Comparative evaluation of *Baccharis trimera*, *Pimpinella anisum* and statin on the biochemical profile of Wistar rats

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**Abstract**

Many are the plants for therapeutic purposes. *Baccharis trimera* is known to treat rheumatism, diabetes, and liver disorders. *Pimpinella anisum* is known to control colds, cough, bronchitis, fever, cramps and inflammation. The aim of this study was to evaluate the use of *B. trimera* and *P. anisum* and compare with statin effects on plasma lipids of Wistar rats. Sixty Animals were divided in control group (CG) and G2 (treated with anise), G3 (*B. trimera*) and G4 (statin). Plants and statin were administrated by intra-gastric route twice a day for 30 days. No modifications in glycaemia were observed in the experimental groups. Reductions were observed in cholesterol levels in treated groups. For LDL-c levels, significant differences were observed in G2 and G4. G3 showed significant reduction in the triglycerides levels and no significant differences were observed in the glycaemia in the studied groups. Increased levels of HDL-c were presented by the groups treated with the plants. The group treated with *B. trimera* showed significant reduction in triglycerides when compared to the control group. Our results suggest that the plants used in this work have similar effects in the lipid profile of Wistar rats when compared to the use of statin.

**Keywords**: *Pimpinella anisum*, *Baccharis trimera*, estatin, cholesterol, LDL-c, HDL-c

**Introduction**

The use of medicinal plants for therapeutic purposes is one of the mankind oldest forms of medical practice and many studies have been designed to show the effects of these plants in many pathologies. As chronic degenerative diseases such as cardiovascular disease, diabetes and obesity are among the leading causes of death in the modern world, they are used as models to investigate the effect of plants on the genesis and treatment of these diseases [1-2]. *Baccharis trimera* (popularly known in Brazil as “carqueja”) is well known for its various medicinal properties and it is used to treat liver and kidney diseases, rheumatism, diabetes, and digestive disorders. Some studies have shown antioxidant, anti-inflammatory and antimutagenic properties, as well as, analgesic effects [3-8]. It presents apigenin, genkwanin, cirsimartitin, eupatorin, hispidulin, 7,4’-di-O-methyl-apigenin, luteolin, nepetin, quercetin, 3-O-methylquercetin and rutin as major flavonoid constituents, essential oils, saponins and diterpenoid [9-10]. *Pimpinella anisum* L. is another well-known plant much used by the population. Also known as anise, it has a strong sweet taste and aroma and is commonly used as a medication for the control of colds, coughs, bronchitis, fever, cramps, inflammation, bad digestion, and loss of appetite as well as a condiment [11]. Many biological effects of *Pimpinella anisum* have been identified. For example, it can display antiepileptic effects, antispasmodic and gastric protection [12-14]. It can also promote hypoglycemic effects and can reduce the effects of oxidative stress by reducing the action of free radicals [15]. Because of the wide range of applications of the above plants, this paper aims to evaluate their effects on the biochemical profile of Wistar rats and compare with those promoted by simvastatin, which is a synthetic lipid lowering drug and belongs to a class of drugs widely used in combating the deviations in lipid profile.

**Materials and Methods**

**Experimental animals**

Sixty male Wistar rats weighing approximately 250g were used. They were kept in the vivarium at UNIMAR (University of Marilia) under a dark/light cycle of 12 hours, room temperature of 22 ± 2°C, and relative air humidity of 60 ± 5%. After a period of seven days of acclimation to the laboratory, the animals were divided randomly into 4 groups (n=15) treated for 30 days, as follows: G1 received water (Control Group); G2 received *P. anisum* by gavage route; G3 received *B. trimera* by gavage route and G4 that received statin also by intra-gastric route. Animals of all groups received water and food *ad libitum* during the treatment period.

This work was approved by the Animal Research Ethics Committee of the University of Marilia (UNIMAR) with registration number 250000764/2007-47 de 18.01.2007. The

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animals were treated according to the “Guide for the Care and Use of Experimental Animals” (that follows principles for the care of laboratory animals).

**Preparation of aqueous extracts of P. anisum and B. trimera**

The extracts of P. anisum seed and B. trimera leaf were prepared by infusion at a concentration of 5 g/mL. The extract was stored in amber glass vials of 30 mL and kept in the freezer for later use.

**Preparation of Statin**

Simvastatin were obtained in local pharmacy and the tablets were ground and mixed in water immediately before administration (5 g/mL).

**Administration of the plants and statin**

The administration of the plant extracts and statin (simvastatin) was done twice a day: in the early morning and late afternoon (according to the weight of animals) and the treatment lasted for 30 days. The administered doses were 200 μl of saline solution for GC and 0.3 mg/kg of aqueous extract of the plants (G2 and G3) and statin (G4).

**Collection of blood samples and determination of the biochemical profile and Atherogenic Index (AI)**

After 30 days of treatment, the animals were anesthetized with Thiopental (sodium pentobarbital) until complete sedation, after which blood samples were drawn to determine their biochemical profile: total cholesterol, LDL-c, HDL-c, triglycerides and glycaemia. The glucose and lipid levels were measured in mg/dL.

The exams were performed at the Clinical Analysis Lab of the University Hospital of UNIMAR (São Francisco Laboratoy) and the results were interpreted according to the ADA [16].

Atherogenic Index (AI) was calculated after Schulpis, Karikas [17] and also used by Munshi, Joshi, Rane [18]: AI = (Total cholesterol – HDL-c)/HDL-c.

**Statistical analysis**

Data analyses were performed using Analysis of Variance (ANOVA) and complemented by the Tukey test at significance level of 5%.

**Results and Discussion**

Table 1 shows the statistical results from the biochemical parameters in the studied groups (G1-G4). Groups treated with plants and statin showed significant reduction on the cholesterol levels. For HDL-c levels, no significant differences between the control group (G1) and the group treated with statin (G4) were observed, but there was a significant increase of this parameter in animals treated with P. anisum (G2) and B. trimera (G3). For LDL-c levels, significant differences were observed in G2 and G4 when compared to control group. G3 showed significant reduction in the triglycerides levels and no significant differences were observed in the glycaemia in the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
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<tbody>
<tr>
<td><strong>Cholesterol</strong></td>
<td>89,18 ± 4,09A</td>
<td>78,25 ± 4,81B</td>
<td>76,31 ± 6,51B</td>
<td>78,59 ± 5,20B</td>
</tr>
<tr>
<td><strong>HDL-c</strong></td>
<td>21,00 ± 1,61A</td>
<td>30,33 ± 1,50C</td>
<td>24,31 ± 1,49B</td>
<td>21,83 ± 2,79A</td>
</tr>
<tr>
<td><strong>LDL-c</strong></td>
<td>34,93 ± 4,61B</td>
<td>21,37 ± 7,11A</td>
<td>33,77 ± 6,63B</td>
<td>25,57 ± 6,29A</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td>118,00 ± 14,62BC</td>
<td>122,50 ± 22,76BC</td>
<td>91,15 ± 18,33A</td>
<td>105,17 ± 21,20AB</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>75,18 ± 4,09A</td>
<td>78,25 ± 4,81B</td>
<td>76,31 ± 6,51B</td>
<td>85,00 ± 11,20A</td>
</tr>
</tbody>
</table>

(1)Means followed by at least one same letter do not differ statistically (Analysis of Variance complemented by the Tukey test at significance level of 5%).

Our results exhibit that animals treated with B. trimera and P. anisum showed no change in blood glucose values. Tirapelli et al [13] evaluated the effects of B. trimera on glycaemia in diabetic and non-diabetic rats and their results suggested that this plant has anti-diabetic activity. Similar effects were found by Oliveira et al [5], Dickel et al [19] and Trojan-Rodrigues et al [6]. In the literature no studies about the effect of P. anisum aqueous extract in relation to glycaemia were found, although Kreydiyyeh et al [20] found that aniseed oil increases glucose absorption by increasing the activity of the Na+K+ ATPase and consequently the sodium gradient needed for the sugar transport in rats. Saddala et al [21] studied the aqueous extract of P. tirupatiensis tuberous root on cardiac oxidative stress and lipid peroxidation in non-diabetic and streptozotocin-induced diabetic rats and found that this extract promoted normalization of glutathione and xanthine oxidase activity in diabetic animals and possible protects heart against oxidative damages promoted by hyperglycaemia. Lee et al [15] studied the effects of ethanol...
extract of *P. brachycarpa* in diabetic mice and concluded that this plant significantly reduces levels of thiobarbituric acid reactive substances. It also increases superoxide dismutase, catalase and glutathione peroxidase activity what can be useful to control glucose levels and oxidative stress what is related to heart diseases. Our results also show that the lipid profile can present similar or better results when animals are treated with the studied plants when compared to those treated with statin in the experimental period of this work. These effects can be explained by the presence of antioxidants and flavonoids, which are also recognized by their effects on the lipid profile. The main antioxidants from *P. anisum* are terpenoids such as linalool, terpinene-4-ol, -terpineol, p-anisaldehyde, foeniculina, anethole, trans-anethole, trans-cespoisoceugenil, 2-metilbuturitate, para-anisaldehyde, estragol and metilcavicul [11, 22-23]. *B. trimera* also possesses bioactive compounds that may be related to the effects observed in the lipid profile of the studied animals. These compounds include flavones, flavonols, saponins and diterpenes, and phenolics such as apigenin, cirsimaritina, eupatorinna, genkwanina, hispidulin, isourcercinna, luteolin, nepelin, quercetin and rutin compounds. Among terpenoid compounds it contains mainly saponins. The presence of these compounds also gives to *B. trimera* antioxidant, anti-inflammatory, analgesic and muscle relaxing effects and liver protection [9, 23-26]. Muneeera, Majeed, Naveed [27] compared the effects of using simvastatin and *Nigella sativa* to treat hyperlipidemia and found that both promoted significant and comparable improvement in the lipid profile of rats after treatment. Low HDL-c levels contrasted with elevated plasma concentrations of triglycerides and LDL-c are related to the metabolic syndrome and increased risk of cardiovascular events and death [28-29]. In order to improve the lipid profile, doctors commonly make prescription of statins to their patients. These drugs are structural inhibitors of 3-hydroxy-3-methylglutaryl CoA reductase (HMG-CoA) that is a limiting enzyme in hepatic cholesterol biosynthesis, resulting in upper regulation of LDL-c receptors which lead to a decrease in LDL-c, total cholesterol and triglycerides levels [16]. However, the use of these drugs may be associated to adverse effects, such as liver damage, development of collateral circulation, stenosis, activation of nitric oxide synthase and increased incidence of diabetes. Moreover, these drugs are not recommended in patients with acute or chronic liver disease what leads patients to seek alternative treatments [30-34]. Table 2 brings the results to the calculation of the Atherogenic Index that is associated with the deposition of foam cells, plaque, fatty infiltration or lipids in the heart, coronaries, aorta or in the liver. It may be also related to the size of the pro and anti-atherogenic lipoprotein particles. When AI increases, there is also an increase in the risk of oxidative stress damages and it is an indication of cardiovascular risk [18]. Our results show that the plants exhibit lower AI than control and the group treated with the simvastatin showing they may have protective effects for cardiovascular diseases probably due to the presence of bioactive compounds described above.

**Table 2**: Atherogenic Index (AI) in groups G1, G2, G3 and G4.

<table>
<thead>
<tr>
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<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
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<tbody>
<tr>
<td><strong>AI</strong></td>
<td>3,25</td>
<td>1,58</td>
<td>2,14</td>
<td>2,60</td>
</tr>
</tbody>
</table>

This work shows important results in the lipid profile after using *P. anisum* and *B. trimera*. This combination of decreasing LDL-c and triglycerides levels and increase HDL-c levels is the desired goal for any treatment for dyslipidemia and metabolic syndrome. Furthermore, the use of plants and its association with the presence of flavonoids and other antioxidants can bring numerous benefits to the body, such as reducing or inhibiting lipid peroxidation, which is a factor implicated in many diseases, including cardiovascular diseases. Padua et al [35] showed that the use of *B. trimera* can act by increasing the antioxidant defense system and decreasing the effects of reactive species. *P. anisum* also exert antioxidant effects because of its potential in reducing nitric oxide radicals and hydrogen and may show metal chelating activities, what are related to the prevention of oxidative damages and their correlated diseases such as diabetes, metabolic syndrome and cardiovascular diseases. Paiva et al [3] found that *B. trimera* has anti-oxidant and neuro-protective effects.

**Conclusions**

Our findings suggest that *B. trimera* and *P. anisum* have potential to be used to control lipid levels. Despite the prospect of the use of medicinal plants is benefic for the population, clinical and laboratory studies in humans are needed to analyze the positive and possible side effects.

**Authors’ contributions**

SMB, ACQ and ELG carried out the conception and design of the study, treated the animals and drafted the manuscript. PCSB performed the statistical analysis. MSSS prepared the extracts of the plants and treated the animals. CGM performed the laboratorial analysis. All authors read and approved the final manuscript.
References


[21]. Sadda RR, Thopireddy L, Ganapathi N, Kesireddy SR. Regulation of cardiac oxidative stress and lipid peroxidation in streptozotocin-induced diabetic rats


