Pharmacogn. Mag.
A multifaceted peer reviewed journal in the field of Pharmacognosy and Natural Products
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ORIGINAL ARTICLE

Hypolipidemic Effect of *Psidium guajava* Leaf Extract against Hepatotoxicity in Rats

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Submitted: 26-04-2017 Revised: 17-05-2017 Published: 20-02-2018

ABSTRACT

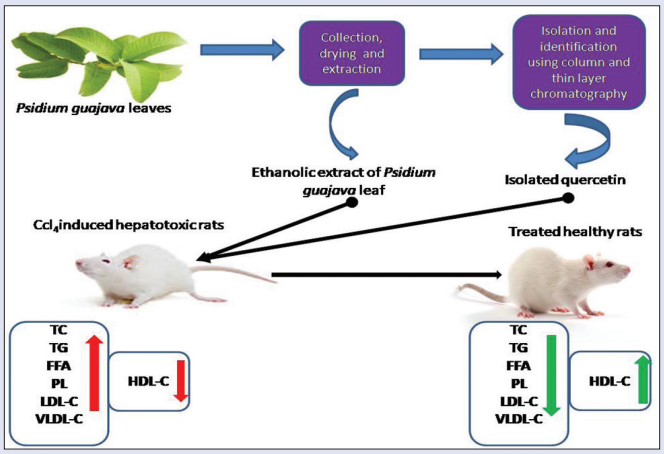
Background: Plant-based natural extracts cure several diseases in human. However, the extract of *Psidium guajava* leaf is not yet evaluated on changes of lipid profile in hepatic disease affected rats. **Objective:** The present study was aimed to evaluate the mitigation effect of the ethanolic extract of *P. guajava* leaf and its isolated quercetin fraction on hepatotoxic rats. **Materials and Methods:** Carbon tetrachloride (CCl_4) was injected to rats for hepatic disease induction and silymarin drug was used as positive control to compare plant ethanolic extract. The lipid profiles were assessed in both plasma and liver tissue of diseased and control rats. **Results:** Levels of total cholesterol, triglycerides, free fatty acids, phospholipids, and low-density lipoprotein cholesterol were increased and the level of high-density lipoprotein cholesterol (HDL-C) was decreased in CCl_4-induced hepatotoxic rats. The treatment of *P. guajava* (100, 200, and 300 mg/kg, bw) and isolated quercetin fraction (20 mg/kg, bw) doses decreased the elevated levels of all these parameters in diseased rats and restored the normal concentration of HDL-C. **Conclusion:** The results of the present study concluded that the *P. guajava* leaf and its isolated quercetin fraction can significantly regulate lipid metabolism in CCl_4-induced hepatotoxic rats and decrease the disease rate.

Key words: Hepatotoxicity, hypolipidemic, *Psidium guajava* and rat

SUMMARY

- *Psidium guajava* leaf extract reduces the hepatotoxicity and disease rate in rats
- Quercetin fraction of leaf extract significantly regulates lipid profile in hepatic diseased rats.

Abbreviations used: CCl_4: Carbon tetrachloride; FFA: Free fatty acids; HDL-C: High-density lipoprotein cholesterol; LCAT: Lecithin cholesterol acyltransferase; LDL-C: Low-density lipoprotein cholesterol; PL: Phospholipids; TC: Total cholesterol; TG: Triglycerides; VLDL-C: Very low-density lipoprotein cholesterol.



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DOI: 10.4103/pm.pm_167_17

Access this article online
Website: www.phcog.com
Quick Response Code:

INTRODUCTION

The liver is the major site for the production and metabolism of cholesterol, bile acids, and phospholipids (PL). The alteration of the fatty acid content frequently occur in liver cells because it is the major organ play a vital role in fat metabolism. Free radicals are essential for many biochemical processes and represent a necessary part of aerobic life and metabolism.[1] Hepatotoxicity is the most common ailment resulting from severe metabolic disorders to even mortality. In most of the cases, free radical is responsible for hepatotoxicity. Hyperlipidemia is one of the major risk factors for heart diseases including atherosclerosis, heart attacks, myocardial infarction, and cerebrovascular diseases.[2] Nowadays, in developing countries, hyperlipidemia and thereby atherosclerosis is one of the major cause of cardiac illness and death. Hypercholesterolemia and hypertriglyceridemia are the autonomous risk factors that only or jointly responsible for the development of atherosclerosis and sequence of atherosclerotic lesions.[3] Numerous hypolipidemic synthetic drugs are available for clinical use, but they have rigorous side effects including harmful syndromes such as diabetes and cardiovascular disease.[4,5] Most of the herbal medicines have excellent hypolipidemic actions without side effects in worldwide. The people are returning to the naturals from synthetic drugs because of its safety and security.

Psidium guajava belong to family Myrtaceae. It is commonly known as guava[6] and is cultivated in tropical regions at all climatic conditions. Conventionally, the *P. guajava* leaves are used as a hypoglycemic agent, antimicrobial, antifungal, cardioprotective, and antispasmodic agent.[7] The *P. guajava* leaves are rich in tannins, phenols, triterpenes, and saponins. The most important bioactive element of the drug is flavonoids such as quercetin. Quercetin is one of the naturally occurring dietary flavonol

Cite this article as: Vijayakumar K, Rengarajan RL, Radhakrishnan R, Anand AV. Hypolipidemic effect of Psidium guajava Leaf extract against hepatotoxicity in rats. Phcog Mag 2018;14:4-8.

compounds which belong to a broad group of polyphenolic flavonoid substances. Isolated fractions have an antioxidant, anti-inflammatory, cardioprotective, and anti-carcinogenic properties.[8,9] The ethanolic extract of *P. guajava* leaves has an antioxidant potential in *in vitro* assays.[10] The above evidence, the present investigation was planned to study the hypolipidemic effect of ethanolic extract of *P. guajava* and its isolated fraction on carbon tetrachloride (CCl_4)-induced hepatotoxic rats.

MATERIALS AND METHODS

Plant material and extraction

The fresh leaves of *P. guajava* (herbarium specimen number: PV001, St. Joseph College, Tiruchirappalli) were collected in Tiruchirappalli, Tamil Nadu. The shade dried *P. guajava* leaves were powdered using mortar and pestle and stored in an airtight container. About 100 g of powder was transferred to soxhlet apparatus and extracted with 250 ml of ethanol for 24 h and filtered through Whatman No. 41 filter paper. The obtained extract was dried under controlled temperature 45°C ± 5°C. The dried extract was preserved in refrigerator for further study.

Extraction and isolation of quercetin from ethanol extract

Fifty gram of dried ethanol extract was dissolved in petroleum ether (60°C–80°C). The marc (35 g) was extracted to exhaustion with 95% ethanol. The crude ethanolic extract was suspended in water and successively extracted with ethyl acetate (2 × 100 ml) and final extract was used to isolated quercetin.[11,12] The ethyl acetate dissolved extract (1.25 g) was passed through silica gel G (60–120 mesh; 100 g) column (75 cm × 2.0 cm) and eluted gradiently with chloroform; chloroform: methanol mixtures (9:1, 8:2, and 7:3) and methanol. The collected fractions were concentrated and separated by thin layer chromatography using toluene:Ethyl acetate:methanol (4.5:0.5:0.5). The glass plates (20 cm × 20 cm) coated with Silica gel "G" (0.2–0.3 mm thick and 30 g/60 ml distilled water) were dried at room temperature. The dried plates were activated at 100°C for 30 min in an oven and cooled at room temperature. The eluted fractions were dissolved in ethanol and spotted 1 cm above the edge of the plate with standard reference compound (quercetin, 5 µl) using a capillary tube on Silica gel "G" plate (Silica gel 60 F 254 precoated aluminum) using toluene:Ethyl acetate:methanol (4.5:0.5:0.5) as mobile phase. The silica gel glass plates were placed in an airtight chromatography chamber, and after running of chromatogram, the plates were air dried. The plates were sprayed with iodine chamber and 5% of ethanolic ferric chloride to observe the color of the spots. The color developed in the chromatogram was photographed and R_f values were calculated for isolated samples and compared with coinciding standard. R_f = distance from the origin to the spot divided by distance from the origin to the solvent front.

Carbon tetrachloride-induced hepatotoxicity and *Psidium guajava* ethanolic treatments in rats

Healthy adult albino Wistar rats, bred and reared in Srimad Andavan College of Arts and Science, Trichy, Tamil Nadu, India were used for the hypolipidemic and hepatotoxicity experiments. The male rats (150–180 g) were chosen for this study. The selected animals were housed in polypropylene cages lined with husk and kept in a semi-natural light/dark condition (12 h light/12 h dark). The animals were allowed free access to water and standard pellet diet (Amrut Laboratory Animal Feed, Pranav Agro Industries Ltd., Bangalore, India), consisting of protein (22.21%), fat (3.32%), fiber (3.11%), balanced with carbohydrates (>67%), vitamins and minerals. Animal handling and experimental procedures were approved by the Institutional Animal Ethics Committee, Srimad Andavan College of Arts and Science, Trichy (Registration Number:/03/ac/CPCSEA) and animals were cared in accordance with the "Committee for the purpose of control and supervision on experimental animals" (CPCSEA, 2004).

Rats were randomly divided into 8 groups of 6 rats each and housed in individual ventilated cages. Feed and water were *ad libitum* provided to the animals. Ethanolic leaf extract of *P. guajava* was suspended in water at three different doses (100, 200, and 300 mg/kg, bw) and isolated quercetin fraction (20 mg/kg, bw) was administered to rats postorally using an intragastric tube daily.

- Group I: Control + normal saline (2 ml/kg, bw)
- Group II: CCl_4 (1.5 ml/kg, bw) hepatotoxic control
- Group III: Control + ethanolic leaf extract of *P. guajava* (300 mg/kg, bw)
- Group IV: CCl_4 + ethanolic leaf extract of *P. guajava* (100 mg/kg, bw)
- Group V: CCl_4 + ethanolic leaf extract of *P. guajava* (200 mg/kg, bw)
- Group VI: CCl_4 + ethanolic leaf extract of *P. guajava* (300 mg/kg, bw)
- Group VII: CCl_4 + isolated quercetin fraction (20 mg/kg, bw)
- Group VIII: CCl_4 + standard drug (silymarin, 25 mg/kg, bw)

After 21 days, all the animals were sacrificed. Blood was collected by cutting the jugular vein, in tubes with a mixture of potassium oxalate and sodium fluoride (1:3) to get plasma for various assays. The collected bloods were centrifuged at 2000 rpm for 10 min, and the plasma was separated by the aspiration.

Liver tissues (250 mg) were sliced into pieces and homogenized in appropriate buffer in cold condition (pH 7.0). The homogenate was centrifuged at 1000 rpm for 10 min at 0°C. The supernatant was separated and used for various biochemical estimations.

Preparation of lipid extract

Tissue and plasma lipids were extracted by the method of Folch *et al.*[13] The lipids were extracted by homogenizing a known weight of tissues (250 mg) with 5 mL of chloroform-methanol mixture (2:1, v/v). The lipid extract was collected and made up to a specific volume. Aliquot of this extract was then used for the estimation of cholesterol, free fatty acids (FFA), triglycerides (TG), and PL.

Estimation of total cholesterol

Total cholesterol (TC) in plasma was estimated by the enzymatic method.[14] To 10 µL of lipid extract, 1.0 mL of enzyme reagent was added, mixed well, and kept at 37°C for 5 min. 10 µL of cholesterol standard and distilled water (blank) were also processed similarly. The absorbance was measured at 510 nm. Cholesterol concentration was expressed as mg/dL plasma or mg/100 g tissue.

Estimation of high-density lipoprotein cholesterol

High-density lipoprotein cholesterol (HDL-C) was estimated using the diagnostic kit based on the enzymatic method.[15] Plasma (0.1 mL) was mixed with 0.1 mL of precipitating reagent and allowed to stand at room temperature for 5 min and centrifuged at 2000–3000 rpm for 10 min. HDL-C was estimated at 500 nm as described earlier. The values were expressed as mg/dL.

Estimation of free fatty acids

FFA was estimated by colorimetric method.[16] Lipid extract (0.5 mL) was evaporated to dryness and dissolved in 6.0 mL chloroform-heptane-methanol solvent and 2.5 mL of copper reagent were added. All the tubes were shaken vigorously for 90 s and were kept

aside for 15 min. The tubes were centrifuged and 3.0 mL of the copper layer was transferred to another tube, containing 0.5 mL of diphenyl carbazide and mixed carefully. The reaction mixture was read at 540 nm against a reagent blank containing 3.0 mL of solvent and 0.5 mL of diphenyl carbazide. The FFA content was expressed as mg/g tissue.

Estimation of triacylglycerols

Triacylglycerols were estimated using the diagnostic kit based on the enzymatic method.[17] Ten microlitter of plasma or 10 µL of lipid extract was added with 1.0 mL of enzyme reagentand mixed well and incubated at room temperature for 10 min. Ten microlitter of triacylglycerols standard and distilled water (blank) were also processed similarly. The absorbance was measured at 510 nm. The triacylglycerol content was expressed as mg/dL plasma or mg/100 g tissue.

Estimation of phospholipids

PL was estimated by the method of Zilversmit and Davis (1950).[18] An aliquot of the lipid extract was evaporated to dryness. One mL of 5.0 N sulfuric acid was added and digested till light brown. Then, 2–3 drops of concentrated nitric acid were added, and the digestion was continued till it became colorless. After cooling, 1 mL of water was added and heated in a boiling water bath for about 5 min. Then, 1.0 mL of ammonium molybdate and 0.1 mL of amino naphthol sulfonic acid were added. The volume was then made up to 10.0 mL with distilled water and the absorbance was measured at 680 nm within 10 min. Standards in the concentration range of 2–8 mg were treated in the similar manner. The values obtained were multiplied with a factor 25 to convert inorganic phosphorus to its PL equivalents. The amount of PL was expressed as mg/dL plasma or mg/100 g tissue.

Very low-density lipoprotein cholesterol and low-density lipoprotein cholesterol

Very low-density lipoprotein (VLDL) and LDL were calculated using the formula Friedewal *et al.*[19]

VLDL cholesterol = TG/5;

LDL cholesterol = TC– (HDL cholesterol + VLDL cholesterol).

The values were expressed as mg/dL.

Statistical analysis

Data were analyzed by one-way analysis of variance using a commercially available statistics software package (SPSS® for Windows, Version 13.0, Chicago, IL, USA). Results were presented as means ± standard deviation $P < 0.05$ was regarded as statistically significant.

RESULTS

The ethanolic extract of *P. guajava* leaves was partitioned with ethyl acetate and 1.25 g of the ethyl acetate soluble fraction was passed to 100 g of silica gel G in a column (75 cm × 2.0 cm) and eluted gradiently with chloroform; chloroform:methanol mixtures 9:1, 8:2, 7:3 and methanol [Figure 1a]. Fifteen fractions [Supplementary Table 1] were collected and all the fractions were checked using TLC pattern [Figure 1b and c]. The fraction (yellow color) eluted using chloroform:methanol (9:1) was subjected with TLC profiling. TLC was performed on analytical plates over silical gel (TLC-grade; Merck India) with standard quercetin using mobile phase toluene: ethyl acetate: methanol (4.5:0.5:0.5). Quercetin was identified after the development of spots and visualized using iodine chamber and 5% ethanolic ferric chloride.

The plasma and tissue (liver) concentrations of TC, TG, FFA, and PL in CCl_4 rats were shown in [Tables 1 and 2]. CCl_4-induced rats had elevated the levels of TC, TG, FFA, and PL in the plasma and liver as compared

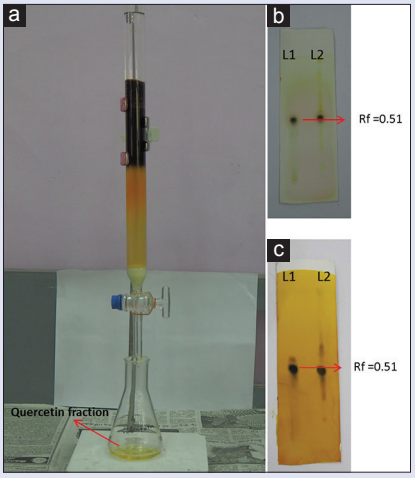

Figure 1: Isolation of quercetin from *Psidium guajava* leaf ethanol extract by column chromatography (a) and identification of quercetin (Rf = 0.51) by thin layer chromatography applied with iodine (b) and 5% $FeCl_3$ reagent (c) L1 = Quercetin standard; L2 = Isolated fraction of *Psidium guajava* leaf ethanol extract

to control. The administration of *P. guajava*, its isolated fraction and silymarin mitigated the CCl_4-induced detrimental effects and reduced the TC, TG, FFA, and PL in infected rats.

Table 3 shows the plasma levels of lipoprotein cholesterols in control and experimental rats. A significant ($P < 0.05$) elevation of plasma low-density lipoprotein cholesterol (LDL-C), VLDL-C, and reduction in HDL-C were observed in CCl_4-induced rats when compared with control rats. The ethanolic extract of *P. guajava*, its isolated fraction and silymarin administered rats, showed the decreased levels of LDL-C, VLDL-C, and increased the level of HDL-C. The results of the present study expressed that the flavonoid-rich fraction (quercetin) was more effective on lipid profile levels in hepatotoxic rats.

DISCUSSION

The presence of flavonoids has been accounted from several plant species such as *Lycium barbarum*,[20] *Passiflora plamer*,[21] *Cassia angustifolia*,[22] and *Jatropa curcas* L.[23] Hidetoshi and Gen-ichi,[24] isolated four compounds from *P. guajava* leaves. Two new flavonoid glycosides, morin-3-O-α-L-lyxopyranoside and morin-3-O-a-L-arabopyranoside, and two known flavonoids, guaijavarin, and quercetin were identified.[25] In accordance with the earlier reports, quercetin is identified in ethanol fraction of *P. guajava*, which is confirmed using standard quercetin.

A high amount of blood cholesterols is the contributory factors of atherosclerosis and many lipid-related complaints including obesity, kidney failure, heart attacks, and stroke. It has been shown that lipid associated disorders are not only attributed to the total serum cholesterol, but also to its distribution among different lipoproteins.[26] In the present study, the elevation in plasma and liver TC levels indicates high rate of cholesterol synthesis, and it was observed in CCl_4-treated rats. Similarly, earlier reports stated that elevation in cholesterol levels was observed in hepatoma 27 cells[27] and N-nitrosodiethylamine-induced hepatocarcinoma.[28]

In the present study, the increased TC level in plasma of CCl_4 treated rats may be due to the decreased uptake of cholesterol from blood. The blood supply to hepatomas was also decreased, and hence 80% decrease in uptake of blood born substances occurred in hepatoma conditions.[29]

Table 1: Effect of *Psidium guajava* leaf extract and isolated quercetin fraction on plasma lipid profile in hepatotoxic rate

Parameters (mg/dL)	Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII
TC	76.41±6.52^{e}	141.07±9.40^{a}	76.37±5.01^{e}	103.68±8.78^{b}	89.42±6.67^{c}	79.87±7.47^{d}	76.74±5.03^{e}	76.96±0.02^{e}
TG	55.86±5.31^{e}	126.81±9.12^{a}	54.70±3.26^{e}	106.47±5.69^{b}	86.47±5.69^{c}	58.26±6.03^{d}	56.78±4.49^{e}	57.92±6.02^{d}
FFA	58.18±4.74^{e}	107.49±8.04^{a}	57.61±4.32^{e}	98.99±3.06^{b}	77.85±4.04^{c}	60.85±3.60^{d}	59.67±2.03^{d}	60.32±6.06^{d}
PL	116.33±7.71^{e}	165.78±12.41^{a}	115.89±8.42^{e}	153.53±10.54^{b}	140.23±3.42^{c}	124.67±8.29^{d}	119.32±4.42^{d}	121.33±8.63^{d}

Values are means±SD for six rats in each group. Means followed by the same letter are not significantly different ($P \leq 0.05$) as determined by DMRT. SD: Standard deviation; FFA: Free fatty acids; TC: Total cholesterol; TG: Triglycerides; PL: Phospholipids; DMRT: Duncan's Multiple Range Test

Table 2: Effect of *Psidium guajava* leaf extract and isolated fraction on liver lipid profile in hepototoxic rats

Parameters (mg/dL)	Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII
TC	3.40±0.25^{c}	5.87±0.53^{a}	3.22±0.30^{c}	5.12±0.05^{a}	4.37±0.04^{b}	3.71±0.3^{c}	3.59±0.07^{c}	3.74±0.27^{c}
TG	3.62±0.34^{e}	7.08±0.56^{a}	3.37±0.24^{e}	6.23±0.60^{b}	5.37±0.36^{c}	4.01±0.28^{d}	3.78±0.21^{e}	3.98±0.33^{d}
FFA	7.46±0.54^{d}	10.23±0.86^{a}	7.28±0.48^{d}	9.15±0.56^{a}	8.5±0.45^{b}	7.96±0.51^{c}	7.64±0.22^{c}	7.89±0.51^{c}
PL	18.29±1.52^{f}	28.37±2.47^{a}	18.15±1.07^{f}	26.32±2.12^{b}	24.13±1.98^{c}	20.15±2.02^{d}	19.04±2.23^{e}	20.81±1.24^{d}

Values are means±SD for six rats in each group. Means followed by the same letter are not significantly different ($P \leq 0.05$) as determined by DMRT. FFA: Free fatty acids; TC: Total cholesterol; TG: Triglycerides; PL: Phospholipids; DMRT: Duncan's Multiple Range Test

Table 3: Effect of *Psidium guajava* leaf extract and isolated fraction on plasma lipoprotein cholesterol in hepoto damaged rats

Parameters (mg/dL)	Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII
HDL-C	46.02±3.58^{a}	27.45±1.33^{d}	46.79±2.85^{a}	33.68±1.78^{c}	39.42±1.67^{b}	44.18±3.30^{a}	45.64±1.03^{a}	44.96±0.02^{a}
VLDL-C	11.17±0.57^{d}	25.36±1.28^{a}	10.94±0.65^{d}	21.94±0.65^{b}	17.29±0.04^{c}	11.65±0.61^{d}	11.35±0.07^{d}	11.58±0.27^{d}
LDL-C	19.21±2.17^{e}	88.26±5.90^{a}	18.64±1.43^{f}	48.70±2.65^{b}	32.70±2.36^{c}	24.03±3.76^{d}	19.73±1.21^{e}	20.41±2.33^{e}

Values are means±SD for six rats in each group. Means followed by the same letter are not significantly different ($P \leq 0.05$) as determined by DMRT. HDL-C: High density lipoprotein cholesterol, VLDL-C: Very low density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; SD: Standard deviation; DMRT: Duncan's Multiple Range Test

The administration of ethanolic leaf extract of *P. guajava*, its isolated fraction and silymarin decreased the cholesterol substances in plasma and liver which might be due to strong hypocholesteromic activity of *P. guajava* and its isolated fraction. Lowering the elevated level of cholesterol was not only retarding progression but can even cause faster deterioration of the toxicity of CCl_4.

The liver injury forms the accretion of abnormal quantities of fats, mainly TG in parenchymal cells. The accumulation of TG can be thought of resulting from an imbalance between the speed of synthesis and the speed of release of TG through the parenchymal cells into the systemic circulation.[30] The elevated plasma TG levels observed might have been partially due to lipoprotein lipase. Modest hypertriglyceridemia occurs in association with alcohol, virus, and drug-induced hepatitis.[31] The mechanism of this process might be involve reduction of lipolytic enzymes, namely, hepatic triglyceride lipase and lipoprotein lipase.[32] The reduction of these enzymes leads to the decreased removal of TG from plasma and the accumulation of TG in tissues.

In the study, the hypertriglyceridemia observed in CCl_4-induced toxicity might be due to the clearance defects associated with deficient lipoprotein lipase activity. Hypertriglyceridemia, which is often observed in different degrees in tumor-bearing animals in blend with increased VLDL-C and decreased HDL-C are defective catabolism rather than elevated hepatic synthesis of triglycerols rich lipoproteins.[33] The present study showed that the decreased concentration of TG in rats after the treatment of ethanolic leaf extract of *P. guajava* and its isolated fraction. The hypolipidemic effect of *P. guajava* leaf extract can be attributed to the presence of flavanoids, which have the ability to reduce serum TG level.[34] This might be due to the optimal activity of serum lipoprotein lipase and the antioxidant effect of the plant extract.

The fatty acids are the principle components present in most lipids of biological importance. The increased FFA accumulation is may be due to the breakdown of lipids. The present study also showed that the higher levels of FFA in liver and plasma of CCl_4-treated rats than controls. The increase of FFA levels can accelerate the synthesis of other major lipids and activate NADPH- or NADH-dependent microsomal peroxidation.[35] On the other hand, the decrease of FFA content in *P. guajava* extract administered rats, can reduce the synthesis of triacylglycerol, cholesterol, PL, and which leads to decrease the lipid peroxidation.

The PL is vital components of biomembranes for their composition which greatly affects the properties and functions of the membranes, including signal transduction.[36] The results of the present study showed that CCl_4-induced rats had significantly increased levels of PL, as shown in earlier findings.[37] Hence, the alteration in the membrane composition might be the reason for the toxic effect induced by CCl_4. The decreased FFA and PL levels following *P. guajava* administration in infected rats might prevent the toxic complication produced by the increased levels of PL.

The reduced level of LDL-C concentration in the plasma might occur due to the defect in LDL-C receptor in the liver, either through failure in its expression or function. HDL-C might be protective by reversing cholesterol transport, inhibiting the oxidation of LDL-C, and by neutralizing the atherogenic effects of oxidized LDL-C. HDL-C, which helps to scavenge cholesterol from extrahepatic tissues in the presence of lecithin cholesterol acyltransferase (LCAT) and brings it to the liver.[38]

CCl_4-treated rats showed the elevated levels of LDL-C and VLDL-C and while the reduced level of HDL-C. The lower amount of HDL-C was due to the reduced activity of LCAT contributed to the increased concentration of cholesterol. A greater increase of LDL-C and VLDL-C causes the reduction of HDL-C, and there was a reciprocal relationship between the concentration of VLDL-C and HDL-C. An elevated activity of plasma lipoprotein lipase increased HDL-C production and reduced the LDL-C constituents.[39] In accordance with the earlier reports, the increased concentration of HDL cholesterol was observed in ethanolic leaf extract of *P. guajava* and its isolated fraction treated rats which might be due to the increased activities of lipoprotein lipase and LCAT.

In the present study, the most active drug seems to be the ethanolic leaf extract of *P. guajava* for HDL cholesterol and followed by the isolated quercetin fraction was also effective in infected rats.

CONCLUSION

The present findings demonstrated that the ethanolic extract of *P. guajava* leaves and its isolated quercetin fraction have a hypolipidemic activity against CCl_4-induced hepatotoxic rats when compared with the standard drug silymarin. These results suggested that *P. guajava* leaves extract and its isolated quercetin fraction can be an alternative medicine for preventing hyperlipidemic and coronary heart disease and fatty liver.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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