Hypolipidemic and Anti-Atherogenic effect of methanol extract of Fennel (Foeniculum Vulgare) in hypercholesterolemic mice

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Abstract

The epidemiological studies suggest that the diets rich in fruits and vegetables, an important vector of the micronutrients and phytochemicals elements, help to prevent the diseases such as cardiovascular diseases. Atherosclerosis and their cardiovascular complications represent a major cause of the mortality in developing country, also called a less-developed country and pose a major public health problem. For these reasons, our study aims to study the anticholesterol and anti-atherogenic of the methanol extracts in the Foeniculum vulgare, most studied in the literature, to show the therapeutic effects of this plant that is most used in Moroccan dishes. In this study, we investigated in mice the effects of methanol extract of fennel on lipid metabolism in plasma, liver and histopathological study. We show here that treatment caused a significant decrease of plasma lipid levels. 24 h after treatment, plasma total cholesterol, triglycerides, LDL-cholesterol and Apolipoprotein B decreased by 35 %, 50 %, 50% and 60%, respectively and increased in HDL-cholesterol and apolipoprotein A-I by 56 % and 52 %, respectively. For histo-pathological study, our results show that Anti-Atherogenic has an important effect. Indeed, it decrease the deposition of triglycerides in the fatty liver form and facilitates the flow of blood in the coronary arteries by preventing the deposition of lipids in the light of the coronary arteries by reducing serum and liver lipids. Fennel is an aromatic and medicinal plant nutrition which showed Hypolipidemic and Anti-Atherogenic and therefore can be used for the prevention of cardiovascular diseases.

Keywords: Foeniculum vulgare, methanol extract, Triton WR-1339, hypolipidemic , anti-Atherogen effect

Introduction

The experimental and epidemiological studies have the important role of the hypercholesterolemia in the pathogenesis of the atherosclerosis. This role has been clarified by studies of seven countries (Kaliman et al., 1981) showing that the total cholesterol is positively correlated with coronary risk. This positive relationship is
linked caused by the LDL fraction (Low Density Lipoprotein) fraction. But, the HDL (High Density Lipoprotein) fraction is opposite negatively correlated with risk. The epidemiological studies have also shown the existence of a correlation between of the triglycerides concentration and the occurrence of a subsequent coronary complication (Jeffrey et al., 2004, Christoffersen et al., 2008; Kromhout et al., 2010).

Atherosclerosis is characterized by liver disease without alcohol which it’s manifested by the significant lipid deposition in hepatocytes of liver parenchyma as a single macro-vesicular steatosis or steatohepatitis, and can develop fibrosis in cirrhosis which is increasingly recognized as an important cause of mortality (Angulo and Lindor, 2002).

High dietary cholesterol causes an important hypercholesterolemia depending on species sensitivity. This phenomenon is generally characterized by an increase in the cholesterol, the triglycerides and the LDL and sometimes a creasing of the HDL. Therefore, the mice develop very quickly hypercholesterolemia (Schreurs et al., 2007).

The beneficial effect of the Mediterranean diet in protecting against of the cardiovascular disease is attributed to its fruit and vegetables rich. Which before act through their nutrients, fiber, Vitamin C, Vitamin E, phenolic composed and polyunsaturated acids (Parejo et al., 2004). These compounds have attracted great interest and continue to be the subject of much research.

Several epidemiological studies have shown the importance of phenolic compounds in reducing of the risk of death from cardiovascular disease (Yiannis et al., 2003). Other studies have shown the Hypolipidemic effect of green tea polyphenols (De Lange et al., 2003). A similar effect was noted for condensed tannins of green tea (Kabouche, 2010). The phenol compounds of the fennel have a large organoleptic and nutritional interest (Weiping and Baokang, 2011).

Given the richness of fennel Hypolipidemic products, our aim consists to search Hypolipidemic and Anti-Atherogenic Effect of methanol extract of Fennel (Foeniculum Vulgare) in hypercholesterolemic mice.

Materials and Methods

Preparation of animals

108 mice C57B1/6 aged than 2 weeks with a mean weight of 20±2 g. These animals were divided into 3 lots. Each lot was divided on 6 groups (n=6). Therefore, each group of mice was treated with intraperitoneal injection of 1 ml of the aqueous extract of the fennel with a concentration determined. The concentrations used were 50%, 41.66%, 34.72%, 28.93%, 24.11% and 20.10%, obtained by diluting 1.2 from a stock solution of the aqueous extract prepared as described above 50 g of fennel ground for 100 ml distilled water. After administration of the extract, the animals are observed every 30 minutes during 8 hours of the first day and every day for a week (Gad, 1999). During the observation period, there is the number of dead and symptomatic disorders.

Method of calculation

The dead mice were recorded for 48 hours and lethal doses 50 are calculated by the Spearman-Karber method:

\[
\text{Log DL50} = \text{Log C0} + \text{Log (Fd)} (0.5 - \frac{M}{n})
\]

C0 : Lethal dose inducing 100% of the mortality.
M : Number of deaths per dose.
n : Number of mice per dose.
Fd : Dilution Factor or growth between 2 doses.

Preparation of Foeniculum vulgare Metanicolic Extract

Foeniculum vulgare was collected in periphery of Casablanca city (Morocco), the fennel bulb dried and crushed,
leaves a night in the methanol 80%, mixed well, filter and evaporated using rotavapour. The methanolic extract obtained is stored at – 20 °C up to use.

Animals and Treatment
Experiments were performed on adult male C57Bl/6 mice weighing 20±2 g. animals bred in the animal house of the Tit Mellil experimental center of the Pasteur Institute of Morocco. They were housed in a controlled room with a 12 h light-dark cycle, at room temperature at 22 ± 02 C°, and kept on standard pellet diet (INAAM Society, Casablanca. Morocco). Animal maintenance and handling were in accordance to internationally accepted standard guidelines for use of laboratory animals.

Experimental Protocol
18 mice were divided into three equal groups. The first group served as control (CG). This group received intraperitoneal administration of normal saline and water by gavages, the second group (HG) was treated with intraperitoneal injection of Triton WR-1339 (Tyloapol, Sigma-Aldrich,USA) at a dose 200 mg/kg and gavaged with water ; in the third group (HG + Fv. EM) the animal were also treated with intraperitoneal injection of Triton (200 mg/kg BW) followed by intragastric administration of Foeniculum vulgare metanolic extract (200mg/kg BW). In the following period of study (24 h), animals had access only to water. At the end of this time, animals were sacrificed and blood samples were immediately centrifuged (2500 rpm/10 min), then plasma was used for lipid analysis. Liver and heart were frozen. Liver was submitted to lipid extraction also liver and heart was fixed for histological study.

Biochemical Analysis
The concentration of lipoproteins was determined in plasma by enzymatic assay using commercial kit reagents: Total cholesterol (Biocon, USA), Triglycerides (Biosystems, France) and HDL-cholesterol (Cromaster, India). LDL-cholesterol level was calculated by using the Friedewald formula. The Apolipoprotein AI and apolipoprotein B levels were measured by electroimmunodiffusion method (Sebia, France).

Extraction of Liver Lipids
After the collection of blood, the liver was submitted to lipid extraction for cholesterol and triglycerides: 1 g of tissue was homogenized with 10 ml of isopropanol, incubated for 48h at 4°C, then centrifuged at 4000 rpm /10 min. Lipids were measured in the supernatant and the results are expressed as mg of cholesterol / Triglycerides per gram of body (Christie, 1993).

Histological Study
Fragments of frozen liver and heart were fixed in formol 10% for cryosectioning. Transverse sections (5 µm thick) were collected throughout the length of segment, and adjacent slides were stained by hématoxylin, eosin and lugol (Soler Rivas et al., 2000).

Determination of Total Polyphenol Contents
One gram of powdered Foeniculum vulgare bulb was used for the extraction of polyphenols. It incubated with 50 ml of 70 % aqueous acetone under 20 min sonication in an ultrasonic bath at 30° C. The extracts were rapidly filtered under vacuum and kept refrigerated until use.

Total polyphenols were determined by Folin-Ciocalteu procedure (Harnafi et al., 2007). Aqueous acetone extracts were diluted 200 folds, and to aliquots of 0.5 ml were added 0.25 ml of Folin Ciocalteu reagent and 1.25 ml 20% aqueous sodium carbonate solution. Samples were homogenized and absorbance of blue colored mixtures recorded after 40 min incubation at 725 nm against a blank containing 0.5 ml of 70% aqueous acetone, 0.25 ml of Folin-Ciocalteu reagent and 1.25 ml 20% aqueous sodium carbonate solution. The amount of total polyphenols was calculated as a catechin equivalent from the calibration curve of catechin standard solutions and expressed as mg
catechin/g dry plant material (Jeffrey et al., 2004). All measurements were done in triplicate.

Quantification of Tannins
Total tannin content was determined by Folin-Ciocalteu procedure as described above, after capture of tannins by their adsorption to hide powder (Boskabady et al., 2002). In brief, 20 ml of aqueous acetone *Foeniculum vulgare* fruit extract were homogenized with 200 mg of hide powder and the mixture was stirred for 1 h at 40 °C. After filtration, no adsorbed phenolics were detected using Folin-Ciocaltelue procedure. Calculated values were subtracted from total polyphenol contents and the amount of total tannins expressed as mg equivalent catechin/g dry plant materiel. All measurements were done in triplicate.

Determination of Flavonoids
One gram of *Foeniculum vulgare* fruit was reduced to a fine powder and homogenized with 20 ml of extracting solvent (methanol-water-acetic acid, 140; 50; 10, v/v/v) and filtered into volumetric flasks. Volume was adjusted to100 ml by addition of extracting solvent. To each 5 ml of analyzed solution, 2.5 ml of AlCl3 reagent were added (133 mg crystalline aluminum chloride and 400 mg crystalline sodium acetate were dissolved in 100 ml of extracting solvent) and absorbance recorded at 430 nm against a blank (5 ml of analyzed solution plus 2.5 ml of water). The flavonoids content was expressed as mg quercetol/g dry fruit. Measurements were done in triplicate (Hamafi et al., 2007).

Statistical Analyzes
The mean and standard deviation of different results and their statistical analysis were released with ANOVA (Tukey test, SigmaStat software). The results for which p<0.01 were considered statistically significant.

Results

**DL50 determination**
The results of the determination of the median lethal dose performed at 3 times were indicated in Table.1:

<table>
<thead>
<tr>
<th>Concentration of the aqueous (C)</th>
<th>Mean Number of the mortality (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 : 50.00</td>
<td>6</td>
</tr>
<tr>
<td>C2 : 41.66</td>
<td>4</td>
</tr>
<tr>
<td>C3 : 34.72</td>
<td>2</td>
</tr>
<tr>
<td>C4 : 28.93</td>
<td>2</td>
</tr>
<tr>
<td>C5 : 24.11</td>
<td>1</td>
</tr>
<tr>
<td>C6 : 20.09</td>
<td>0</td>
</tr>
</tbody>
</table>

The mean lethal dose calculated by the Spearman-Karber formula: is of the 542.50 ± 14.20 mg/kg of body weight. Indeed, it suffices to apply the above to a number of mice to cause the death of half of its total effective.

**Determination of Hypolipidemic effect of fennel**
The values of serum and hepatic lipid concentrations, lipoproteins, apolipoproteins were presented in Table.2, which shows a net decrease in total cholesterol, triglycerides, C-LDL and Apo. B of 35%, 50%, 50% and 60% respectively, and increased C-HDL and Apo. AI of 56% and 52% comparing the group (HG) with group (HG+ Fv.EM).
The LDL/HDL and TC/HDL atherogenic index showed a significant increase in hypercholesterolimical mice with a total more than 5 whereas mice treated with fennel these index were decreased from 60% to 65% respectively.

**Table 2. Plasma concentration of serum lipids in mice treated with methanol extract of fennel (g/l)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total Cholesterol</th>
<th>Triglycerides</th>
<th>C-HDL</th>
<th>C-LDL</th>
<th>Apo.AI</th>
<th>Apo.B</th>
<th>Atherogenic index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group CG</td>
<td>0.95±0.09</td>
<td>0.70±0.11</td>
<td>0.26±0.01</td>
<td>0.5±0.10</td>
<td>1.47±0.20</td>
<td>1.11±0.07</td>
</tr>
<tr>
<td></td>
<td>Group HG</td>
<td>1.48±0.15</td>
<td>1.83±0.05</td>
<td>0.14±0.01</td>
<td>0.9±0.15</td>
<td>0.59±0.04</td>
<td>3.1±0.15</td>
</tr>
<tr>
<td></td>
<td>Group HG + Fv.EM</td>
<td>0.95±0.13</td>
<td>0.91±0.02</td>
<td>0.32±0.05</td>
<td>0.45±0.18</td>
<td>1.22±0.04</td>
<td>1.25±0.26</td>
</tr>
<tr>
<td>Probability</td>
<td>CG/HG</td>
<td>0.078</td>
<td>0.074</td>
<td>0.00013</td>
<td>0.072</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Probability</td>
<td>HG/HG+Fv.EM</td>
<td>0.00001</td>
<td>0.00285</td>
<td>0.0001</td>
<td>0.00023</td>
<td>&lt;0.0001</td>
<td>0.00002</td>
</tr>
</tbody>
</table>

- **X**: mean g/l ± DS: Déviation standard.
- **Xa b**: Means with different letters for the same lipid parameters were significantly different at the 5% level.
- (*) : NS: Not significant difference.
- (**) , (***) : Respectively with significant differences 1% and 1‰.

**Hepatic concentration of total cholesterol and triglycerides**

The concentrations of triglycerides and total cholesterol liver were significantly reduced by 42% and 64% respectively (Table 3).

**Table 3. Liver concentrations of triglycerides and total cholesterol treated with methanol extract of fennel (mg/g of liver)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Triglycerides</th>
<th>Total Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group CG</td>
<td>4.76 ± 0.58</td>
</tr>
<tr>
<td></td>
<td>Group HG</td>
<td>17.81 ± 0.69a</td>
</tr>
<tr>
<td></td>
<td>Group HG+Fv.EM</td>
<td>10.37 ± 0.76a</td>
</tr>
<tr>
<td>Probability</td>
<td>CG/HG</td>
<td>P = 0.000000278 (***)</td>
</tr>
<tr>
<td>Probability</td>
<td>HG/HG+Fv.EM</td>
<td>P = 0.000000231 (**)</td>
</tr>
</tbody>
</table>

**Quantification of antioxidants**

**Determination of polyphenols, tannins and flavonoids**

The quantification of antioxidants: polyphenols, tannins and flavonoids by the Folin-Ciocalteu method showed the presence of a very high concentration of the polyphenols 95.78 ± 2.13 (mg/g), the tannins 39.68 ± 3.05 (mg/g) and the flavonoids of 4.10 ± 0.04 (mg/g). But, the tannins represent 28.50% and flavonoids represents 3% in relation to total polyphenols. We note that the polyphenols are presented in large quantities compared with tannins and flavonoids of the 68.62% (Table 4).

**Histo-pathology study**

Microscopic observation of organ tissues collected revealed numerous anomalies compared to the organs of animals and particularly in the liver and heart of the animals.
Table 4. Quantification of polyphenols, tannins and flavonoids

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Quantity of the plant (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyphenols(^a)</td>
<td>95.78 ± 2.13</td>
</tr>
<tr>
<td>Tannins(^a)</td>
<td>39.68 ± 3.05</td>
</tr>
<tr>
<td>Flavonides(^b)</td>
<td>4.10 ± 0.04</td>
</tr>
</tbody>
</table>

\(^a\): Expressed as mg of catechin/g of fruit.
\(^b\): Expressed in quercetin mg/g of fruit.

a. Liver

The normal liver tissue is formed of lobules of the polyhedral form (Figure 1a). The centrolobular vein was found in the center of the lobules. The hepatocytes have a polygonal form. Each a hepatocyte contains a rounded nucleus. The cytoplasm contains a very abundant endoplasmic reticulum.

In the liver hypercholesterolemic, we noted of steatosis liver presenting in the form empty white vacuoles which are only deposits of triglycerides in hepatocytes (Figure 1b). In liver tissue treated with fennel, we observed a clearly decrease of the hepatic steatosis.

![Figure 1](image1.png)

Figure 1. Effect of methanolic extract of fennel in deposit hepatic steatosis in liver mice.

a. Control group, b. Hypercholesterolemic group, c. Hypercholesterolemic liver treated by methanol extract of fennel.

b. Heart

The microscopic study of the coronary arteries of the mice of hypercholesterolemia groups revealed a net lipid deposition and debris including the accumulation of triglycerides in the coronary arteries caused by treatment of Triton WR 1339 (Figure 2a). But, the fennel treatment with showed a significant decrease in blood vessel obstruction (Figure 2b).

![Figure 2](image2.png)

Figure 2. Effect of methanol extract on lipid deposition in the coronary arteries of mice.

Discussion

Several studies have used the Triton WR-1339 to block the storage of lipoproteins that rich of the triglyceride to induce acute hyperlipidemia in several animals. The accumulation of serum lipids by this detergent seems to be particularly caused by inhibition of the activity of the lipase lipoprotein (Otway and Robinson, 1967). This model has been used by several authors (Fiser et al., 1974; Kalopissis et al., 1980) and in particular, for the mice, it was used to examine the hypolipidemic plants (Schurr et al., 1972). Many plants such as Ocimum basilicum Vaccinum (Cignarella et al., 1996) and Phyllanthus niruri (Khanna et al., 2002) were studied for their acute hypolipidemic activity by Triton WR-1339 that induced hyperlipidemic animals.

The study of the several authors showed that administration intraperitoneal triton WR-1339 in adult mice induced hyperlipidemia with increased triglycerides and total serum cholesterol that were achieved after 24 h compared to control groups (Srikanth and Muralidharan, 2009).

Similar results were described by Harnafi et al. 2007 and Amrani et al. 2006 using the same protocol to study the hypolipidemic effect of the Erica multiflora and Ocimum basilicum, respectively. Similar for the study of the Jingjing and Xiangrong 2007, which shown in mice a very significant increase of the serum lipids after administration of the triton WR-1339 after 24 hours.

In our study, we were used the mice as soon as model and our results are similar with those literature. Indeed, a significant change in lipid profile after 24 hours after injection intraperitoneal TritonWR-1339 was reported. The tables 1 and 2 showed demonstrated the feasibility of using this protocol of acute hyperlipidemia. To examine the hypolipidemic activity of the methanol extract of fennel demonstrate significant decrease total cholesterol, triglycerides, C-LDL and Apo. B of 35%, 50%, 50%, 60%. But a significant increase of 56% and 40% for HDL-C and Apo. AI respectively.

Our results clearly show that the methanol extract of fennel with a dose of 0.2 g/kg (body weight) causes significantly lower concentrations of liver lipids as soon as cholesterol and triglycerides of 64% and 42% respectively. The increase of the serum and liver lipids caused by the injection of the Triton WR-1339 is caused to increased of the secretion of VLDL by liver accompanied with a strong reduction in catabolism of VLDL and C-LDL (Amrani et al., 2006).Thus, the proportion of triglycerides in the VLDL is higher multiple than those the cholesterol. It's not surprising that the hypolipidemic action of fennel was significantly higher for triglycerides followed by cholesterol. This result suggests that the extracts can restore, at least partially, the catabolism of β-lipoproteins.

The important mechanism of this activity has not been elucidated in this study. However, it has been studied by other studies (Campillo et al., 1994. Pérez et al., 1999). The metabolism of VLDL may be due to the increased stimulation of the lipolytic activity of the serum lipoprotein lipase (LPL).

Moreover, several authors showed that the phenolic compounds of the grape seed increases the action of the LPL (Del Bas et al., 2005) and it reduces the lipid profile indicating the reduction of total cholesterol and the C-LDL fraction extracts of fennel, which was associated with an increase in serum C-HDL in our study. This plays a role in the transport of the cholesterol from peripheral tissues to the liver. This result suggests that cholesterol decreased by the activity of extracts of fennel stimulates the mobilization of cholesterol from peripheral tissues to the liver for elimination as bile acids, this hypothesis has been advanced by several authors (Piyachaturawat et al., 1999).

However, the hypcholesterolemic effect of turmeric on the India with elimination of cholesterol in the bile secretion was indirectly validated by Del Bas et al., 2005 have shown that the grape procyanidins increase important enzymes of bile acid synthesis.

Although specific experiments will be designed to test this hypothesis, these results are consistent with reports of the Lee, 2004 ; Kabouche, 2010 ; and Sabatini, 2010 showing that the methanol extracts and water-soluble extracts have cholesterol-suppressive capabilities and capacity to mitigate the accelerated atherosclerosis in hypercholesterolemic development models, we found that the flavonoids and the polyphenols are present in the methanol extract of the Foeniculum vulgare, which are responsible for the Hypolipidemic effect and anti-atherogenic. The authors Weiping and Baokang (2011) identified polyphenols and antioxidants by HPLC chromatographic
methods coupled with mass spectrometry, they showed a series of pharmacological activities, including the hypocholesterolemia.

The comparison of mean lipid parameters noted in the treated mice compared to hypercholesterolemic us to calculate the indices of atherogenic LDL/HDL and TC / HDL. Our results show that the Triton WR-1339 has increased 2 reports, while after administration of fennel these two reports are reduced significantly from 60% and 65% respectively for the methanol extract of the fennel. The study of the Jingjing and Xiangrong (2007) showed that flavonoids reduce the report C-LDL/C-HDL which can accelerate the movement of cholesterol from peripheral tissues to the liver for catabolism and excretion, which makes reduce the risk of cardiovascular disease.

The experimental data in this study show that all the changes at the tissue level induce acute hyperlipidemia in several animals is caused by the administration of Triton WR1339, which promotes the storage of triglyceride-rich lipoproteins and specifically inhibits the activity of lipoprotein lipase by accumulating triglycerides level as hepatic steatosis (Otway and Robinson, 1967).

The first stage of the hepatic steatosis corresponds at the accumulation of triglycerides in the liver due to an imbalance between the channels leading to the formation and breakdown of triglycerides. The development of steatosis weakens hepatocytes which are then more vulnerable to attacks. The second phase corresponds to the development of cell injury and the development of liver fibrosis caused by the oxidative stress (Marchesini et al., 2003).

In our studies, the formation of liver steatosis by the significant deposition of triglycerides in liver parenchyma shows the important effect of Triton WR 1339 in the induction of hyperlipedemiac wholes in which of the mice tested in accordance with the serum and liver assayed. So after administration of extracts of fennel showed a net decrease of steatosis. In the coronary arteries, our study showed a significant lipid deposition in 50% of mice, which over time can cause a blockage of the arteries and increase thereafter atherosclerotic disease. The animals are treated with methanol extract of *Foeniculum vulgare*, show a decrease of the lipid deposition in hepatocytes and also in the coronary arteries. Various studies have shown that the presence of antioxidants such as polyphenols may limit some tissue damage and delay the onset of these diseases (Tijburg et al., 2000). It was thought that the antioxidant mechanisms responsible for the protection of fat by polyphenols could also play a role in protecting blood vessels, and thus delay the development of the atherosclerosis. It seems that more complex phenomena involved (Kabouch, 2010)

The study of the Zhenhua et al. (1991) showed that flavonoids are responsible for inhibiting the oxidation of LDL induced by activation of vascular cells. Polyphenols isolated from green tea were able to inhibit the oxidation of LDL by macrophages in culture, but there is little information on the effectiveness of individual flavonoids fennel. Catechin and quercetin protected the LDL oxidation when incubated with different cells in culture, such as human monocytes derived macrophages, endothelial cells of human umbilical vein cells or lymphoid (Gurinder and Daljit 2010). It has been suggested that this phenomenon was due to the ability of flavonoids to inhibit lipoprotein activity in vitro (Robak et al., 1988) and in vivo (Katiyar et al., 1992). In addition to inhibiting the oxidation of LDL-C cell-mediated, catechin and quercetin also protect lymphoid cells against the cytotoxic effects of oxidized LDL previously. This effect is probably caused by the increase of antioxidant present in the flavonoids.

The development of cardiovascular disease is a function several environmental factors (including diet) and results of epidemiological studies indicate that a diet rich in fruits and vegetables have a protective effect (Ness and Powles 1997).

Dietary studies have shown that flavonoids of the soy and lemon bioflavonoids may reduce cholesterol esters and triglycerides and extent of steatosis liver in mice (Peluso et al., 2000; Kim et al., 2005). The mechanism responsible for the attenuation of lipogenesis by flavonoids in cultured liver cells has not been elucidated, and similar effects are clearly demonstrated in vivo. Biosynthetic pathways in addition, the weight of the neutral lipids in the hepatocytes cytosolic body is controlled by the hydrolysis of lipid (Kawakami et al., 2005).

The Atherosclerosis is a hardening and narrowing of the arteries, which progresses and blocks arteries. Atherosclerosis is the most common cause of heart attacks and peripheral vascular disease (Benavente et al., 2008).
The disease is reported mainly in LDL, cholesterol, cholesterol esters and triglycerides that are transported by LDL (particularly Apo.B).

Actually, epidemiological studies have found that the Mediterranean diet, rich in fruits and vegetables, using largely plants such as *Foeniculum vulgare* as popular salads or dishes (tagine). This plant contains high levels of antioxidants and reduces the risk of cardiovascular disease (Paulo et al., 2010).

The current results show that the methanolic extract of *Foeniculum vulgare* has a very high antioxidant power, which can contribute to the potential possibilities of this plant foods or supplements to therapeutically data to be beneficial in hyperlipidemic and anti-atherogenic and preventing the development of related diseases. The composition of fennel fatty acids has been described by Cosge et al. (2008). Namely, linoleic, palmitic and oleic acid, were major factors in the acetone extract (Singh et al., 2006) who proved the benefic protective effect against atherosclerosis even for compounds phenolic (Parejo et al., 2004) and flavonoids (Weiping and Baokang 2011).

**Conclusion**

In conclusion, our results show that the administration of the methanol extract of fennel caused a Hypolipidemic and anti-Atherosclerotic effect in reducing the lipids concentrations of serum and liver as well as the deposition of triglycerides in the form of lipids and fatty liver facilitating the blood circulation in the coronary arteries preventing deposition of lipids in the lumens of the coronary arteries by the reduced serum and liver lipids.

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