STUDY OF IN VIVO ANTIDYSLIPIDEMIC ACTIVITY OF SOLANUM XANTHOCARPUM SCHRAD. & WENDL. ON TRITON INDUCED DYSLIPIDEMIA IN RATS

Anitha Mary Mathews1*, Arockiasamy Josphin Maria Christina2
1Department of Pharmacology, Pushpagiri College of Pharmacy, Thiruvalla-689101, Kerala, India.
2Department of Pharmacology, Taylor’s University, No. 1 Jalan Taylor’s, 47500 Subang Jaya, Selangor Darul Ehsan, Malaysia.

ARTICLE INFO

ABSTRACT

*Solanum xanthocarpum Schrad. and Wendl.(solanaceae) is otherwise called Indian nightshade or yellow berried night shade. Decoction of root is used as febrifuge, effective diuretic and expectorant. The aerial parts and fruits were subjected to our study using triton induced model of dyslipidemia in rats. The aerial parts in the dose of 400mg/kg produced significant alteration in lipid profile whereas fruit in the dose of 400mg/kg produced significant positive alterations in the lipid profile of rats though at a lesser extent compared to the aerial parts. The in-vitro studies showed that the aerial parts of the plant produced considerable inhibition of fat formation. Since adipogenesis and abnormal lipid profile are risk factors for the development of T2DM, the progression of its cardiovascular and cerebrovascular complications and insulin resistance, the present study was directed towards seeking the possibilities of the plant in the treatment of dyslipidemia as well. The aerial part of the plant in the dose of 400mg/kg was found to possess antidyslipidemic activity comparable to the standard drug gemfibrozil. The fruits too possess comparable effects.

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INTRODUCTION

T2DM is associated with a group of lipid abnormalities like slightly increased, denser LDL, elevated triglycerides, lower HDL and elevated levels of VLDL cholesterol. Type 2 diabetics have elevated levels of C-reactive protein levels and other markers of inflammation and thrombogenesis. Their CVD risk is 2 to 4 times compared to similar age risk-controlled patients. The recommended reduction of LDL cholesterol is to less than 70mg/dl. Though statin is the mainstay of treatment, statin monotherapy was not sufficient to reach the LDL goal in 38% CAD high risk patients in a Canadian observational study in 2009. Statins deplete the natural antioxidant in the body- Coenzyme Q10. Fibrates produce a reversible deterioration of renal function and fibrates in combination with statins may increase the incidence of myopathy. Bile acid binding resins are contraindicated in hypercholesterolemia with elevated levels of triglycerides. The situation infers the need to identify an alternative approach and therapy in dyslipidemia which may help to raise HDL levels and to lower the LDL, triglyceride levels with proper glycemic control, thereby lower the CHD risk in diabetes and prediabetes states. These therapies include treatment with substances like niacin, plant sterols and omega-3 fatty acids. It is an approach that helps to increase the number of patients who are able to meet the lipid goals with good glycemic control without significant adverse effects. Solanum Xanthocarpum Schrad. and Wendl. (Solanaceae) is a plant with multiple constituents like triterpenoids, phenolics, alkaloids, flavonoids, sterols, saponins, and their glycosides. The plant as a whole is used in traditional systems of medicine for its antiasthmatic, hypoglycaemic, anti-inflammatory, antitumour, antitussive, antipyretic, antispasmodic, antihistaminic, hypotensive and cytotoxic activity. The aerial part of the plant bearing ripe yellow fruits were extracted and the ethanolic extract was tested in rats for its antidysslipidemic activity.

MATERIALS AND METHODS

Plant material

The plant was collected in the month of April when the first flowers of the season developed into fruits and when the fruits were ripe and leaves were healthy and green. The materials were separated into fruit bearing aerial parts and fruits, shade dried and powdered. The powdered fruit and aerial parts were extracted separately in a Soxhlet with 80% ethanol as the solvent. The waxy extractives obtained were stored in a refrigerator.

Preliminary phytochemical screening

Preliminary phytochemical analyses showed the presence of glycosides, flavonoids, phenolics and tannins in the aerial parts and the fruit showed the presence of glycosides, saponins, alkaloids, flavonoids, phenolics, tannins, phytosterols and triterpenoids, fixed oils and fats.

Chemicals and Kits

Triton WR1339 was procured from Sigma Aldrich, St. Louis, USA. Ready to use Citrate buffer and CMC were purchased from Himedia, Mumbai. All biochemical kits were procured from ERBA diagnostics, India.

Experimental animals

Male Wistar rats, 42 in number, weighing 200-250 g were divided into 7 groups of 6 animals each. The animals were maintained at 22±3°C and relative humidity of 60-80% with 12:12 hour light-dark cycle, they were fed on normal pellet diet. Animals were starved throughout the experimental period, but water was provided ad libitum.

Grouping and drug treatment

The animals 42 in number were initially divided into two groups, rats in Group I were maintained as the untreated control. Triton (Tyloxapol) was administered via intraperitoneal route to the rats of groups II-VII, at a dose of 200 mg/kg body weight to produce a state of acute hyperlipidaemia. Group 2 was left without dosing after triton administration. After 72 hours of triton administration, animals of group 3-7 were treated with different doses of test extracts. The details of treatment to different groups are as given below.

A total of 42 rats (n = 6) were randomly divided into seven experimental groups (Group I to Group VII) as follows:

Group I: Rats treated with water orally once a day for 7 days.
Group II: Rats treated with water orally once a day for 7 days.
Group III: Rats treated with Test extract SXA (200 mg/kg b.wt.) orally once a day for 7 days.
Group IV: Rats treated with Test extract SXA (400 mg/kg b.wt.) orally once a day for 7 days.
Group V: Rats treated with Test extract SXF (200 mg/kg b.wt.) orally once a day for 7 days.
Group VI: Rats treated with Test extract SXF (400 mg/kg b.wt.) orally once a day for 7 days.
Group VII: Rats treated with triton and Gemfibrozil 50 mg/kg orally once a day for 7 days.

Blood collection

On the 8th day blood was collected by retro-orbital sinus puncture under mild ether anaesthesia. The collected samples were centrifuged for 10 minutes at 15-24°C. Then serum samples were separated and used for various biochemical investigations. Then animals were sacrificed under proper anaesthesia and collected the liver and kidneys.
Biochemical analysis

The serum samples were assayed for total cholesterol, triglycerides, phospholipids, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL). The serum cholesterol level, triglycerides, phospholipids, serum HDL, LDL and VLDL were calculated using standard methods.

RESULTS

Intraperitoneal administration of triton in the dose of 200mg/kg elevated the levels of LDL, VLDL, phospholipids, serum triglycerides, and lowered the HDL levels. The ethanolic extract of aerial parts of *Solanum Xanthocarpum Schrad. and Wendl.* (Solanaceae) in the dose of 200mg/kg reduced the serum LDL level and VLDL to 232.83±2.38 and 29.17±3.66mg/dl respectively. The level of HDL was raised to 39.83±6.65mg/dl. The standard drug gemfibrozil reduced the LDL and VLDL to 189.67±3.93 and 23.50±1.85 and raised HDL to 42.50±8.69mg/dl.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>LDL mg/dl</th>
<th>HDL mg/dl</th>
<th>VLDL mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>29.00 ±1.82</td>
<td>47.33±2.25</td>
<td>19.32 ± 4.13</td>
</tr>
<tr>
<td>II</td>
<td>Triton treated control</td>
<td>289.15±0.88</td>
<td>29.50±5.42</td>
<td>33.33± 2.74</td>
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<tr>
<td>III</td>
<td>TRT + SXA (200 mg/kg)</td>
<td>232.83±2.38</td>
<td>34.33±4.63</td>
<td>29.17± 3.66</td>
</tr>
<tr>
<td>IV</td>
<td>TRT + SXA (400 mg/kg)</td>
<td>195.25±1.45</td>
<td>39.83±6.65</td>
<td>25.33±1.35</td>
</tr>
<tr>
<td>V</td>
<td>TRT + SXF (200 mg/kg)</td>
<td>235.54±3.07</td>
<td>36.33±9.51</td>
<td>30.17±1.37</td>
</tr>
<tr>
<td>VI</td>
<td>TRT + SXF (400 mg/kg)</td>
<td>212.33±1.21</td>
<td>37.17±8.94</td>
<td>27.50±3.51</td>
</tr>
<tr>
<td>VII</td>
<td>TRT + GFZL (50 mg/kg)</td>
<td>189.67±3.93</td>
<td>42.50±8.69</td>
<td>23.50±1.85</td>
</tr>
</tbody>
</table>

Statistical significance test was done by ANOVA followed by Dunnet’s ‘t’ test (n=6)

Values are mean±SEM of 6 animals per group

*P<0.01 vs triton treated control

The extract of aerial parts in the dose of 200mg/kg reduced the total cholesterol, triglycerides and phospholipid levels to 326.50±1.72mg/dl, 289.42±2.99mg/dl, and 438.26±0.36 mg/dl respectively. Aerial parts of the plant SXA in the dose of 400mg/kg reduced the levels to 303.67±2.47, 255.67±2.00 and 376.81±0.42mg/dl respectively. The SXF treated group in the dose of 200mg/kg reduced the levels to 338.33±1.13mg/dl, 275.33±1.91mg/dl and 441.02 ±0.46mg/dl respectively. SXF in the dose of 400mg/kg reduced the levels of total cholesterol, triglycerides and phospholipids to 311.12±3.09mg/dl, 261.00 ±1.41mg/dl and 384.63 ±0.54 mg/dl respectively compared to the triton treated group. Gemfibrozil in the dose of 50mg/kg reduced the levels of total cholesterol, triglycerides and phospholipids to 299.00±2.63mg/dl, 250.17±1.12 and 369.18±0.29 mg/dl respectively (Table 2).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Total Cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
<th>Phospholipids (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>95.3±2.12</td>
<td>86.1±3.88</td>
<td>75.32±0.19</td>
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<tr>
<td>II</td>
<td>Triton treated control</td>
<td>439.17±1.35</td>
<td>369.00±1.95</td>
<td>534.09±0.37</td>
</tr>
<tr>
<td>III</td>
<td>TRT + SXA (200 mg/kg)</td>
<td>326.50±1.72</td>
<td>289.42±2.99</td>
<td>438.26±0.36</td>
</tr>
<tr>
<td>IV</td>
<td>TRT + SXA (400 mg/kg)</td>
<td>303.67±2.47</td>
<td>255.67±2.00</td>
<td>376.81±0.42</td>
</tr>
<tr>
<td>V</td>
<td>TRT + SXF (200 mg/kg)</td>
<td>338.33±1.13</td>
<td>275.33±1.91</td>
<td>441.02 ±0.46</td>
</tr>
<tr>
<td>VI</td>
<td>TRT + SXF (400 mg/kg)</td>
<td>311.12±3.09</td>
<td>261.00 ±1.41</td>
<td>384.63 ±0.54</td>
</tr>
<tr>
<td>VII</td>
<td>TRT + GFZL (50 mg/kg)</td>
<td>299.00±2.63</td>
<td>250.17±1.12</td>
<td>369.18±0.29</td>
</tr>
</tbody>
</table>

Statistical significance test was done by ANOVA followed by Dunnet’s ‘t’ test (n=6)

Values are mean±SEM of 6 animals per group

*P<0.01 vs triton treated control
DISCUSSION

Elevated levels of glucose in diabetes may lead to oxidative stress which in turn precipitates protein oxidation and dyslipidemia. Hypercholesterolemia and triglyceridemia are risk factors that may precipitate cardiovascular and cerebrovascular complications especially in type 2 diabetes patients, resulting in considerable mortality. Adipocytes become resistant to insulin and release more fatty acids into the circulation. This flux of free fatty acids into the liver stimulates the secretion of VLDL resulting in hypertriglyceridemia. ApoA-1 dissociates from TG-rich HDL and availability of HDL for reverse cholesterol transport is reduced. TG-rich LDL undergoes lipolysis and become smaller, more dense LDL. The triton treated experimental rats showed all the characteristics of acute dyslipidemia namely, hypercholesterolemia, triglyceridemia and elevated levels of phospholipids compared to the normal control animals.

CONCLUSION

Dyslipidemia is a major risk factor for coronary heart diseases, stroke and death, all over the world and there is a need for multiple strategies for its treatment. *Solanum Xanthocarpum Schrad. and Wendel.(solanaceae)*, was evaluated for its potential in the treatment of dyslipidemia. The aerial parts and fruits were subjected to our study using triton induced model of dyslipidemia in rats. The aerial parts in the dose of 400mg/kg produced significant alteration in lipid profile whereas fruit in the dose of 400mg/kg produced significant positive alterations in the lipid profile of rats though at a lesser extent compared to the aerial parts. The results were comparable to those produced by the standard control gemfibrozil. The positive outcome of the study might be attributed to the phytoconstituents in fruit and aerial parts namely phytosterols, phenolics, flavonoids, glycosides, saponins, alkaloids and tannins. Fruits are rich in sterols like carpesterol, campeserol, stigmasterol and T-sitosterol. The plant is rich in flavones like apigenin, quercetin and triterpenoid lupeol and fatty acids namely stearic acid, palmitic acid and oleic acid. The active constituents may help to increase the HDL level by stimulating the synthesis of HDL and increased transport of HDL. The constituents of leaves, stem and fruits may synergise the actions of each other that the antiadipogenic activity is produced. The plant may be considered a potential candidate for the treatment of dyslipidemia associated with T2DM and the antihyperglycemic effects have been elucidated by the communicating author which would provide good glycemic control too. The ethanolic extract of fruit bearing aerial parts with healthy green leaves were found to produce antidyslipidemic effect that was comparable to the standard drug gemfibrozil.

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REFERENCE