflammatory response and tissue damage. To protect themselves from reactive oxygen species, living organisms have developed several effective mechanisms *(McEneny, 2001).* The antioxidant defense mechanisms of the body include enzymes such as superoxide dismutase, catalase, and glutatione peroxidase, but also nonenzymatic counterparts such as glutathione, ascorbic acid, and α-tocopherol. The increased production of reactive oxygen species during injury results in consumption and depletion of the endogenous scavenging compounds.

Quercetin may have an additive effect to the endogenous scavenging compounds. Quercetin can interfere with different free radical producing systems and can also increase the function of the endogenous antioxidants. So, quercetin can prevent injury caused by free radicals in various ways. One way is the direct scavenging of free radicals *(Kamada et al., 2005 and Odbayar et al., 2006).* Quercetin stabilizes the reactive oxygen species by reacting with the reactive compound of the radical due to the

high reactivity of the hydroxyl group of quercetin *(Cai et al., 1997; Zern et al., 2003 and Sanchez et al., 2006)*.

In the experimental number two, the administration of quercetin enhances all studied parameters in obese rats dependent on the time of administration (Tables 3-6). Different studies have previously described quercetin as an efficient hypohyperlipidemic, hypocholesterolemic and antiatherosclerotic agent in several experimental models of obese rats when administered *(Auger et al., 2005 and Kamada et al., 2005)*. This enhancement effect has been related to the beneficial properties of quercetin on endothelial dysfunction and, although these mechanisms are not yet fully explained, the antioxidant properties of this flavonol seem to be involved in this effect. It can be concluded that quercetin's antioxidant effects also extend to the cardiovascular system.

Our results are in harmony with those obtained by *Gnoni et al. (2009); Chuang et al. (2010) Shanely et al. (2010) and Lee et al. (2011)*. The authors attributed these results to the powerful of quercetin which improves dyslipidemia and decreases oxidative stress *via* stimulates lipolysis activity and increases the expression of adipocytes genes (3T3-L1) in adipose tissue with increases the beta-oxidation of lipids in the matrix of mitochondria. Also, they explained the decrease in the level of serum triglycerides due to decrease the synthesis of triglycerides by the liver or by inhibition of triglyceride release from the liver.

As regard to the marked reduction of serum the levels of lipid profile (cholesterol, triglycerides and LDL) induced in hyperlipidemic group supplemented with quercetin in rats dependant on the time of treatment and based on the known adverse relationship between serum lipid profile and circulating thyroid hormone concentrations, the levels of serum $T_3$ and $T_4$ recorded herein are not surprised. Table (4) shows that the effects of quercetin on the levels of serum $T_3$ is more pronouncing than they do on $T_4$.

In the current work, the maximum correction was occurred in all investigated parameters [lipid profile (cholesterol, triglycerides, HDL, LDL and VLDL); hormonal profile ($T_3$, $T_4$ and resistin); cardiac profile (AST, CK and LDH) activities and the levels of serum total nitric oxide, endothelin-1 and ADMA and TNF-α in the obese animals group which treated with both taurine and quercetin dependent on the time of treatment. These data may be due to the synergistic effects of both antioxidants by improving their pharmacodynamics and pharmacokinetics properties, so they are considered bio-tonic agents. For this reason, this combination might represent a treatment option for cardiovascular diseases (CVD) with obesity-related diseases.

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