Enhancement of the Role of Mixed Hypolipotropic Agents in Male Albino Rats

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ABSTRACT

Thirty adult male albino rats were used in the present study to assess the effect of using tryptophan or/and hawthorn extract with coenzyme Q10 in ameliorating the effect of high fat diet (HFD) intake on hyperlipidemia, hormonal imbalance and body weight. Six animals were served as a control group while the other twenty four rats were supplemented with 20 g butter/100 g standard laboratory diet (HFD) for 8 weeks prior to the experiment. These HFD rats were divided randomly into four equal groups; hyperlipidemic group, tryptophan and hawthorn groups where animals of the latter two groups were supplemented with 100 mg/kg B.W. tryptophan and 50 mg/100 g B.W. hawthorn extract respectively, and mixed group that was daily administrated with a mixture of 100 mg/kg B.W. tryptophan, 50 mg/100 g B.W. hawthorn extract and 50 mg/kg B.W. coenzyme Q10. Body weight was recorded twice/week, after 30 days animals were decapitated and sera were collected for determination of total lipids, triglycerides, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triiodothyronine (T₃), Thyroxine (T₄), testosterone and corticosterone hormones. The data revealed that tryptophan, hawthorn extract alone or mixed with CoQ10 improved the dreadful effects induced by HFD, but the most profit was achieved by mixing these three antioxidants on hyperlipidemia, tested hormones and body weight.

Keywords: CoQ10, Tryptophan, Hawthorn, Antioxidants, Hyperlipidemia, Thyroid hormones, Testosterone, Corticosteroids.

INTRODUCTION

Tryptophan is an essential amino acid that cannot be synthesized by the organism and it must be provided in diet (¹). Amino acids, including tryptophan, act as building blocks in protein biosynthesis. In addition, tryptophan functions as a biochemical precursor for serotonin (²), niacin (³) and auxin (⁴).
Hawthorn is a berry-like fruit that is commonly used in traditional Chinese medicine\(^5\). Hawthorn has received much attention because of its potentiality to reduce plasma cholesterol and triglyceride concentrations\(^6\) and to treat heart arrhythmia\(^7, 8\). Hawthorn fruit is also an excellent source of antioxidants as they prevented the peroxy free radical–induced oxidation of α-tocopherol in human LDL\(^9\).

Coenzyme Q is present in mitochondria, other subcellular fractions and plasma. Coenzyme Q is the only lipid soluble antioxidant synthesized endogenously. Ubiquinol, the reduced form of CoQ10, inhibits protein and DNA oxidation and its effect on lipid peroxidation has been most deeply studied. Ubiquinol inhibits the peroxidation of cell membrane lipids and that of lipoprotein lipids present in the circulation. Dietary supplementation with CoQ10 results in increased levels of ubiquinol-10 within circulating lipoproteins and increased resistance of human low-density lipoproteins to the initiation of lipid peroxidation. Moreover, CoQ10 has a direct anti-atherogenic effect and could have a direct effect on endothelial function\(^10\).

Excess fat intake causes in addition to hyperlipidemia increase deposition of adipose tissue. The fatty tissue is an endocrine and paracrine organ that produces many cytokines and hormone interfering with many diseases such as atherosclerosis, hypertension, infertility and osteoporosis\(^11\). The adipocytes have the ability to synthesize hundreds of adipokines, some are proinflammatory mediators, others offer protection against inflammation; the later, however, appears to decrease with increasing degree of obesity\(^12\).

**Aim of work:**

In a previous study, conflicting results about the role of CoQ10 as a beneficial agent for controlling the hormonal changes associated with hyperlipidemia were obtained. These results were referred to the nature of the CoQ10, its dose, duration of administration and/or the need for another complimentary antioxidant\(^13\). In this research, the authors investigate the effect of another two hypolipotropic agents either separately or combined with CoQ10 in order to optimize or attain the most beneficial effects for the studied hormones associated with hyperlipidemia. Since obesity is an important predictor of many diseases; the present study will also deal with the effect of these agents on the reduction in body weight gain.
MATERIALS AND METHODS

In this study, thirty male albino rats (120-130 g) were obtained from the Animal House of the Nuclear Research Center at Anshas Area. Under standard laboratory conditions, six rats were kept and fed *ad libitum* a standard laboratory diet and served as a control group. The other twenty four rats were supplemented with 20 g butter/100 g standard laboratory diet (HFD) daily for 8 weeks to attain hyperlipidemia prior to the experiment then they were divided randomly into four equal groups (6 rats each). Each group received a specific treatment for 30 days as follows:

Hyperlipidemic group (Group I): still receive a high fat diet (HFD).

Tryptophan group (Group II): received a HFD and was daily administrated orally with 100 mg L-tryptophan (Fluka-grantie, Switzerland) /kg b.w. supplemented in one ml deionized distilled water.

Hawthorn treated group (Group III): received a HFD with oral daily administration of 50 mg hawthorn extract (Nature’s Way Company, USA) /100g b.w. supplemented in one ml deionized distilled water.

Mixture group (Group IV): received a HFD and was daily administrated orally with a mixture of coenzyme Q10 (50 mg/kg B.W.), hawthorn extract (50 mg/100g B.W.) and L-tryptophan (100 mg/kg b.w. supplemented in one ml deionized distilled water.

In all groups, the body weight was recorded twice/week. Diet was withdrawn from cages 12 hours before blood sampling that performed by decapitation. Blood was collected in plastic tubes and incubated at 37°C for 15 minutes then sera were obtained by centrifugation at 1500 rpm for 15 minutes.

Serum total lipids, triglycerides, total cholesterol and high density lipoprotein (HDL) were colorimetrically determined using Randox kits (U.K.). The values of low density lipoprotein cholesterol (LDL) were calculated according to the equation: LDL=total cholesterol−(HDL+serum triglycerides/5). Serum total T₃, T₄, testosterone and rat corticosterone hormones were determined by RIA kits from Diagnostic Product Corporation, LA, U.S.A.

ANOVA (one-way classification F-test), Duncan (Multiple Range-test) and correlation coefficient analysis were carried out for the statistical analysis studies (¹⁴).
RESULTS

Table (1) demonstrates the effect of feeding animals a high fat diet (HFD) on the lipid profile. The findings were severely apparent in the lipogram pattern in the HFD group where total lipids, triglycerides and total cholesterol and LDL levels were significantly (p < 0.01) increased while HDL showed a significant (p < 0.01) decrease. Treating the hyperlipidemic rats with tryptophan, hawthorn and a mixture of both plus coenzyme Q10 for 30 days lessened the dreadful alteration happened in the lipid profile and endocrine parameters. The results were optimistic since they showed a remarkable significant (p < 0.01) decrease in total lipids and triglycerides, total cholesterol and LDL levels while HDL showed a significant increase compared to the levels of the same parameters in the hyperlipidemic animal group reaching almost the control group.

Table (1): Effect of high fat diet and lipotropic agents on lipid profile in male rats.

<table>
<thead>
<tr>
<th>Groups Parameters</th>
<th>Control</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lipids (mg/dl)</td>
<td>350.5±7.43 b</td>
<td>748.2±5.76 a*</td>
<td>363.7±6.18 b</td>
<td>351.5±4.96 b</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>117.3±2.96 b</td>
<td>179.5±4.15 a*</td>
<td>120.4±2.93 b</td>
<td>107.6±3.1 b</td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>98.2±1.95 b</td>
<td>132.2±2.76 a*</td>
<td>100.1±1.56 b</td>
<td>92.7±2.14 b</td>
<td></td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>20.7±0.5 b</td>
<td>17.1±0.49 a*</td>
<td>19.8±0.39 b</td>
<td>21.9±0.60 b</td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>49.2±1.91 b</td>
<td>75.9±0.92 a*</td>
<td>49.3±1.07 b</td>
<td>46.5±1.56 b</td>
<td></td>
</tr>
</tbody>
</table>

Values with different superscript in the same row differ significantly (P<0.05), *: p<0.01

The dreadful effect of feeding HDF has been reflected also on the thyroid hormones T3, T4 and testosterone hormone that demonstrated a significant (p < 0.01) decrease while corticosterone hormone showed a significant (p < 0.01) increase as shown in Table (2).

At the same time, administration of either tryptophan, hawthorn and their mixture with CoQ10 resulted in a significant (p < 0.01) increase of T3, T4 and testosterone levels and a significant (p < 0.01) decrease of corticosterone level compared to their corresponding levels in hyperlipidemic animal group reaching almost the control level.
Table (2): Effect of high fat diet and lipotropic agents on T<sub>3</sub>, T<sub>4</sub>, testosterone and corticosterone concentrations in male rats.

<table>
<thead>
<tr>
<th>Groups Parameters</th>
<th>Control</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;sub&gt;3&lt;/sub&gt; (ng/dl)</td>
<td>421.5±6.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>381.4±5.24&lt;sup&gt;a*&lt;/sup&gt;</td>
<td>409.7±5.17&lt;sup&gt;b&lt;/sup&gt;</td>
<td>416.2±6.78&lt;sup&gt;b&lt;/sup&gt;</td>
<td>423.3±5.82&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>T&lt;sub&gt;4&lt;/sub&gt; (ng/dl)</td>
<td>45.5±2.19&lt;sup&gt;b&lt;/sup&gt;</td>
<td>36.2±1.68&lt;sup&gt;a*&lt;/sup&gt;</td>
<td>42.9±1.36&lt;sup&gt;b&lt;/sup&gt;</td>
<td>41.4±1.36&lt;sup&gt;b&lt;/sup&gt;</td>
<td>44.3±1.43&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Testosterone (ng/dl)</td>
<td>69.9±4.69&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47.1±3.57&lt;sup&gt;a*&lt;/sup&gt;</td>
<td>62.3±4.84&lt;sup&gt;b&lt;/sup&gt;</td>
<td>65.5±2.47&lt;sup&gt;b&lt;/sup&gt;</td>
<td>67.9±2.24&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Corticosterone (ng/dl)</td>
<td>276.3±3.99&lt;sup&gt;b&lt;/sup&gt;</td>
<td>346.7±3.36&lt;sup&gt;a*&lt;/sup&gt;</td>
<td>285.8±4.57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>282.3±4.43&lt;sup&gt;b&lt;/sup&gt;</td>
<td>278.8±5.88&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values with different superscripts in the same row differ significantly (P<0.05), *: p<0.01

Total body weight gain was postulated in Figure (1) that showed a significant (p<0.01) increase in body weight gain due to feeding rats on a HFD. This increase was ameliorated as a response to the administration of tryptophan, hawthorn independently and their mix with coenzyme Q10 that exhibited the least total body weight gain at the end of the experiment.

Correlation test is complementary to ANOVA test in this study. It clarifies the relationship between two variables, on the individual’s level, and how they affect each other. Table (3) illustrated the correlation between total body weight and the other parameters in the different tested groups.

Values with different superscripts differ significantly, *: p<0.01

Figure (1): Average total body weight of different experimental groups at the end of experimental period (30 days).
Table (3): Correlation between body weight and the other parameters under different experimental treatments.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lipids</td>
<td>0.200</td>
<td>-0.753*</td>
<td>0.159</td>
<td>0.033</td>
<td>0.300</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-0.032</td>
<td>-0.933*</td>
<td>0.194</td>
<td>-0.400</td>
<td>-0.033</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.860*</td>
<td>-0.481</td>
<td>-0.740*</td>
<td>-0.157</td>
<td>0.611*</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.870*</td>
<td>0.100</td>
<td>0.653*</td>
<td>0.133</td>
<td>0.148</td>
</tr>
<tr>
<td>LDL</td>
<td>-0.321</td>
<td>0.558</td>
<td>0.134</td>
<td>0.139</td>
<td>0.172</td>
</tr>
<tr>
<td>T₃</td>
<td>-0.057</td>
<td>-0.500</td>
<td>0.507</td>
<td>0.723*</td>
<td>0.275</td>
</tr>
<tr>
<td>T₄</td>
<td>-0.106</td>
<td>-0.165</td>
<td>0.052</td>
<td>-0.106</td>
<td>-0.479</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.440</td>
<td>0.215</td>
<td>0.489</td>
<td>-0.050</td>
<td>-0.660*</td>
</tr>
<tr>
<td>Corticosterone</td>
<td>0.138</td>
<td>0.115</td>
<td>0.200</td>
<td>0.494</td>
<td>-0.693*</td>
</tr>
</tbody>
</table>

In the control group, total body weight showed a positive significant correlation with cholesterol and negative significant correlation with HDL. Surprisingly, the hyperlipidemic group of rats revealed a negative significant correlation between total body weight and both total lipids and triglycerides. In the same time treating hyperlipidemic rats with tryptophan resulted in a negative and positive significant correlation between body weight and cholesterol and HDL, respectively. Total body weight showed a positive significant correlation with T3 hormone after one month of oral administration of hawthorn to hyperlipidemic rats with no significant correlation with lipid profile. On the other hand, treating hyperlipidemic rats with a mixture of tryptophan, hawthorn and coenzyme Q10 resulted in a positive significant correlation between total body weight and cholesterol and negative significant correlation with testosterone and corticosterone hormones.

**DISCUSSION**

HFD resulted in significant alterations in lipid profiles and a depressed antioxidant defense system (15). These results were established in the present work since serum cholesterol, triglycerides and LDL were significantly (p<0.01) increased in hyperlipidemic rats as compared to their relevant levels in normolipidemic rats (Table 1). The long-term high-fat diet can induce chronic pancreatic injuries and pancreatic microcircula-tory disturbances and oxidative stress that may play an
important part in the underlying pathogenesis\textsuperscript{(16)}. Similarly, Zhang\textsuperscript{(17)} indicated that chronic HFD increased pancreatic free fatty acids and lipid peroxidation associated with pancreatic injuries and collagen synthesis by activated pancreatic stellate cells in rats, further, hypertriglycerideremia and hypercholesterolemia were associated with oxidative modification of LDL, protein glycation and glucose autooxidation, thus leading to excess production of lipid peroxidation products which may cause elevation of oxidative stress in higher lipid and hyperlipidemic subjects.

The group of hyperlipidemic animals that was supplemented orally with tryptophan showed an ameliorated lipid profile, all the parameters experienced levels around the control one (Table 1). Tryptophan acts as a biochemical precursor for some compounds, the most of our concern are serotonin and niacin. Serotonin, in turn, can be converted to melatonin\textsuperscript{(2)}. This may explain the ameliorating effect of tryptophan on lipid profile. Both melatonin and niacin have antioxidant and hypolipidemic effect. Pita\textsuperscript{(18)} concluded that long-term melatonin administration modifies the fatty acid composition of rat plasma and liver lipids and ameliorates the arterial fatty infiltration induced by cholesterol. Also, Rodriguez\textsuperscript{(19)} explained that melatonin also influences both antioxidant enzyme activity and cellular mRNA levels for the antioxidative enzymes glutathione peroxidase, superoxide dismutases and catalase both under physiological and under conditions of elevated oxidative stress. Moreover, Hoyos\textsuperscript{(20)} reported that the increase in total cholesterol and low-density lipoprotein (LDL)-cholesterol induced by a cholesterol-enriched diet was reduced significantly by melatonin administration and prevented the decrease in high-density lipoprotein (HDL)-cholesterol induced by the same diet. Our results come in agreement with the findings of Subramanian et al.\textsuperscript{(21)} who reported that melatonin caused a significant decrease in lipid peroxidation and the levels of cholesterol, phospholipids, triglycerides and free fatty acids in the examined tissues.

Interestingly, tryptophan contains the amino acid niacin (nicotinic acid) that favorably affects very-low-density lipoprotein (VLDL), low-density lipoprotein, and lipoprotein (a) and increases high-density lipoprotein. Recent evidence indicates that niacin acts on G protein-coupled receptor 109A (GPR109A). GPR109A activation reduces triglyceride lipolysis, resulting in decreased free fatty acid mobilization to the liver. Evidence indicates that niacin directly inhibits diacylglycerol acyltransferase-2 resulting in accelerated hepatic apolipoprotein B (apo B) degradation and decreased apo B secretion, thus
explaining reductions in VLDL and LDL\textsuperscript{(22)}. \textbf{Kamanna et al.} \textsuperscript{(23)} focused on the mechanism of hypolipemic action of niacin. The authors indicated that niacin inhibits hepatic diacylglycerol acyltransferase 2, resulting in inhibition of triglyceride synthesis and decreased apolipoprotein B-containing lipoproteins and it decreases the surface expression of hepatic adenosine triphosphate synthase beta-chain, leading to decreased holoparticle high-density lipoprotein catabolism and increased high-density lipoprotein levels.

Hawthorn extraction has the function of depressing the concentration of blood-fat, it co-adjusted lipid metabolism by regulating the transcription expression of adipogenesis genes in fat and muscle tissue of hyperlipidemic animals\textsuperscript{(24)}. This conclusion runs in agreement with the present study concerning the remarkable recovery in the lipid profile (Table 1). The underlying mechanisms for hypocholesterolemic activity of hawthorn may be related to its up-regulation effect of LDL receptors on cell surfaces, or/and inhibition of cholesterol and bile acid absorption or increased excretion of these neutral and acidic sterols\textsuperscript{(6)}. Hawthorn fruit is not only hypolipidemic but also an excellent source of antioxidants; \textbf{Chang et al.}\textsuperscript{(25)} referred the hypolipidemic effect of hawthorn to the presence of antioxidant flavonoids components, similarly \textbf{Zhang}\textsuperscript{(9)} attributed the antioxidant status to the reduction in the production of free radicals, the damage of the tissue and the deposition of oxidized LDL cholesterol. Moreover, \textbf{Pittler et al.}\textsuperscript{(26)} assessed the benefits of hawthorn extract for treating patients with chronic heart failure. The authors' conclusions suggested that there is a significant benefit in symptom control and physiologic outcomes from hawthorn extract as an adjunctive treatment for chronic heart failure. Our results are in agreement with those of \textbf{Hong}\textsuperscript{(27)} who reported that a diet included hawthorn can be considered for the treatment of hyperlipidemia and prevention of atherosclerosis and \textbf{Luo et al.}\textsuperscript{(28)} who illustrated that a health-promoting diet against dyslipidemia combined with polyphenol from hawthorn postulate as a functional formula diet and would be a potent alternative as a health-promoting diet, simultaneously targeting on the complexity and redundancy of dyslipidemia.

Undoubtedly, hyperlipidemia altered some hormonal functions\textsuperscript{(13)}. This alteration was evident in Table (2) where $T_3$, $T_4$ and testosterone hormones significantly decreased ($p<0.01$) and corticosterone hormone significantly increased ($p<0.01$) in hyperlipidemic rats. Tryptophan functions as a biochemical precursor for serotonin that in turn, can be converted to melatonin, via N-acetyltransferase and 5-hydroxyindole-O-methyltransferase activities \textsuperscript{(2)}.
Previous studies have provided evidence that free radicals increase during hyperthyroidism\(^{29}\). Melatonin has been proposed to be useful for the prevention of oxidative stress during hyperthyroidism. It has been reported to be protective in various models of oxidative stress, both through its free radical scavenging effect as well as by directly increasing antioxidant activity\(^{30}\). The hypothesis of an inhibitory effect of melatonin on thyroid hormones may elucidate the effect of tryptophan administration on the recovery of elevated levels of thyroid hormones due to hyperlipidemia (Table 2). Our results are congruent with the findings of Makay et al.\(^{31}\) who reported that thyrotoxicosis stimulates the oxidative stress response and the production of inflammatory cytokines (IL-10 and TNF-alpha); there is a relationship between oxidative stress parameters and inflammatory cytokines; melatonin prevents the increase in \(T_3\) and \(T_4\) and melatonin-based antioxidative treatment inhibits thyroid hormone increasing levels.

The same ameliorating effect of melatonin may run on the testosterone hormone levels after long term administration of tryptophan to hyperlipidemic rats (Table 2). Melatonin triggers gonadotropin releasing hormone (GnRH) secretion in the mediobasal hypothalamus and thus leads to increase follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion, which results in an elevated testosterone response \(^{32, 33}\). These findings came in agreement with those of Faigl et al.\(^{34}\) who concluded that the use of melatonin had a positive effect on the endocrine function of the testicles reflected in improving testicular testosterone production.

Corticosterone is a stress hormone that shows increased levels in response to chronic stress \(^{35}\). This was evident in the hyperlipidemic rats (Table 2) putting in consideration that hyperlipidemia act as an oxidative stressor by decreasing free radical scavenger enzyme gene expression \(^{15}\). On the other hand, melatonin, which is an end product of tryptophan reaction, is known with its stimulating effect on antioxidative enzymes, such as glutathione reductase (GR) and glutathione peroxidase (GPx). These enzymes convert oxidized glutathione to glutathione (GSH), leading to increased GSH activity \(^{36}\). This may explain the regaining of corticosterone hormone to its control level after oral administration of tryptophan to hyperlipidemic group of rats (Table 2).

Total antioxidant activity of hawthorn was assessed by measuring its ability to reduce the hydroxyl radical and hydrogen peroxide and it showed a high ability (81.04\%) to scavenge the radicals \(^{37}\). Moreover Raudonis et al.\(^{38}\)
reported that hawthorn contains the active antioxidant chlorogenic acid in the leaves and flowers, meanwhile, Bahri et al.\textsuperscript{39} identified eight antioxidants of phenolic type in hawthorn extract that presented a strong radical-scavenging activity. These findings could explain the profitable outcome of hawthorn administration represented here in returning the hormonal disorders of hyperlipidemic rats near to the control value (Table 2) considering that hyperlipidemia is an oxidative factor and the multiple antioxidant activity available in hawthorn could minimize this factor.

Coenzyme Q10, which has both energizing and anti-oxidative effects\textsuperscript{40}, plays three well-characterized functions in mitochondria: transfer of reducing equivalents in the electron transport chain, generation of superoxide anion radical and quenching of free radicals. Dietary supplementation of mice and rats with CoQ10 has been demonstrated to augment the endogenous Co Q content (CoQ9+ CoQ10) in mitochondria and homogenates of various tissues, albeit to varying extent \textsuperscript{41}. Consequently, mixing CoQ10 with tryptophan and hawthorn could lessen the hormonal changes induced by hyperlipidemic oxidative stress (Table 2).

Total body weight is one of the biomarkers of obesity demonstration\textsuperscript{42}. Jin Son et al.\textsuperscript{43} reported a substantially higher body weight in mice fed with high fat diet than that of the normal control mice. This was obvious in our work where the group of rats fed on the HFD recorded a total body weight almost the double of the control group at the end of the experimental period (Figure 1). This increase may be due to perivascular adipose inflammation and oxidative stress \textsuperscript{44}. Moreover, Hageman et al.\textsuperscript{45} stated that HFD led to weight gain and attributed this gain to the dietary fatty acids that were partially metabolized and converted in both liver and fat tissues; saturated fatty acids were converted in the liver to mono-unsaturated fatty acids and poly-unsaturated fatty acids, and oleic acid was the preferred mono-unsaturated fatty acid for storage of excess energy in all tissues of HFD-fed mice. Transcriptional changes largely reflected the tissue-specific fat deposition. The increased body weight gain in this research came in agreement with that of Ferreira et al.\textsuperscript{46} who reported that obesity may represent a state of chronic low-grade inflammation associated with infiltration of adipose tissue by inflammatory cell, body weight increased by approximately 20% in mice fed the HFD compared with mice fed the control diet and the results have shown that the nature of nutrients influences the type of proinflammatory cytokines in target organs and may contribute to the comorbidities of obesity. The negative correlation between body weight, total
lipids and triglycerides may point to the suggestion that dyslipidemia not necessarily related to body weight (Table 3).

No wonder that tryptophan, the precursor for serotonin, melatonin\(^2\), and niacin\(^3\); hawthorn that regulate the transcription expression of adipogenesis genes in fat and muscle tissue of hyperlipidemic subjects\(^{24}\) and CoQ10 that tends to decrease hepatic stress gene expression involved in reactive oxygen species production\(^{47}\), in addition to their antioxidants capability previously mentioned could control the over body weight gained due to HFD. This was clear in decreasing the total body weight when administrated independently or mixed to hyperlipidemic rats (Figure 1). Moreover, it seems that hawthorn influence the thyroid hormone in playing a role in reduction of body weight as evidenced by the positive significant correlation of \(T_3\) and body weight in the group administrated with hawthorn (Table 3). Similarly, the negative correlation between body weight and corticosterone in the mixed group pointed to the beneficial effect of these combined antioxidants in minimizing the chronic stress induced by corticosterone.

For conclusion we may state that mixing three potent antioxidant, tryptophan, hawthorn and coenzyme Q10, consequently allowed a powerful formula that could minimize the dreadful oxidative effects of hyperlipidemia articulated in this study as impaired lipid profile, hormonal dysfunction and overweight. This mixture when administrated orally to hyperlipidemic rats resulted in attaining all the investigated parameters almost to the control values (Table 1 and Figure 1). This may point to the most profit achieved by mixing three antioxidants in ameliorating the oxidative damage of hyperlipidemia.

REFERENCES


تعظيم دور مخلوط من المواد المخفضة للليبيدات في ذكور الجرذان البيضاء

ميخائيل إبراهيم ميخائيل - ماجد محمد عامر

قسم التطبيقات البيولوجية - شعبة تطبيقات النظم المشعة - هيئة الطاقة الذرية

استخدم في هذه الدراسة ثلاثون من ذكور الجرذان البيضاء لدراسة تأثير استخدام التريتوفات أو/مع مستخلص نبات الزعور و كوازنزيم كيو10 لتخفيف أثر تعاطي وجهة مرتفعة الدهون على الدهون المرتفعة، الاضطرابات الهرمونية ووزن الجسم. تم فصل ستة حيوانات ومعاملتهم كمجموعة ضابطة أما بباقي الأربعة وعشرون جرذًا فتم تغذيتهن على وجهة عملية قياسية ولكن مضاف إليها 20جم/100جم دهن لتصلب وجهة مرتفعة الدهون وذلك لمدة ثمانية أسابيع قبل بدء التجربة. بعد ثماني أسابيع تم تقسيم هذه الجرذان التي تغذت على وجهة مرتفعة الدهون عشوائيا إلى أربعة مجموعات متساوية: مجموعة الدهون المرتفعة، مجموعة معاملة بالتريتوفان (100جم/كجم من وزن الجسم)، مجموعة معاملة بمستخلص نبات الزعور (50جم/100جم من وزن الجسم) ومجموعة معاملة بمخلوط من التريتوفات والزعور وكوازنزيم كيو10 (50جم/100جم من وزن الجسم). تم تسجيل وزن الجسم مرتين أسبوعيا طوال فترة التجربة.

بعد ثلاثون يوما تم ذبح الجرذان وتجميع المصل لقياس كل من الدهون الكلية والجليريدات الثلاثية والكوليستيرول الكلي والكوليستيرول عالي ومنخفض الكثافة وكل من هرمونات الغدة الدرقية والنسوتيسترونين والكورتيكسترونين.

وقد أظهرت النتائج أن المعاملة بالتريتوفات أو مستخلص نبات الزعور منفرد أو مخلوطين مع كوازنزيم كيو10 قد حسنا من الآثار السيئة التي أحدثها التعاطي على وجهة مرتفعة الدهون، و كان التحسن الأمثل في المجموعة التي أعطيت المخلوط من الثلاثة مضادات للأمراض على كل من ارتفاع الدهون والهرمونات ووزن الجسم.