LIPID-LOWERING EFFECT OF *ALTERNANTHERA SESSILIS* EXTRACTS IN HIGH FAT DIET-INDUCED HYPERLIPIDEMIA RATS

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Abstract
This study was conducted to investigate the potential antihyperlipidemic effect of extract of *A. sessilis* leaf in high fat diet-induced hyperlipidemic rats. *A. sessilis* extracts were prepared using sequential extraction to obtain petroleum ether, chloroform, methanol, and water extracts. Extracts at the dose of 1000 mg/kg body weight were orally administered to hyperlipidemic rats for 28 consecutive days. Serum lipid profile, liver function enzymes, hepatic and fecal fat as well as total bile acid were evaluated. In vitro antioxidant activities were also assessed. Water extracts of *A. sessilis* significantly ($p < 0.05$) reduced the level of serum total cholesterol, triglycerides, low-density lipoprotein, and CRI ratio ($p < 0.05$) when compared to the hyperlipidemic control. Water and methanol extracts did not significant changes in liver enzymes when compared to the controls ($p < 0.05$). Methanol and water extracts decreased liver total cholesterol ($p < 0.01$) and triglycerides ($p < 0.001$) when compared to hyperlipidemic control and significantly ($p < 0.05$) increased fecal total bile acid as compared to controls. Both water and methanol extracts exerted potential antioxidant activities. *A. sessili*s extracts elicit antihyperlipidemic activity partly by reducing hepatic fat, increasing fecal fat and bile acids as well as scavenging the free radicals. This suggests a preventive effect of *A. sessili*s against hyperlipidemia.

Keywords**:** *Alternanthera sessili*s, Antihyperlipidemic, Antioxidant, High-fat diet

Introduction

Hyperlipidemia refers to a group of inherited and acquired disorders characterized by an elevated level of low-density lipoprotein, total cholesterol, and triglycerides in the blood. It is a significant contributor for the development of atherosclerosis and subsequent cardiovascular diseases (1). Atherosclerosis is a disease that arises from the excessive passage of cholesterol through the arteries followed by the formation of plagues, thereby blocking the passage of blood (2). Thus, interventions that lower serum lipids can reduce the risk of atherosclerosis and may benefit cardiovascular health (3). Apart from synthetic medications such as clofibrates and statins, attempts are continuously being made to discover herbal pharmaceuticals with lipid-lowering properties.

Medicinal plants play a vital role in lowering lipid profile (4). Alternanthera sessilis (sessile joyweed) is a widespread aquatic plant commonly growing in tropics and subtropics countries. It is traditionally used to alleviate fever, increase the breast flow in breastfeeding mothers and neutralize snake venom (5). Several pharmacological activities of this plant, including hypoglycemic, (6), anti-inflammatory (7), antimicrobial and wound healing (8) as well as antioxidant (9) have been reported. The presence of bioactive compounds namely cycloeucalenol, stigmasterol, campesterol, beta-sistosterol, and alkaloids were also reported (10). Although extensive research has documented various pharmacology activities of *A. sessilis*, there is limited data discussing the potential antihyperlipidemic activity of this plant. A study conducted by Othman (11) has investigated the therapeutic effect of methanolic and water leaf extracts of *A. sessilis* red (ASR) in diet-induced obesity rats. ASR extract at 175 mg/kg body weight normalized plasma lipid profile and reduced leptin level after 2 months of daily therapy. In this study, the possible prophylactic effect of *A. sessilis* leaf extracts in preventing antihyperlipidemic was studied in hyperlipidemic rat

model. Serum lipid profile, hepatic and fecal fat as well as in vitro antioxidant activities were evaluated.

Methods

Sample preparation

The fresh whole plant of *A. sessilis* was collected from Pulau Pinang, Malaysia. The specimens were identified by Associate Professor Dr. Rahmad Zakaria and placed in the Herbarium Unit of the School of Biological Sciences at Universiti Sains Malaysia (USM) with the specimen ID 1694. To prepare the samples, the plant was first cleaned and dried in an oven at a temperature of 45-50^{o}C and then ground into a powder. The powdered plant (500g) was macerated serially to extract its active components with petroleum ether, chloroform, methanol, and water in water bath at 45-50^{o}C. The plant was macerated for 3 days in each solvent at a volume of 2.5 L. The extracts of organic solvents were distilled using a rotary evaporator (Buchi Labortechnik, AG CH-9230 Flawil, Switzerland) and then dried in an oven at 40-50°C. The water extract was freeze-dried. All extracts were kept in a dessicator prior to the experiments.

Experimental animals

Sprague-Dawley male rats (180-220 g) were supplied by the Animal Research and Service Centre, USM. The rats were kept in the transit room in School of Pharmaceutical Science, USM and acclimatized for seven days before the commencement of the experiment. During the period of acclimatization, the animals were kept in regular environmental settings with a 12-hour light/dark cycle and had unlimited access to food pellets and water. All the procedures were approved by the animal ethic committee of USM [USM/Animal Ethics Approval/ 2013/ (90) (522)].

Induction of hyperlipidemia

In this experiment, hyperlipidemia was induced by feeding the rats with high-fat diet. This diet was made by blending a commercial food pellet with cholesterol at 1%, cholic acid at 0.5%, margarine at 15%, and basal diet at 83%. The mixture was formed into small pellets and dried at 60°C.

Experimental design

Randomly, the rats were grouped into seven and administered orally either a high-fat diet with the extracts or atorvastatin twice daily for 28 days, as below:

Group 1: Normal control (normal diet + vehicle)
Group 2: Hyperlipidemic control (high-fat diet + vehicle)
Group 3: Positive control (high-fat diet + atorvastatin, 30 mg/kg)
Group 4: Treatment (high-fat diet + petroleum ether extract, 1000 mg/kg)
Group 5: Treatment (high-fat diet + chloroform extract, 1000 mg/kg)
Group 6: Treatment (high-fat diet + methanol extract, 1000 mg/kg)
Group 7: Treatment (high-fat diet + water extract, 1000 mg/kg)

The dose of atorvastatin was applied as suggested by Arora et al. (12). The extracts and atorvastatin were suspended in distilled water containing 10% tween 80. Rat food intake was recorded daily, and their lipid profiles were examined weekly. On the final day of the experiment, the feces were collected from each rat, dried at 50°C, weighed and kept into a glass container, and stored at -20°C. The livers were harvested and kept at -80°C until further processing.

Biochemical parameters

The blood was collected using the cardiac puncture method and put in the non-heparin blood tubes for liver function tests and lipid profiles analyses. To obtain serum, the blood was centrifuged at 3000 rpm for 10 minutes. Lipid profiles. Total cholesterol (TC), triglycerides (TG) and high-density lipoprotein (HDL) levels were measured using automated analyzer (Selectra Junior, Vital Scientific B. V., Netherlands).

The following equations were used to determine low-density lipoprotein (LDL) and coronary risk index (CRI):

$$LDL = TC - HDL - TG/5$$

$$CRI = TC/HDL$$

Hepatic fat extraction

The hepatic fat was extracted to determine the content of cholesterol and triglycerides. The extraction was conducted according to the modified method of Folch et al. (13). Briefly, 1 g of liver was homogenized with the chloroform-methanol-water mixture at the ratio of 2:1:0.2 and filtered. The filtrate was allowed to separate into two layers and the lower layer was evaporated. Then, ELISA kits (Thermo Scientific Infinity, UK) were used to quantify the liver's total cholesterol and triglyceride content.

Fecal fat extraction

The feces were collected at the last day of the experiment, dried and kept in -20^{o}C until used. Powdered fecal samples were dissolved in distilled water and acidified with hydrochloric acid and incubated for 10 min. Chloroform-methanol mixture (2:1), shaken vigorously, sonicated for 30 min, filtered and lastly evaporated to remove the organic solvents. The procedure was repeated three times with the residue. the concentration of cholesterol, triglycerides and total bile acids contents were measured using commercial kits (Thermo Scientific (Infinity) UK).

In vitro antioxidant activity

2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity.

The modified Brimson et al. (14) method was applied to measure the scavenging activity of the extracts against DPPH radical. The DPPH solution at the concentration of 200 µg/ml was prepared by dissolving DPPH in methanol. The extracts were prepared by dissolving them in distilled water. In the 96-well plate, 100 µL of DPPH solution was mixed with 100 µL of the extracts at various concentrations. A blank for the extracts was made by replacing DPPH with water. The blank for the DPPH was prepared by replacing the extract with methanol. The plate was incubated in the dark at room temperature for half an hour. After that, the absorbance at 517 nm was determined. Butylated hydroxytoluene and quercetin were used as the standard compounds for comparison purpose. The measurement of each sample was done in triplicate.

Using the following formula, the percentage of radical scavenging activity was quantified:

DPPH scavenging activity (%) = $((A_s - A_b) - A_{dpph} \times 100)/A_{dpph}$

A_s = absorbance of the sample

A_b= absorbance of blank

A_{dpph} = absorbance of DPPH control

The value of EC_{50} was used to express the samples' DPPH scavenging activity. This EC50 represents the concentration at which 50% of the DPPH scavenging activity is inhibited.

2,2'*-Azino-bis(3-ethyl) benzothiazoline-6-sulphonic (ABTS) acid decolorization assay*

The ABTS+ radical was prepared by dissolving ABTS (2 mM) and potassium persulphate (7 mM) in methanol in the ratio of 50:0.3 (15). This mixture was incubated in the dark at room temperature overnight. Before conducting the assay, the absorbance of ABTS+ at 734 nm was adjusted to 0.7 via dilution. *A. sessilis* extracts were prepared in methanol. These extracts were serially diluted to achieve a concentration between 10 mg/ml and 0.3125 mg/ml. In a 96-well plate, 100 µL of the extracts in various concentrations were added to the 100 µL of ABTS+ solution. The mixtures were incubated at room temperature for 30 minutes. Finally, the absorbance at 734 nm was recorded. L-Ascorbic acid (10 µg/ml-0.156 µg/ml) was used as the standard antioxidant. All measurements were performed in triplicate.

Reducing capacity

The reducing capacity of the *A. sessilis* extracts was conducted by adapting the previous study (16). The extracts were prepared in the concentrations ranged from 5 mg/ml to 0.156 mg/ml. One ml of the extract was incubated with 2.5 ml of the respective 1% potassium ferricyanide and 0.2 M phosphate buffer (pH 6.6) at 50°C for 20 minutes. After that, 2.5 ml of 10% trichloroacetic acid was added. The mixture was centrifuged for 10 minutes at 3000 rpm. The supernatant was collected and 2.5 ml of distilled water and 0.5 ml of 0.1% ferric chloride were added. The absorbance was measured at 700 nm. Each sample was tested in triplicates.

Statistical analysis

Values were reported as mean ± standard error of the mean (S.E.M). To understand the statistical significance between control and treatment groups, one way ANOVA was performed. Dunnett's test was used as the post-hoc. P-value less than 0.05 was considered as significantly different.

Results

Extraction yield of A. sessilis

Table 1 shows the weight of extracts in grams obtained from extracting 2.5 kg of A. sessilis powder serially with organic solvents of different polarity, namely petroleum ether, chloroform, methanol and water respectively. Extraction using polar solvents, methanol and water produced high extracts yield as compared to non-polar ones.

Table 1: Yield of *A. sessilis* crude extracts

Extracts	Weight (g)	Color of extract
Petroleum ether extract	18.88	Orange brown
Chloroform extract	25.40	Dark green
Methanol extract	278.11	Dark yellow
Water extract	259.22	Black

Effect of A. sessilis extracts on serum lipid profile.

There was significant increase in serum TC, TG and LDL after administration of high fat diet in the hyperlipidemic control when compared the normal control. Among all extracts, only water extracts significantly lowered the levels of TC, TG, LDL and CRI ratio when compared to the hyperlipidemic control. None of the extract and standard drug significantly increased HDL level. The result is shown in Table 2.

Table 2: Effect of *A. sessilis* extracts on serum lipid profile and coronary risk index (CRI) ratio on high fat diet-induced hyperlipidemic rats.

Treatment Groups	Serum Lipid Profile (mg/dl)				CRI Ratio
	TC	TG	HDL	LDL	
Normal Control	74.34 ± 6.28	86.43 ± 13.07	52.55 ± 5.45	33.95 ± 3.17	1.47 ± 0.16
Hyperlipidemic control	444.92 ± 26.50$^{\#}$	302.90 ± 10.42$^{\#}$	30.37 ± 4.67	302.51 ± 19.94$^{\#}$	16.60 ± 2.54$^{\#}$
Atorvastatin	217.40 ± 18.00***	120.90 ± 15.24***	33.98 ± 4.73	128.27 ± 5.25***	7.62 ± 2.04*
Petroleum ether extract	384.31 ± 32.66	302.23 ± 30.47	30.04 ± 8.38	288.01 ± 8.12	15.72 ± 2.35
Chloroform extract	396.07 ± 22.92	274.52 ± 19.43	40.05 ± 10.55	298.55 ± 19.09	14.43 ± 3.77
Methanol extract	337.35 ± 21.71	192.22 ± 28.78**	36.30 ± 4.52	264.61 ± 6.30	10.18 ± 1.76
Water extract	229.62 ± 15.19***	171.31 ± 27.60**	31.59 ± 4.03	133.13 ± 4.36***	7.91 ± 1.19*

$^{\#}$ $p < 0.001$ statistically significant compared to normal control. *** $p < 0.001$, ** $p < 0.01$ and * $p < 0.05$ statistically significant compared to hyperlipidemic control. Values are expressed as mean ± SEM (n=6). SEM: standard error of mean, TC: total cholesterol, TG: triglycerides, HDL: high-density lipoprotein, LDL: low-density lipoprotein, CRI: cardiac risk index

Effect of A. sessilis extracts on liver function.

Table 3 shows the effect of extracts of *A. sessilis* on the biochemical parameters in liver functions test of high-fat diet-induced hyperlipidemic rats. Hyperlipidemic control had significantly ($p < 0.001$) higher ALP and GGT as compared to the normal control. There was no significant difference in the levels of total protein, albumin, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in methanol, water and atorvastatin treated groups, as compared with both controls. When compared with the normal control, chloroform-treated group significantly rose the level of total protein, ALP, GGT, AST, and ALT.

Table 3: Effect of extracts of *A. sessilis* on liver function test of high-fat diet-induced hyperlipidemic rats

Treatment Groups	Parameters					
	Total Protein (g/dl)	Albumin (g/dl)	ALP (IU/l)	GGT	AST (IU/l)	ALT (IU/l)
Normal Control	6.83 ± 0.15	3.96 ± 0.11	51.70 ± 3.85	32.66 ± 2.90	28.50 ± 1.87	29.83 ± 2.65
Hyperlipidemic Control	7.88 ± 0.55	4.90 ± 0.51	134.33 ± 8.91$^{\#\#\#}$	59.50 ± 4.94$^{\#\#\#}$	38.83 ± 3.40$^{\#}$	43.66 ± 4.12
Atorvastatin	6.96 ± 0.19	4.18 ± 0.14	58.88 ± 2.33	35.66 ± 2.36	31.83 ± 2.93	33.16 ± 3.87
Petroleum Ether Extract	7.36 ± 0.25	4.48 ± 0.19	106.38 ± 10.75$^{\#\#\#}$	41.33 ± 4.02	28.50 ± 3.49	45.50 ± 4.96
Chloroform Extract	9.08 ± 0.53$^{\#\#}$	5.08 ± 0.46	143 ± 7.92$^{\#\#\#}$	53.16 ± 3.30$^{\#\#}$	41.83 ± 4.89$^{\#}$	48.83 ± 4.80$^{\#}$
Methanol Extract	7.51 ± 0.35	4.91 ± 0.31	89.71 ± 9.21	43.50 ± 3.36	33.00 ± 2.59	36.50 ± 3.70
Water Extract	6.88 ± 0.31	4.23 ± 0.18	63.33 ± 4.59	36.83 ± 3.26	35.16 ± 3.34	35.16 ± 4.36

$^{\#\#\#}$ $p < 0.001$, $^{\#\#}$ $P < 0.01$, $^{\#}$ $P < 0.05$ statistically significant compared to normal control. Values are expressed as mean ± SEM (n=6). SEM: Standard error of mean, ALP: alkaline phosphatase, GGT: gamma-glutamyltransferase, AST: aspartate aminotransferase, ALT: alanine aminotransferase

Effect of A. sessilis extracts on hepatic fats.

The hyperlipidemic control showed significant increase in liver total cholesterol and triglycerides when compared to normal control ($p < 0.001$). Atorvastatin managed to significantly reduce liver total cholesterol and triglycerides, as compared with HFD group. Methanol and water extracts showed a significant decrease in liver total cholesterol ($p < 0.01$) and triglycerides ($p < 0.001$) when compared to hyperlipidemic control. There was a significant difference in liver triglycerides of chloroform extract treated group ($p < 0.01$) compared to the normal control, respectively (Figure 1).

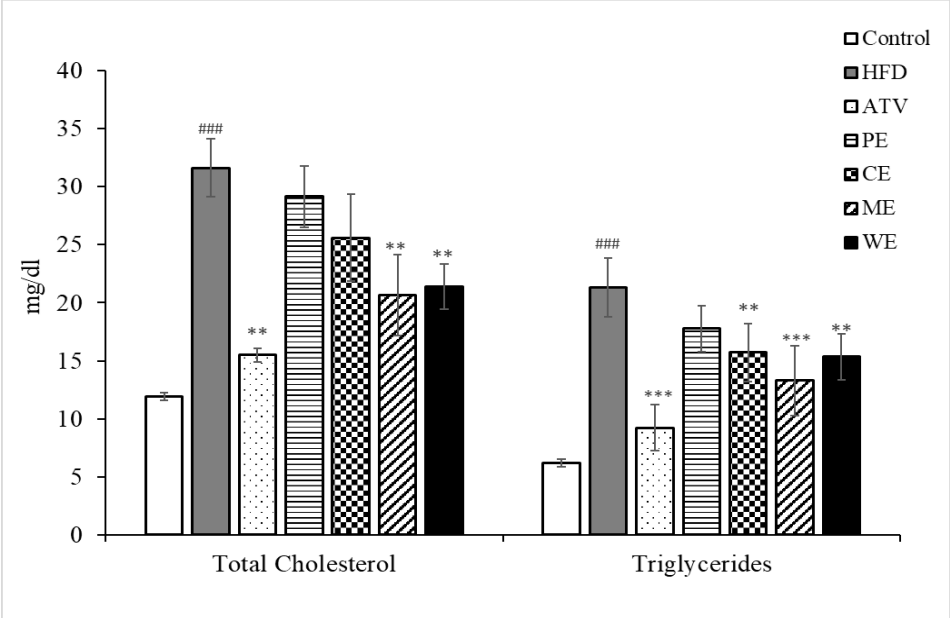

Figure 1: Effect of *A. sessilis* on liver cholesterol and triglycerides on high-fat diet-induced (HFD) hyperlipidemic rats. Each bar represents mean ± SEM of rats. ### P<0.001 statistically significant compared to Control group, ** P<0.01, *** P<0.001 statistically significant compared to HFD group. ATV: atorvastatin, PE: petroleum ether extract, CE: chloroform extract, ME: methanol extract, WE: water extract

Effect of A. sessilis extracts on fecal fat and total bile acids.

As shown in Figure 2, the water extract treated group significantly increased fecal total cholesterol and total bile acid, as compared to normal and hyperlipidemic controls. Meanwhile, methanol extract exhibited a significant increase in fecal triglycerides and total bile acid when compared with both controls.

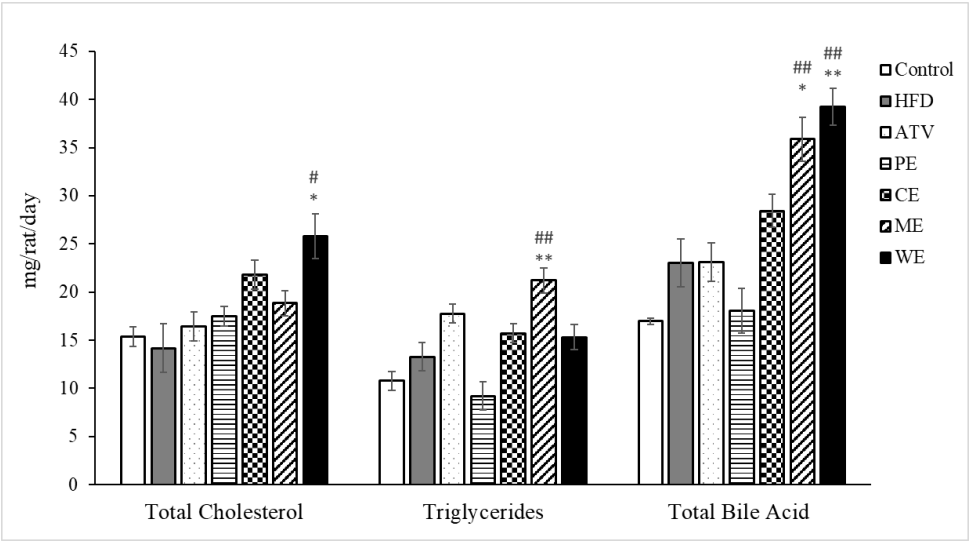

Figure 2: Effect of *A. sessilis* on fecal cholesterol, triglycerides, and total bile acids on high-fat diet-induced (HFD) hyperlipidemic rats. Each bar represents the mean ± SEM of rats. # P<0.05, ## P<0.01 statistically significant compared to Control group, * P<0.05, ** P<0.01 statistically significant compared to HFD group. ATV: atorvastatin, PE: petroleum ether extract, CE: chloroform extract, ME: methanol extract, WE: water extract

Antioxidant activity of A. sessilis extracts

Extracts of *A. sessilis* were tested for their in vitro antioxidant activity using DPPH, ABTS, and reducing power assays (Table 4). In the DPPH test, methanol extract exerted the strongest antioxidant activity against DPPH radical, with the EC_{50} value of 0.07 ± 1.21 mg/mL, followed by water and petroleum ether extracts with the respective EC_{50} value of 1.47 ± 1.92 mg/mL and 6.60 ± 0.61 mg/mL.

Table 4: DPPH, ABTS and reducing power assays of the *A. sessilis* extracts.

Extracts	DPPH (EC_{50}, mg/mL)	ABTS (EC_{50}, mg/mL)	Reducing Capacity (mg BHT/100 g extract)
Petroleum Ether	6.6 ± 0.61	2.11 ± 0.99	5.21 ± 0.19
Chloroform	10.95 ± 0.92	5.93 ± 0.72	2.71 ± 0.23
Methanol	0.07 ± 1.21	0.48 ± 0.29	12.99 ± 0.26
Water	1.47 ± 1.92	1.65 ± 0.37	10.69 ± 0.30
Quercetin	0.0092 ± 1.02	-	-
BHT	0.0052 ± 0.21	-	-
L-ascorbic acid	-	0.0006 ± 0.16	-

Values represent mean ± SD (n=3). DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), BHT: butylated hydroxytoluene, EC_{50}: half maximal effective concentration

A similar finding was recorded in ABTS; methanol extract showed the strongest antioxidant activity, and the weakest activity was observed in chloroform extract. The radical scavenging of the extracts against ABTS, expressed as EC_{50} value, varied from 0.48 ± 0.29 mg/mL to 5.93 ± 0.72 mg/mL. Interestingly, a similar pattern of antioxidant strength was observed in the reducing power as those seen in the DPPH and ABTS assays. The pattern was as follows: methanol extract > water extract > petroleum ether extract > chloroform extract.

Discussion

High-fat diet (HFD) has been used to induce hyperlipidemia in animals. This model has been reported to be an ideal in vivo model for studying antihyperlipidemic drugs (17). Rats on a high-fat diet showed observable changes in blood lipoproteins, which altered the distribution of apolipoproteins. Apolipoproteins regulate lipoprotein metabolism and lipid transport. The change in apolipoproteins influenced the distribution of β-VLDL, LDL-c, and HDL-c (18). These alterations result in the accumulation of cholesteryl ester in macrophages and human monocyte (19).

As expected, the HFD rats showed a significant increase in serum TC, TG, and LDL levels, when compared with the normal rats. Our preliminary result showed 1000 mg/ kg B.W. as the minimum effective dose for *A. sessilis*. Thus, it was applied in this study. Of all four extracts of *A. sessilis*, water extract showed the most potent preventive effect against hyperlipidemia. It notably reduced the levels of serum TC, TG, LDL, and CRI ratio, thus suggesting its potential role in normalizing lipid profiles. The antihyperlipidemic effect of *A. sessilis* has been demonstrated previously by Rayilla and Goverdhan (20) and Rohini and Doss (21). These studies demonstrated that extracts of *A. sessilis* significantly ($p < 0.05$) lowered the serum TC, TG, and LDL cholesterol levels and effectively elevated the HDL level in diabetic rat models.

As the liver is the central organ in lipid metabolism, liver enzymes were also assessed to have an insight into the hepatic function in high-fat diet rats. ALT, AST, and GGT are the common enzymes tested in liver function tests. ALT and AST are the markers for hepatocellular injury whereas GGT reflects the function of the biliary tract (22). Lipids play an intriguing role in the development of fibrosis, hepatocellular carcinoma, and cirrhosis in the liver. Hence, any disturbances in the lipoprotein uptake, storage, and circulation will affect the function and morphology of the liver and alter the level of liver enzymes (23). Methanol and water extracts normalized the lipid profile despite being challenged with high-fat diet. An insignificant change in lipid profile was observed in these groups when compared to the normal control. On contrary, chloroform extract significantly elevated the levels of ALP, AST, ALT and GGT. Elevated levels of these enzymes reflect possible liver diseases. Sattar et al. (24) have associated increased level of transaminases in hepatic steatosis due to non-alcoholic fatty liver disease. Meanwhile, several studies have shown the correlation of GGT levels with the prevalence of hypercholesterolemia and hypertriglyceridemia (25, 26). AST however, was observed to have a weak positive correlation with lipid profile.

The mechanisms underlying the lipid-lowering effect of *A. sessilis* extracts in high-fat diet rats were scrutinized by evaluating hepatic and fecal fats as well as total bile acid. The result demonstrated that water and methanol extracts along with atorvastatin significantly decreased the hepatic total cholesterol and triglycerides. *A. sessilis*

extracts decreased hepatic cholesterol may be partly by stimulating hepatic cholesterol-7-alpha hydroxylase activity, a rate-limiting enzyme in bile acid biosynthesis (27). The fecal triglycerides and bile acid excretion were significantly increased in the water and methanol extracts, as compared to the hyperlipidemic control. The biosynthesis of bile acid is one of the major pathways in cholesterol degradation and elimination (28). Bile acid is synthesized from cholesterol which occurs exclusively in the hepatocytes by a sequence of enzymatic reactions and secreted into the intestinal lumen to facilitate dietary fat absorption (29). Enterohepatic circulation permits bile acid reabsorption from the distal ileum and is conveyed back to the liver via portal circulation (30). Any disturbance in the reabsorption of bile acids aids in its elimination in the feces and the excreted bile acids will be replenished via de novo synthesis in the liver using cholesterol as a precursor (29). This mechanism aids in cholesterol excretion in the body which is followed by decreased hepatic cholesterol. It had been demonstrated that hepatic cholesterol deficiency leads to increased LDL receptor expression which subsequently results to increased plasma LDL clearance (31).

Furthermore, the antihyperlipidemic activity and antioxidant effects of *A. sessilis* extracts displayed similar tendencies. In alignment with antihyperlipidemic activity, polar extracts exerted stronger antioxidant activity than non-polar extracts. Several studies have demonstrated the association of antioxidants with lipid-lowering effects of different plant extracts, for example *Ulva pertusa* (32), *Costus speciosus* (33) and *Aframomum melegueta* (34). Based on the reported phytochemical analyses, the chromatograms of *A. sessilis* shows the presence of several alkaloids, phenolic acid and flavonoids with predominance of ferulic acid, rutin, and quercetin (35). These compounds are not only known for their antioxidant activity but also antihyperlipidemic effect. Quercetin, for example, reduced serum cholesterol and triglycerides in rabbit receiving high-fat diet by obstructing cholesterol accumulation and increasing the expression of LCL receptors (36). It has been hypothesized that alkaloids exert the antihyperlipidemic effect partially through inhibition of carbohydrate absorption and metabolism as well as the lipogenesis process (37).

This study has several limitations that might be addressed in future research. A histology study of the liver was not carried out. Through histological study, the effect of *A. sessilis* on the accumulation and distribution of lipids in the hepatocytes, the formation of fibrosis, and signs of liver abnormalities can be observed. In addition to that, a study on the isolation and identification of the bioactive compound(s) that are responsible for the antihyperlipidemic should be considered.

Conclusion

Conclusively, this study demonstrated that *Alternanthera sessilis* extracts have potential antihyperlipidemic and antioxidant activities. The protective effects of *A. sessilis* against hyperlipidemia may be partially mediated via the reduction of endogenous synthesis of hepatic total cholesterol and triglycerides and increased excretion of fecal triglycerides and bile acid. Additionally, the plant is also shown to possess an antioxidant effect which may have provided protection against oxidative damage, hyperlipidemia, and liver damage.

Conflict of Interest

No conflict of interest is associated with this work.

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