Original article

Antihyperlipidemic effect of Angiosifa, a polyherbal formulation, in Sprague–Dawley rats

Subramani Parasuraman a,*, Seevalen Shahul Hamid Babuji a, Gan Siaw Thing b, Kuppusamy Sreevidya Kumari b, Athitan Yoganishalinib, Chua Wei Lian b, Manimaran Kumuthab, Tajudeen Kassimc, Sokkalingam Arumugam Dhanarajd

a Unit of Pharmacology, Faculty of Pharmacy, Asian Institute of Medicine, Science and Technology (AIMST) University, Bedong 08100, Kedah, Malaysia
b Faculty of Pharmacy, AIMST University, Bedong 08100, Kedah, Malaysia
c East West Oriental Enterprises, No. 36 B, Chow Thye Road, Penang 10050, Malaysia
d Unit of Pharmaceutical Technology, Faculty of Pharmacy, AIMST University, Bedong 08100, Kedah, Malaysia

A R T I C L E   I N F O

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A B S T R A C T

Objective: To study the antihyperlipidemic effect of Angiosifa, a polyherbal formulation (PHF), in Sprague–Dawley (SD) rats.

Methods: The rats were divided into seven groups, each having five animals: normal controls, high fat diet (HFD)-fed controls and HFD-fed animals treated with atorvastatin (10 mg/kg), petroleum ether extract of the PHF (200 and 400 mg/kg) and methanol extract of the PHF (200 and 400 mg/kg). The test and standard drugs were administered orally once daily for 28 consecutive days. During the experiment, changes in body weight were noted and alterations in biological and biochemical parameters were monitored at regular intervals.

Results: HFD-fed animals showed significant increases in body weight and total cholesterol, triglyceride and VLDL levels. They also showed a significant reduction in HDL levels compared with the control and drug treatment groups. Animals treated with atorvastatin and methanol extract of PHF showed significant reductions in total cholesterol, triglyceride and VLDL levels compared with HFD-fed animals. But there was no significant hypolipidemic effect in animals treated with petroleum ether extract of PHF, and the ether caused piloerection and led to cannibalism.

Conclusion: Methanol extract of PHF has a significant hypolipidemic effect against HFD-induced hyperlipidemia in SD rats. The petroleum ether extract of PHF did not show any significant hypolipidemic effect on HFD-fed rats.

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1. Introduction

The concept of polyherbalism has been highlighted in the Sarangdh Samhita, an Ayurvedic work dating back to 1300 A.D.1 In a polyherbal formulation (PHF), a combination of herbs is used rather than a single herb. The individual constituents may not be sufficiently active to achieve the desired therapeutic effect. By acting on multiple targets at the same time, the PHF enhances the therapeutic efficacy by improving the bioavailability thereby reducing the doses required of the individual components in the formulation.2 Besides, synergism attenuates undesirable side effects.3 Raghavendra et al studied the combined effect of the methanol extract of Tribulus terrestris (whole plant) and Annona squamosa leaves against hyperlipidemia, and they concluded that a combination of the two herbs has better hypolipidemic activity compared with the individual effects.4 Parasuraman et al demonstrated the superior antihyperlipidemic effect of a commercially available PHF that has extract of 10 herbs, viz., Terminalia arjuna, Cissus quadrangularis, Boerhaavia diffusa, Commiphora mukul, Phyllanthus emblica, Terminalia bellercia, Terminalia chebula, T. terrestris, Allium sativum and Trigonella foenumgraecum.5 Angiosifa, a PHF, is used in the management of coronary atherosclerosis, hypercholesterolemia and ischemic heart diseases. Angiosifa contains seven herbs, viz., Cinnamomum zeylanicum, Glycyrrhiza glabra, Nelumbo nucifera,
Hibiscus rosa-sinesis, Sausurrea lappa, Spermacoce hispida and T. arjuna. The hypolipidemic effect of H. rosa-sinesis, S. hispida, N. nucifera, S. lappa and T. arjuna are known, but the synergistic effect of these plants in the formulation has not been elucidated so far. Combinations of these herbs may have an enhanced hypolipidemic effect even with low dose levels of the individual herbs. Angiosifa consists of a raw herbal mixture, and the concentrations of the herbs are high for therapeutic efficacy. Extracts of individual plants or a formulation containing these may require a smaller dose and may have enhanced therapeutic efficacy. Hence the present study was planned to investigate the antihyperlipidemic effect of the petroleum ether and methanol extract of the PHF in rodents using the high fat diet (HFD)-induced hyperlipidemic model.

2. Materials and methods

2.1. Polyherbal formulation

Angiosifa (manufactured by East West Oriental Enterprise, Georgetown, Penang, Malaysia) is a PHF available in Malaysia. It is formulated using dried, powdered herbs, namely C. zeylanicum, G. glabra, N. nucifera, H. rosa-sinesis, S. lappa, S. hispida and T. arjuna.

2.2. Animals

Healthy adult male Sprague–Dawley (SD) rats, weighing 100 ± 10 g, were obtained from Happy Pets, Sungai Petani, Malaysia. The animals were housed in large, spacious polycrylic cages at ambient temperature with a 12-h-light/12-h-dark cycle. The animals were acclimatized to laboratory conditions for a period of one week. The rats were fed with normal rodent pellets and water ad libitum. During the experiment, normal control animals were fed with a normal diet; the rest of the animals were fed with a high fat diet. The compositions of the normal and hyperlipidemic diets (HFD) are provided in Table 1. The study was approved by the Institute Animal Ethics Committee, and the study was conducted according to the guidelines of the Animal Research Review Panel (ARRP).

2.3. Extraction of PHF using petroleum ether and methanol

The PHF was packed into a Soxhlet extractor and extracted with petroleum ether at 50 °C over 6 h. The petroleum ether extract was concentrated to a dry mass using simple distillation, and the dry mass was stored under reduced pressure at room temperature. The same marc was successively extracted with methanol at 45 °C over 6 h. The methanol extract was also distilled, and the dry mass was preserved under reduced pressure at room temperature. The percentage yields of the petroleum ether and methanol extracts of the PHF were 2.56% w/v and 12.61% w/v, respectively. The extracts thus obtained were subjected to phytochemical analysis and pharmacological screening.

2.4. Phytochemical analysis of petroleum ether and methanol extract of PHF

Petroleum ether and methanol extract (500 mg) was dissolved in a minimal volume of its own mother solvent and used for phytochemical analysis. The Salkowski reaction, Tschugajev test, Dragendorff’s reaction, ferric chloride test and Baljet test were carried out to detect the presence of phytosterols, triterpenoids, alkaloids, flavonoids/phenolic compounds/tannins and glycosides, respectively.

2.5. Acute toxicity testing

A single dose oral acute toxicity test was performed using the fixed dose method. Female SD rats were used for this study. The petroleum ether and methanol extract of the PHF was administered successively to different groups at fixed dose levels of 500, 1000 and 2000 mg/kg (n = 3 per dose) and observed for the next 14 days.

2.6. Antihyperlipidemic effect of PHF

Thirty-five young, healthy male SD rats were divided into seven groups containing five animals each. The diet and treatment were as follows.

Group 1 (normal diet): Normal diet + drug vehicle (1 ml/kg)
Group 2 (HFD control): HFD + drug vehicle (1 ml/kg)
Group 3: HFD + atorvastatin (10 mg/kg)
Group 4: HFD + PHF (petroleum ether extract, 200 mg/kg)
Group 5: HFD + PHF (petroleum ether extract, 400 mg/kg)
Group 6: HFD + PHF (methanol extract, 200 mg/kg)
Group 7: HFD + PHF (methanol extract, 400 mg/kg)

The locomotor activities of all the animals were measured, and the animals that had abnormal locomotor activities were excluded from the study. All the animals were provided with 15 g normal/HFD diet per day. The drug vehicle, standard drug (atorvastatin) and PHF were administered once daily as an oral suspension for 28 days. The oral suspension was prepared with 0.5% w/v carboxymethyl cellulose (CMC). All the experimental procedures were carried out between 9:00 am and 11:00 am to avoid chronopharmacological variations. Throughout the study, the behavioral alterations, body weight variations and biochemical changes were monitored at regular intervals. At the end of the study, all the animals were sacrificed by cervical dislocation. The liver and kidney were excised, and the absolute organ weights were measured. A part of the liver tissue of each of the experimental animals was preserved in 10% v/v buffered neutral formalin for histopathological examination.

2.7. Measurement of locomotor activity

The activity of the rats was recorded in a rodent activity cage (actophotometer) provided with an acrylic cage and with 16 beams of infrared light along both the x and y axes. The activity of each rat was monitored at room temperature over 10 min.
2.8. Body weight analysis

The body weight of each rat in each group was recorded initially and at weekly intervals. The percentage change in body weight was calculated.

2.9. Collection of serum

A blood sample (0.5 ml) was collected from each experimental animal on the day preceding the commencement of the study and on the 14th and 28th days. The samples were drawn from the retro-orbital sinus under mild ether anesthesia. The blood samples were collected in sodium EDTA tubes and centrifuged at 3000 RPM for 20 min. The plasma obtained was maintained at –80 °C until analysis.

2.10. Biochemical estimations

The plasma was used to estimate the plasma lipid profile. The total cholesterol, triglyceride and HDL levels were measured using a Reflotron biochemical analyzer (Reflotron Plus System, Hoffmann-La Roche, USA) and lipid profile analytical strips. The LDL, HDL ratio and atherogenic index (AI) were calculated mathematically.

2.11. Histopathological study

A part of each liver sample was embedded in paraffin after being dehydrated in alcohol and subsequently cleared with xylene. Liver sections of thickness 5 μm were prepared from paraffin blocks, stained with hematoxylin and eosin and mounted in neutral DPX medium. The sections were examined under a light microscope.

2.12. Statistical analysis

All the values are represented as the mean ± S.E.M. Statistical differences among the groups were determined using One-way repeated measures ANOVA, followed by the Bonferroni post hoc test. P < 0.05 was considered to be significant.

3. Results

3.1. Phytochemical analysis of petroleum ether and methanol extract of PHF

The primary phytochemical analysis of the petroleum ether extract of the PHF showed the presence of phytosterols, triterpenoids, alkaloids, flavonoids, phenolic compounds and tannins, and analysis of the methanol extract of the PHF showed the presence of phytosterols, triterpenoids, flavonoids and glycosides.

3.2. Acute toxicity testing

No mortality or signs of toxicity were noted on the first day or during the study period of the single-dose oral toxicity testing of the petroleum ether and methanol extracts of PHF at dose levels of 500, 1000 and 2000 mg/kg. Hence, the present study was initiated with dose levels of 200 and 400 mg/kg. Repeated administration (antihyperlipidemic study) of the petroleum ether extract of the PHF produced signs of toxicity including altered locomotor activity, piloerection and cannibalism.

3.3. Antihyperlipidemic effect of petroleum ether and methanol extract of PHF

3.3.1. Body weight analysis

HFD-fed animals exhibited a significant increase in body weight compared with normal diet-fed animals from the third week onwards (P < 0.01). The effects of the PHF on the body weight over the period of 28 days of treatment were studied and recorded in all the groups. The percentage changes in body weight were calculated from the weights noted before the study and on the 7, 14, 21 and 28th days (Fig. 1). The HFD-fed animals that were administered the petroleum ether extract of the PHF showed significant increases in body weight; those administered atorvastatin and the methanol extract of the PHF did not show any significant increase in body weight compared with the control animals.

3.3.2. Locomotor activity

The HFD-fed animals showed a significant decrease in locomotor activity at the end of the study compared with the controls (P < 0.05). The groups treated with the PHF and with atorvastatin did not display altered locomotor activity (Table 2). There were no significant alterations in absolute organ weight in the HFD control group and the treatment groups. This may be due to the short duration of the study.

3.3.3. Effect of petroleum ether extract of PHF on central nervous system

Repeated administration of the petroleum ether extract of the PHF at 200 and 400 mg/kg caused rigidity and dorsiflexion of the rats’ tails (piloerection reaction/Straub tail phenomenon) and cutis anserina. Cannibalism was noted in the group treated with the petroleum ether extract of the PHF at 200 mg/kg after the 12th day of drug administration (Table 3).

3.3.4. Intake analysis

Control animals consumed more food and water (Figs. 2 and 3) compared with the other groups. There were no significant changes in the food and water intake of the animals treated with atorvastatin or the PHF. A quantitative decrease in food intake and a significant decrease in water intake were observed with HFD-fed animals.

3.3.5. Serum lipid profile

The effects of the PHF on the biochemical parameters (total cholesterol, triglyceride, HDL, VLDL and LDL levels; HDL ratio; and AI) were assessed from measurements made before the commencement of the study and on the 14th and 28th days of treatment (Tables 4–6).

The HFD-fed rats showed significant increases in total cholesterol and triglyceride levels from the second week onwards. The petroleum ether and methanol extract of the PHF inhibited the hyperlipidemia caused by the HFD. Compared with the petroleum ether and methanol extract of the PHF, the methanol extract of the PHF showed better activity.

In the second week of the study, there were significant increases in the total cholesterol (28.98%) and triglyceride (49.87%) levels of the HFD-fed animals compared with the controls. In contrast, the atorvastatin- and PHF-treated groups did not have significant alterations in the total cholesterol and triglyceride levels compared with the controls.

At the end of the study, the HFD-fed animals had significant increases in total cholesterol (34.66%) and triglyceride (60.40%) levels compared with the controls. The atorvastatin- and PHF-treated groups did not have significant alterations in their total cholesterol and triglyceride levels compared with the controls. The
methanol extract of the PHF at dose levels of 200 and 400 mg/kg reduced the total cholesterol by 4.99% and 0.29%, respectively, compared with the controls.

Throughout the experiment, decreased HDL levels and increased VLDL levels were noted in the HFD-fed animals compared with the controls. The LDL and VLDL levels of atorvastatin were significantly reduced at the end of the study compared with the HFD-fed controls, and the methanol extract of the PHF (at 200 and 400 mg/kg) were significantly reduced the LDL level compared with the HFD controls. Throughout the study, atorvastatin and PHF treatment did not have any significant influence the AI values.

3.4. Histopathological analysis

The liver of HFD-fed animals had diffuse fatty infiltration affecting all the hepatocytes, leading to peripherally compressed nuclei, and minimal periportal inflammation (Plate 1). This infiltration was not seen in the controls. Normal morphological features were observed in normal control, atorvastatin and PHF treated animals liver.

4. Discussion

Phytochemical screening of the petroleum ether and methanol extract of the PHF showed the presence of phytosterols, which may contribute to the hypolipidemic effect of the PHF by reducing cholesterol absorption in the gastrointestinal tract. Cholesterol may be displaced from micelles by the phytosterols, thereby limiting the solubility of cholesterol in the small intestine. Flavonoids, which are among the contents of the PHF, are generally known to display hypolipidemic activity, and they may act through inhibition of HMG CoA reductase as well as increasing resistance to LDL oxidation. Increased HDL levels and HDL ratios were observed in the atorvastatin and PHF-treated groups, and these effects may help modulate endothelial function.

The results of the present study support the assertion that the PHF has a hypolipidemic effect. The methanol extract of the PHF significantly inhibited diet-induced hyperlipidemia in rats compared with the petroleum ether extract. The HFD control group had significant increases in the plasma lipid parameters (TG, TC, LDL, and VLDL) compared with the controls. Atorvastatin and PHF treatment reversed the effects of HFD, and this effect may be due to inhibition of either the cholesterol metabolism or a reduction in food intake. Both atorvastatin and PHF do not produce any significant changes in LDL, VLDL, HDL ratio and AI. This may be due to the short duration of the study and the small sample size. If we had only conducted our study with more than eight animals in each group or increased the duration of the study to 60/90 days, we would have made a statistical difference to the LDL, VLDL, HDL ratio and AI. At the end of the study, none of the animals from the treatment groups had any changes in the absolute organ weights or histopathological changes.

Throughout the experiment, the normal control animals were found to have increased food and water intake, but HFD-fed animals had increased food intake only till the second week. Except

### Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Locomotor count (10 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>534 ± 10.30</td>
</tr>
<tr>
<td>HFD control</td>
<td>302 ± 62.45</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>552 ± 64.66</td>
</tr>
<tr>
<td>PHF-I 200 mg/kg</td>
<td>442.5 ± 92.51</td>
</tr>
<tr>
<td>PHF-I 400 mg/kg</td>
<td>687 ± 77.31***</td>
</tr>
<tr>
<td>PHF-II 200 mg/kg</td>
<td>435 ± 37.82</td>
</tr>
<tr>
<td>PHF-II 400 mg/kg</td>
<td>551 ± 35.01</td>
</tr>
</tbody>
</table>

PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5); *P < 0.05 as compared to control; **P < 0.01, ***P < 0.001 compared to HFD control, One-way ANOVA followed by Bonferroni post hoc test.

### Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>History of cannibalism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Nil</td>
</tr>
<tr>
<td>HFD control</td>
<td>Nil</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Nil</td>
</tr>
<tr>
<td>PHF-I 200 mg/kg</td>
<td>12th day of dosing – 2 animals</td>
</tr>
<tr>
<td>PHF-I 400 mg/kg</td>
<td>18th day of dosing – 1 animal</td>
</tr>
<tr>
<td>PHF-II 200 mg/kg</td>
<td>Nil</td>
</tr>
<tr>
<td>PHF-II 400 mg/kg</td>
<td>Nil</td>
</tr>
</tbody>
</table>

PHF-I: Pet-ether extract; PHF-II: Methanol extract.
Fig. 2. Effect of petroleum ether and methanol extracts of PHF on food intake (g). PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5) except PHF-1 200 mg/kg (n = 3 in 3rd week and n = 2 in 4th week) *P < 0.05, **P < 0.01 as compared to control, One-way repeated measures ANOVA followed by Bonferroni post hoc test.

Fig. 3. Effect of petroleum ether and methanol extracts of PHF on water intake (ml). PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5) except PHF-1 200 mg/kg (n = 3 in 3rd week and n = 2 in 4th week). *P < 0.05, **P < 0.01, ***P < 0.001 as compared to control, One-way repeated measures ANOVA followed by Bonferroni post hoc test.

Table 4
Effect of petroleum ether and methanol extracts of PHF on lipid profile in plasma (pre-study) on HFD fed SD rats.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total cholesterol (mg/dl)</th>
<th>Triglyceride (mg/dl)</th>
<th>HDL cholesterol (mg/dl)</th>
<th>LDL cholesterol (mg/dl)</th>
<th>VLDL-c (mg/dl)</th>
<th>HDL ratio</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>106.43 ± 3.62</td>
<td>70.86 ± 2.80</td>
<td>12.65 ± 2.18</td>
<td>79.61 ± 3.24</td>
<td>14.17 ± 0.56</td>
<td>13.59 ± 2.43</td>
<td>1.14 ± 0.02</td>
</tr>
<tr>
<td>HFD control</td>
<td>106.19 ± 2.52</td>
<td>67.31 ± 5.31</td>
<td>13.14 ± 1.72</td>
<td>79.58 ± 3.13</td>
<td>13.46 ± 1.06</td>
<td>14.28 ± 2.09</td>
<td>1.14 ± 0.02</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>106.73 ± 2.45</td>
<td>76.17 ± 7.20</td>
<td>12.93 ± 1.29</td>
<td>78.57 ± 3.76</td>
<td>15.23 ± 1.44</td>
<td>14.05 ± 1.91</td>
<td>1.14 ± 0.02</td>
</tr>
<tr>
<td>PHF-I 200 mg/kg</td>
<td>103.71 ± 2.62</td>
<td>74.40 ± 9.12</td>
<td>14.72 ± 1.43</td>
<td>74.11 ± 3.58</td>
<td>14.88 ± 1.82</td>
<td>16.59 ± 1.65</td>
<td>1.17 ± 0.02</td>
</tr>
<tr>
<td>PHF-I 400 mg/kg</td>
<td>106.42 ± 4.05</td>
<td>77.94 ± 8.12</td>
<td>11.46 ± 1.54</td>
<td>79.37 ± 3.52</td>
<td>15.59 ± 1.62</td>
<td>12.11 ± 1.62</td>
<td>1.12 ± 0.02</td>
</tr>
<tr>
<td>PHF-II 200 mg/kg</td>
<td>103.88 ± 3.50</td>
<td>70.86 ± 9.29</td>
<td>13.70 ± 2.38</td>
<td>76.01 ± 5.68</td>
<td>14.17 ± 1.86</td>
<td>15.89 ± 3.58</td>
<td>1.16 ± 0.04</td>
</tr>
<tr>
<td>PHF-II 400 mg/kg</td>
<td>110.12 ± 1.20</td>
<td>76.17 ± 6.01</td>
<td>12.97 ± 1.90</td>
<td>81.92 ± 3.05</td>
<td>15.23 ± 1.20</td>
<td>13.63 ± 2.41</td>
<td>1.14 ± 0.02</td>
</tr>
</tbody>
</table>

PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5).
the normal controls, all other experimental animals (HFD-fed animals) showed a significant reduction in food and water intake. Ghalami et al also reported a reduction in food and water intake in HFD-fed animals, and this effect might be due to increased plasma leptin levels. These increased levels may reduce protein and water intake.21

The petroleum ether extract of the PHF produced reductions in the TC, TC and LDL levels in rats at both a low dose (200 mg/kg) and high dose (400 mg/kg), but this effect was not comparable with that of the methanol extract of the PHF. Administration of the petroleum ether extract of the PHF resulted in Straub tail, cutis anserina, increased locomotor activity and cannibalism in the rats. This may have been due to stimulation of the central nervous system/behavioral alteration/neurological disorders or changes in environmental factors such as deficient diets and group size.22 The effect of stimulating the central nervous system may be due to chemical changes that occurred when the PHF was extracted with petroleum ether or may be due to the solvent effect of petroleum ether. Further studies are required to study the effect of petroleum ether as a solvent on the central nervous system.

Before inducing hyperlipidemia through diet in SD rats, the authors tried to induce hyperlipidemia chemically using Triton X-100. Triton X-100 is a non-ionic surfactant, widely used in animal models to increase the concentration of lipids in the blood progressively.23 In our experiment, Triton X-100 (100 mg/kg; i.p.) caused mortality to the extent of 60% within 2 days. Because of the high mortality rate, HFD-induced hyperlipidemia was chosen as an alternative. Sodipo et al also reported a high mortality rate with Triton X-100 (400 mg/kg; i.p.). This is probably due to high osmotic fragility and altered red blood cell (RBC) morphology, causing icterus, leading to the death of the rats.23

Table 5
Effect of petroleum ether and methanol extracts of PHF on lipid profile in plasma (week 2) on HFD fed SD rats.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total cholesterol (mg/dl)</th>
<th>Triglyceride (mg/dl)</th>
<th>HDL cholesterol (mg/dl)</th>
<th>LDL cholesterol (mg/dl)</th>
<th>VLDL-c (mg/dl)</th>
<th>HDL ratio</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>109.10 ± 3.74</td>
<td>69.09 ± 3.32</td>
<td>13.06 ± 1.86</td>
<td>82.22 ± 2.14</td>
<td>13.82 ± 0.66</td>
<td>13.55 ± 1.78</td>
<td>1.14 ± 0.02</td>
</tr>
<tr>
<td>HFD control</td>
<td>136.97 ± 6.71**</td>
<td>100.97 ± 7.20*</td>
<td>9.45 ± 0.54</td>
<td>107.32 ± 6.05</td>
<td>20.19 ± 1.44*</td>
<td>7.56 ± 0.74</td>
<td>1.08 ± 0.01</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>114.44 ± 2.50</td>
<td>72.63 ± 9.03</td>
<td>23.63 ± 10.93</td>
<td>76.28 ± 11.09</td>
<td>14.53 ± 1.81</td>
<td>19.13 ± 26.45</td>
<td>1.39 ± 0.26</td>
</tr>
<tr>
<td>PHF-I 200 mg/kg</td>
<td>118.21 ± 6.76</td>
<td>76.76 ± 5.90</td>
<td>11.18 ± 1.16</td>
<td>91.67 ± 4.48</td>
<td>15.35 ± 1.18</td>
<td>10.40 ± 0.54</td>
<td>1.10 ± 0.01</td>
</tr>
<tr>
<td>PHF-I 400 mg/kg</td>
<td>119.80 ± 3.95</td>
<td>83.26 ± 6.63</td>
<td>16.12 ± 5.17</td>
<td>87.02 ± 7.33</td>
<td>16.65 ± 1.33</td>
<td>17.57 ± 7.47</td>
<td>1.18 ± 0.07</td>
</tr>
<tr>
<td>PHF-II 200 mg/kg</td>
<td>121.66 ± 4.29</td>
<td>86.80 ± 8.12</td>
<td>16.61 ± 4.95</td>
<td>87.68 ± 4.65</td>
<td>17.36 ± 1.62</td>
<td>16.78 ± 6.01</td>
<td>1.17 ± 0.06</td>
</tr>
<tr>
<td>PHF-II 400 mg/kg</td>
<td>113.72 ± 1.76</td>
<td>70.86 ± 4.85</td>
<td>17.68 ± 4.21</td>
<td>81.86 ± 5.60</td>
<td>14.17 ± 0.97</td>
<td>19.57 ± 5.95</td>
<td>1.20 ± 0.06</td>
</tr>
</tbody>
</table>

PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5). *P < 0.05, **P < 0.01 as compared to control, One-way repeated measures ANOVA followed by Bonferroni post hoc test.

Table 6
Effect of petroleum ether and methanol extracts of PHF on lipid profile in plasma (week 4) on HFD fed SD rats.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total cholesterol (mg/dl)</th>
<th>Triglyceride (mg/dl)</th>
<th>HDL cholesterol (mg/dl)</th>
<th>LDL cholesterol (mg/dl)</th>
<th>VLDL-c (mg/dl)</th>
<th>HDL ratio</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>110.60 ± 1.54</td>
<td>81.49 ± 7.09</td>
<td>11.67 ± 2.42</td>
<td>82.63 ± 1.13</td>
<td>16.30 ± 1.42</td>
<td>10.58 ± 1.17</td>
<td>1.12 ± 0.03</td>
</tr>
<tr>
<td>HFD control</td>
<td>143.00 ± 5.16***</td>
<td>108.06 ± 9.86</td>
<td>10.72 ± 0.70</td>
<td>10.67 ± 5.87</td>
<td>21.61 ± 1.97</td>
<td>8.12 ± 0.51</td>
<td>1.08 ± 0.01</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>117.66 ± 5.47</td>
<td>70.86 ± 4.85**</td>
<td>33.50 ± 7.77</td>
<td>69.99 ± 10.58**</td>
<td>14.17 ± 0.97</td>
<td>14.17 ± 0.97</td>
<td>4.58 ± 13.63</td>
</tr>
<tr>
<td>PHF-I 200 mg/kg</td>
<td>112.16 ± 0.76</td>
<td>70.43 ± 0.43**</td>
<td>10.52 ± 0.50</td>
<td>87.55 ± 0.34</td>
<td>14.09 ± 0.09</td>
<td>10.35 ± 0.47</td>
<td>1.10 ± 0.00</td>
</tr>
<tr>
<td>PHF-I 400 mg/kg</td>
<td>114.64 ± 6.72</td>
<td>86.80 ± 8.12**</td>
<td>9.43 ± 0.53</td>
<td>87.85 ± 5.51</td>
<td>17.36 ± 1.62</td>
<td>9.22 ± 0.98</td>
<td>1.09 ± 0.01</td>
</tr>
<tr>
<td>PHF-II 200 mg/kg</td>
<td>101.11 ± 0.40</td>
<td>77.95 ± 7.62**</td>
<td>27.61 ± 7.48</td>
<td>57.91 ± 8.15**</td>
<td>15.59 ± 1.52</td>
<td>43.07 ± 14.33</td>
<td>1.14 ± 0.14</td>
</tr>
<tr>
<td>PHF-II 400 mg/kg</td>
<td>103.58 ± 4.16</td>
<td>76.17 ± 3.54**</td>
<td>24.04 ± 8.43</td>
<td>64.30 ± 10.96**</td>
<td>15.23 ± 0.71</td>
<td>41.29 ± 21.11</td>
<td>1.41 ± 0.21</td>
</tr>
</tbody>
</table>

PHF-I: Pet-ether extract; PHF-II: Methanol extract. All the values are mean ± SEM (n = 5). ***P < 0.001 as compared to control, One-way repeated measures ANOVA followed by bonferroni post hoc test.

Plate 1. (a) Normal architecture of rat hepatic lobules (×100) H&E stained; (b) Fatty liver tissue with diffuse fatty infiltration, compressed nuclei, and minimal periportal inflammation (×100) H&E stained.
5. Conclusions

The methanol extract of the PHF showed a significant hypolipidemic effect against HFD-induced hyperlipidemia in SD rats. The petroleum ether extract of the PHF did not show a significant hypolipidemic effect against HFD-induced hyperlipidemia in SD rats but produced hyperlocomotion in HFD-fed rats.

Conflicts of interest

All authors have none to declare.

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References