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ORIGINAL ARTICLE

Preclinical Study on Effects of *Acalypha indica* on Streptozotocin-induced Liver Damage in Diabetic Rats

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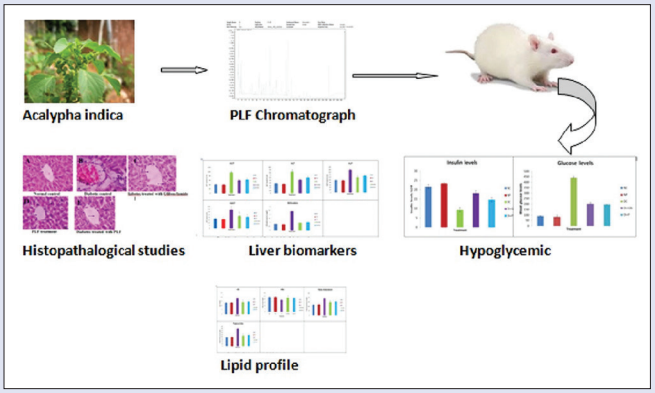
ABSTRACT

Background: Diabetes is one of the most common non-communicable global diseases. It is the fourth leading cause of death, thus posing a serious threat to human beings. The conventional drugs developed along the principles of Western medicine are often limited in efficacy in diabetes management. However, significant evidences suggest that polyphenol-rich diet has the ability to protect diabetes complications. **Objective:** In this study we investigated the quantifying and profiling of phenols in *Acalypha indica* polyphenol-rich fraction (PLF) and their therapeutic potential on hepatic tissue damage in streptozotocin (STZ) induced diabetic rats. **Materials and Methods:** In this study,PLF was subjected the gas chromatography–mass spectrometry and High Resolution Liquid Chromatograph Mass Spectrometer HR-LC-MS and evaluate the liver biomarkers includes aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin content, lipid profiles like low-density lipoprotein (LDL), total cholesterol (TC), triglycerides (TGs), and high-density lipoprotein (HDL), insulin and body weights in diabetic, PLF, and glibenclamide-treated diabetic and normal rats. **Results:** The result showed that PLF was significantly decreased the blood glucose levels, liver biomarkers such as AST, ALT, ALP, bilirubin content, lipid profiles like LDL, TC, and TGs and decreased the tissue damage in diabetic rats. Subsequently, insulin, body weight, and HDL levels were increased in diabetic rats. Subsequently, insulin, body weight, and HDL levels were increased. **Conclusion:** We concluded that Ai (Acalypha indica) leaves have a rich number of polyphenolic compounds and those were may be protected from STZ-induced toxicity in liver of diabetic rats. Further research is necessary for this area to isolate bioactive polyphenolic compounds from Ai leaves and to be validated against STZ-intoxicated liver damage with assessing mechanism of action.

Key words: *Acalypha indica*, diabetes, lipid profile, liver markers, polyphenol-rich fraction

SUMMARY

- Polyphenol-rich fraction (PLF) of Ai reduced the blood glucose and body weights and increased the insulin levels in diabetic condition. PLF of Ai significantly affects the lipid profile and liver biomarkers under diabetic condition. Liver structure was significantly rehabilitated with supplementation of PLF of Ai in diabetic rats.



Abbreviations used: GC-MS: Gas chromatography–mass spectrometry, PLF: Polyphenol-rich fraction, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder which was associated with hyperglycemia results in a lack of insulin or insulin resistance.[1,2] DM is the most prevalent disease affecting 25% of the population worldwide, and it is predicted to be rise to 552 million by 2030.[3] Sustained hyperglycemic condition could ensure diabetic complications besides the dysfunction or damage of insulin-dependent organs due to the generation of high amount of free radicals.[4,5]

Etiology of liver diseases is important in the incidence of DM. As a consequence, liver is a large and complex insulin-dependent organ which plays a major role in glucose homeostasis and involved in carbohydrates and lipid metabolism. Lack of insulin, liver could ensure the glycogenolysis which oftenhypertriglyceridemia and hypercholesterolemia.[6,7] Chronic mild elevations of transaminases are frequently found in diabetes due to oxidative injury of hepatocytes by free radicals.[8] Consequently, this could lead to develop the micro and macrovascular diseases which are the major causes of morbidity and death.[9,10] Therefore, it is an immediate search for more effective and safer antidiabetic drugs. Currently, for diabetes management, a number of antidiabetic drugs including biguanide, thiazolidinedione, and sulfonylurea were used. However, the usage of these agents was restricted due to several considerable side effects.[11] Many herbal medicinal plants and their bioactive constituents have been recommended to

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treat diabetes and its complications from hundreds of years throughout the World.[12] Plants mostly contain carotenoids, flavonoids, phenols, tannins, terpenoids, alkaloids, and glycosides which have antidiabetic properties.[13,14] *Acalypha indica* (Ai) is extensively grown in tropical India, Sri Lanka, South Africa, and Pakistan. It has antivenom, wound healing, antioxidant, anti-inflammatory,[15] diuretic, antibacterial,[16] and antidiabetic properties. Ai has rich in polyphenolic compounds (phenols, tannins, and flavonoids) and other phytochemicals. However, to the best of our knowledge, hepatoprotective activity under diabetic condition by polyphenol-rich fraction (PLF) of Ai leaves remains to be ascertained. In order to obtain more knowledge about Ai, this study was made to attempt an investigation on therapeutic potentiality of PLF of leaves against streptozotocin (STZ)-induced liver damage in rats.

MATERIALS AND METHODS

Chemicals

Polyvinylpolypyrrolidone (PVPP) and STZ were purchased from Sigma-Aldrich, and Ultra-sensitive ELISA kit for rat insulin purchased from Linco Research, Inc., St. Charles, MO, USA. liver biomarkers, bilirubin test kits were purchased from Reckon Diagnostics, Ltd., Vadodara, India. All other chemicals used in the study were of analytical grade and were obtained from standard commercial suppliers.

Plant material

Leaves of Ai were collected from Raghavarajapuram, Kodur, Kadapa, Andhra Pradesh, India. The identity of the plant (Ai*)* was confirmed by a taxonomist of the Department of Botany, Sri Venkateswara University, Tirupati, India, and deposited a voucher specimen (Voucher No. SVU-BOT-926) in the same department.

Preparation of polyphenol-rich fraction

PLF was prepared according to the method.[17] Of briefly, dried leaf powder was macerated overnight in dichloromethane and then filtered with Whatman No. 1 filter paper. The filtrate was separated to get the defatted residue. Further, this residue was macerated in methanol/water (70:30 v/v) for a day and filtered. The filtrate was concentrated in a rotary evaporator until complete evaporation of methanol from the mixture. The obtained water extract was adjusted to pH 4 with the help of 1N HCl. To 100 ml of water extract, 5 g of PVPP was added as an adsorbent. The PVPP adsorbed "OH" group contained moieties that were reside in residue of filtration. This PVPP-OH group mixture was mixed with acetone/water (70:30 v/v) and stirred for a while, and then again, filtration was done. Finally, filtrate (acetone/water) was dried where acetone was evaporated and polyphenols in water. The complete dry form of polyphenols has been stored in the refrigerator for future use.

Quantitative estimation of phenols

The quantitative estimation of phenols present in the separated fraction was assessed using Folin–Ciocalteu method.[18] Briefly, the reaction mixture was made with 1 ml of fraction (0.5 mg)/gallic acid (different concentrations include 5, 10, 15, 20, and 25 µg/ml), 5 ml of double-distilled water, and 1.5 ml of the Folin–Ciocalteu reagent. The total mixture was kept at room temperature for 5 min. To this mixture, 2 ml of Na_2CO_3 solution was added and the final volume was made up to 15 ml with distilled water and now incubated for another 30 min, and reaction was read at 765 nm in a spectrophotometer. The total phenolic content of fraction was calculated from calibration curve of gallic acid. The phenolic content of fraction was expressed in gallic acid equivalent/gram weight of fraction.

OH group phytochemical (polyphenol) identification

The obtained polyphenol mixture from PVPP procedure has been subjected to HR-LC/Q-TOF/MS to explore individuals from concoction. We followed the same method for this analysis which is available in our previous publication.[19] All the obtained phytochemical compounds have been drawn in Marvin sketch, a free tool for chemical structure calculations.

Animals

Male Wistar rats (200–220 g) were purchased from the Indian Institute of Science, Bengaluru, India. The study was carried out according to the principles guided for the care and use of experimental animals as per CPCSEA. The animals received a standard pellet diet and water *ad libitum* and were maintained under laboratory environmental conditions (23°C ± 2°C, 40%–60% relative humidity and 12 h of light–dark cycle).

Induction of diabetes

One-week acclimatized healthy animals were fasted overnight, and diabetes was induced by a single intraperitoneal injection of freshly prepared STZ (50 mg/kg b.w) in 0.1 M cold citrate buffer (pH 4.5). The animals were considered as diabetic when their blood glucose levels reached above 250 mg/dL on the 3rd day after STZ injection. The dosage studies were conducted on polyphenol fraction according to Ravi *et al*.[19] and selected effective dose of 100 mg/kg b.w. for the treatment.

Grouping of animals

The rats were divided into five groups of six rats each, and the oral treatment was given every day for 1 month.

Group I, normal control (NC): Rats received 0.9% saline and fed with normal diet.

Group II, diabetic control (DC): STZ (STZ 50 mg/kg b.w.) was given intraperitoneally for the induction of diabetes.

Group III, polyphenolic fraction treatment (Pt): Rats received polyphenolic fraction (100 mg/kg b.w.) orally for a period of month.

Group IV, diabetics + polyphenolic fraction treatment (Di + Pt): Diabetic rats received polyphenolic fraction, as described in Group III, for a month treatment.

Group V, diabetics + glibenclamide treatment (Di + Glbt): Diabetic rats received glibenclamide (20 mg/kg b.w.) for 1 month treatment.

Collection of blood and analysis

After completion of treatment period, blood was collected in EDTA coated vials from overnight-fasted animals by retro-orbital sinus puncture under mild ether anesthesia. Plasma was obtained by centrifugation at 3000 rpm for 10 min at 4°C and stored at −20°C until estimation of liver biomarkers and lipid profile.

Body weight measurement and estimation of blood glucose levels

Blood glucose was measured using a one-touch glucometer (Accu-Chek). After 24 h of the last dose, blood glucose levels were measured from overnight-fasted rats in each group. Body weights of all the animals were recorded prior to the treatment and sacrifice.

Estimation of insulin levels in plasma

Insulin levels were analyzed in all groups before and after the treatment. Insulin was measured by ELISA assay (Linco, Millipore).

Determination of liver biomarkers in plasma

Estimation of alkaline phosphatase

Plasma ALP activity was measured by Reckon Diagnostics kit which was followed by Bassey *et al.*, method[20] that is modified by Wright *et al.*[21] with the help of Reckon Diagnostics kit. Briefly, 10 µl of plasma was mixed with 500 µl of the reagent. Initial to 3 min, absorbance was read at 405 nm. The mean absorbance per every minute was considered and the final values were expressed in U/L.

Estimation of alanine transaminase (ALT) activity in plasma

Plasma ALT activity was measured by Reckon Diagnostics kit which was followed by IFCC method[22] 50 µl of the sample was added to1 ml of working reagent and incubated at 37°C for 60 s. The absorbance was read at 340 nm continuously for 2 min at an interval of 30 s. The values were expressed in U/L.

Estimation of aspartate transaminase (AST) activity in plasma

Plasma AST activity was measured by Reckon Diagnostics kit which was followed by IFCC method[22] using Reckon Diagnostics kit. Briefly, 0.05 µl of sample was added to 1 ml of working reagent and incubated at 37°C for 60 s. The absorbance was read at 340 nm for 2 min with an interval of 30s. The values were expressed in U/L.

Estimation of γ-glutamyltransferase activity in plasma

Plasma γ-glutamyltransferase (GGT) activity was measured by Reckon Diagnostics kit which was followed by Szasz method[23] using Reckon Diagnostics kit. Briefly, γ-glutamyl-p-nitroanilide in ammediol-HCl buffer at pH 8.2 was used as a substrate and was added to 0.1 ml of plasma. The absorbance was read at 405 nm in UV/visible spectrophotometer.

Estimation of bilirubin levels in plasma

Plasma bilirubin levels were measured by BioVision assay kit which was followed by Mauro *et al.*,[24] using BioVision assay kit. Briefly, 50 µl of sample was added to sodium nitrite and sulfanilic acid solutions. Pink-colored azo compound was read at 546 nm in UV/visible spectrophotometer.

Determination of lipid profile in plasma

Triglyceride (TG) and total cholesterol (TC) levels were measured using commercially available kits (Merck India Ltd.), whereas high-density lipoproteins (HDLs) levels were estimated enzymatically by colorimetric kits (Merck India Ltd.) and low-density lipoproteins (LDLs) were calculated as per the method.[25]

Histopathology

The liver tissues were isolated from sacrificed animal groups followed by immediate fixation in 10% formalin for 24 h. The tissues were further processed with washing and dehydrated with the help of an increased concentration of alcohol. The dehydrated tissues were embedded in paraffin wax and then cut into sections about 5 µ thick using microtome. All the sections were deparaffinized in xylene and hydrated with reverse process of alcohol treatment on glass slides. Initial staining with hematoxylin and counterstain with eosin were done for tissues fixed on slides.

Statistical analysis

Statistical evaluation of the data was done by one-way ANOVA, followed by Dunnett's multiple comparison test. The results were expressed as mean ± SD using ($P < 0.01$) IBM-SPSS version 20 (IBM Corp, Armonk, New York, USA) and Microsoft Excel version 2008 (Albuquerque, New Mexico, United States).

RESULTS

Quantity of polyphenols and chemical composition of polyphenol-rich fraction of *Acalypha indica* leaves

Quantitative estimation of phenols in the fraction revealed that it has 368 mg/g of gallic acid equivalent. The phytochemical profile analysis of PRF of Ai using HR-LC-MS revealed that the OH group-contained

Table 1: OH group-contained phytochemicals of *Acalypha indica* of polyphenol-rich fraction separated using polyvinylpolypyrrolidone and profiling with the help of high resolution liquid chromatograph mass spectrometer

S. No	Name of the compound	Compound structure
01	1,4 Dideoxy 1,4 Imino D Arabintol	
02	2-Hydroxy-3-(4-methoxyethylphenoxy)-propanoic acid	
03	2-methylglutaconic acid	
04	2-Naphthaleneacetic acid, 6-hydroxy	
05	3,5-Pyridinedicarboxylic acid,2-(hydroxymethyl)-6-methyl-4-(3-nitrophenyl)-, 5-(2-hydroxyethyl) est	
06	3-Methyl-tetradecanedioic	
07	4,7-Dioxo-octanoic acid	
08	4-Chloro-N1-methyl-N1-(4-carboxy-2 hydroxy 2methylbutyl)m-benzenedisulfonamide	
09	4-Hydroxy-L-threonine	
10	4-Methyl-decanoic acid	
11	5-(4-Hydroxy-3-methoxyphenyl)-5-phenylhydantoin	
12	8R-hydroxy-nonanoic acid	
13	Ala His Ala	
14	Arg Pro	
15	Asn Met Asp	
16	Beta-nonylenic acid	
17	Choline	
18	D-Pantetheine 4'-phosphate	
19	L-2-Aminoadipic acid	
20	Lactone of PGF-MUM	
21	N-(2- hydroxyethyl) stearamide	
22	N-Acetyl-b-neuraminic acid	
23	O-Acetylserine	
24	Pro Ile	
25	Tiapride	
26	Trans-aconitate	

26 phenolic compound structures and names are represented in Table 1 and Figure 1. These structures strongly supported the quantity of phenols present in fraction measured from Folin–Ciocalteu method.

Effect of polyphenol-rich fraction of *Acalypha indica* on body weight

The effect of PLF of Ai on body weight in normal and diabetic rats is represented in Figure 2. The body weight of NC rats increased in 1 month of treatment period. However, the body weight of DC rats were significantly decreased when compared with NC rats. PLF did not alter the body weight in normal rats, while treated the diabetic rats with PLF significantly increased the body weight compared to DC rats.

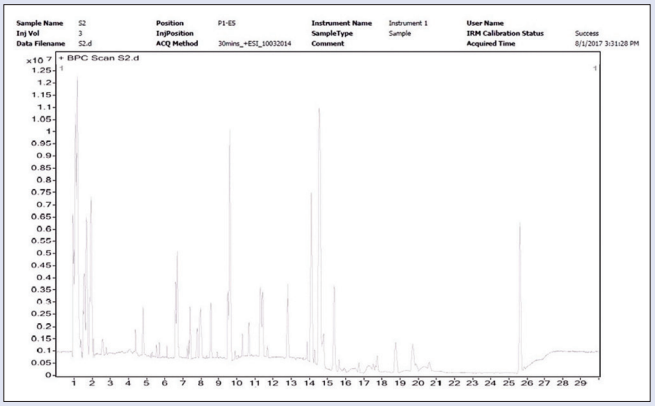

Figure 1: Methanolic extract of PLF of Ai leaves GC-MS chromatograph

Effect of polyphenol-rich fraction of *Acalypha indica* on blood insulin and glucose levels

As shown in Figure 2, the plasma insulin level in diabetic rats was decreased significantly compared with normal rats. After 1-month treatment with PLF of Ai (40 mg/kg), the plasma insulin level of diabetic rats was significantly increased compared with DC rats. After treatment of normal rats with PLF of Ai, there were no significant changes in insulin level compared with normal rats alone.

The hypoglycemic effect of PLF of Ai was examined by measuring the blood glucose levels from 0 to 4 weeks of the treatment period. As shown in Figure 2, the blood glucose levels of the DC group were increased significantly ($P < 0.01$) after injection of STZ compared with NC rats. Administration of PLF significantly decreased the plasma glucose level in diabetic rats compared with DC rats, while in PLF treated normal rats there was no effect on the plasma glucose level.

Effect of polyphenol-rich fraction of *Acalypha indica* on liver biomarkers in plasma (AST, ALT, ALP, GGT, and bilirubin)

Figure 3 shows that the effect of PLF of Ai on plasma AST, ALT, and ALP levels in normal and diabetic rats. Plasma AST, ALT, and ALP levels were significantly increased in rats after STZ injection when compared with the normal rats while in PLF treated diabetic rats the plasma AST, ALT and ALP levels significantly decreased. However, normal rats treated with PLF of Ai there was no effect on the plasma AST, ALT and ALP levels.

The plasma GGT and bilirubin levels in the diabetic group were significantly increased compared with the NC group, as shown

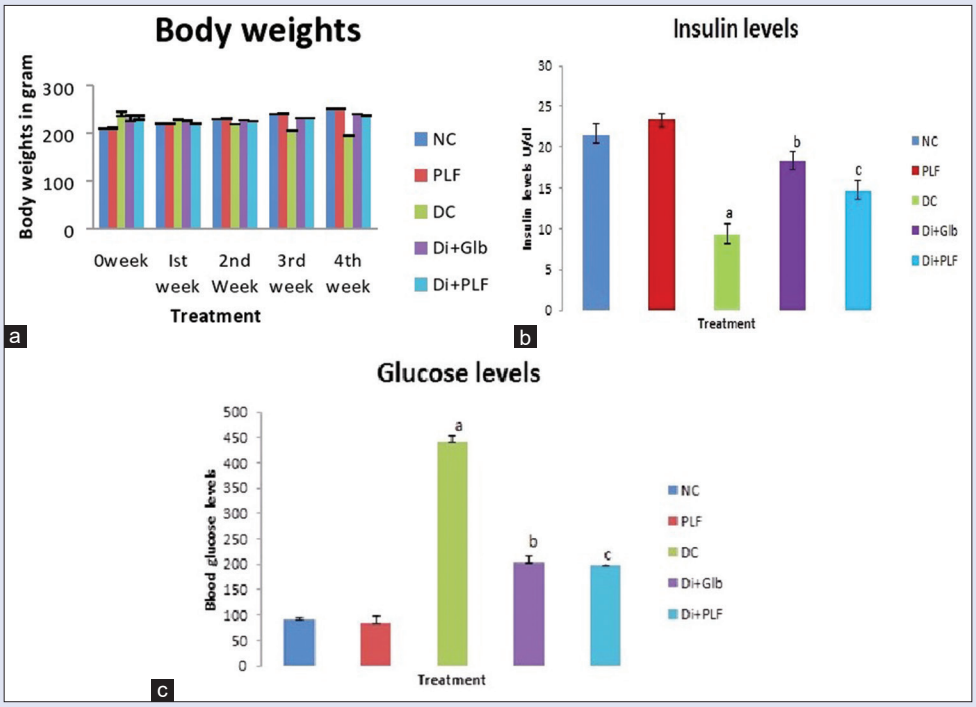

Figure 2: Effect of PLF on body weights (a) insulin (b) and glucose levels (c) in plasma under diabetic condition. The groups which not have the same alphabet letter are significant ($P < 0.01$) to the control and those groups have not alphabet letter are not significant to the control. Values are means ± SD for six rats per group

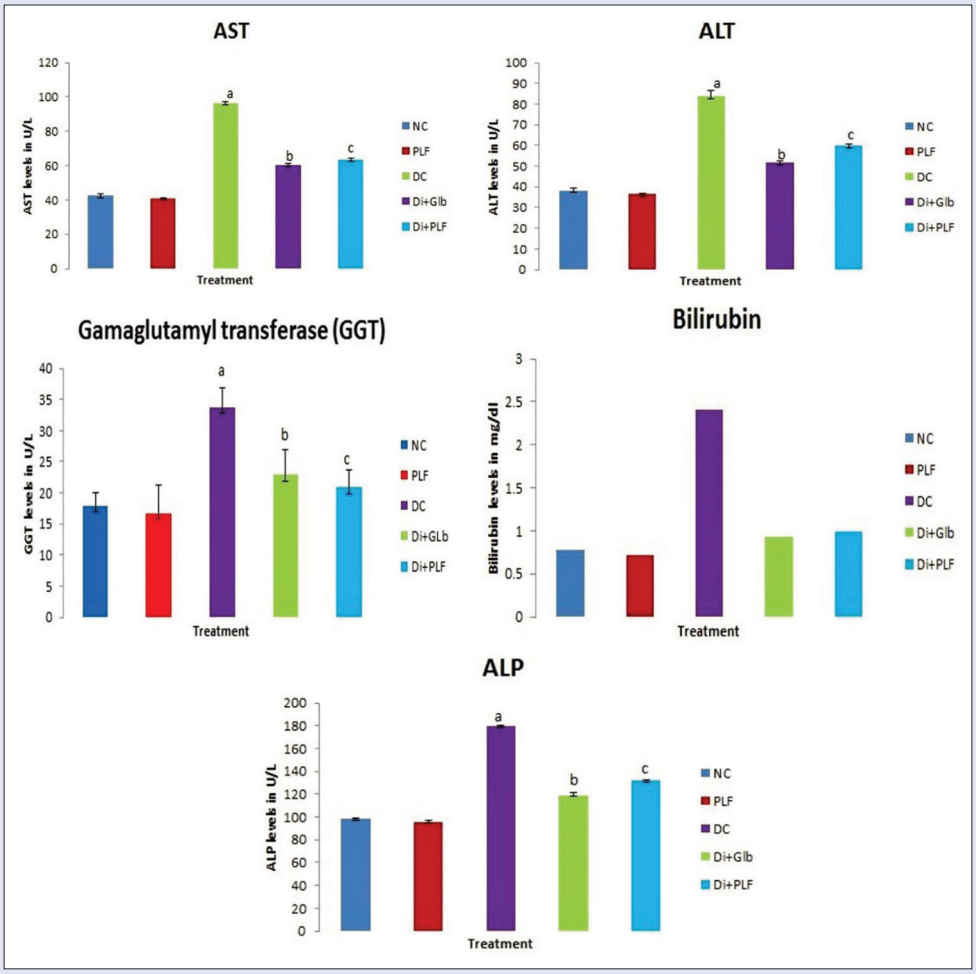

Figure 3: Effect of PLF on AST, ALT, GGT, bilirubin, and ALP levels in plasma under diabetic condition. The groups which not have the same alphabet letter are significant ($P < 0.01$) to the control and those groups have not alphabet letter are not significant to the control. Values are means ± SD for six rats per group

in Figure 3. A significant decrease in GGT and bilirubin levels was observed in the diabetic group when treated with PLF of Ai while normal rats treated with PLF of Ai were not shown any significant change in GGT and bilirubin levels compared to the NC rats.

Effect of polyphenol-rich fraction of *Acalypha indica* on lipid profile in plasma (total cholesterol, triglycerides, HDL, and LDL)

As shown in Figure 4, plasma TC and TG levels were significantly increased after administration of STZ compared with the normal group. Administration of PLF was significantly decreased the plasma TC and TG levels in diabetic rats compared with DC rats, while in normal rats PLF was no effect on the plasma TC and TG levels when compared with the normal group. Plasma LDL levels were increased whereas HDL levels decreased after administration of STZ to the normal rats when compared with the NC group. However, LDL levels decreased whereas HDL levels increased in diabetic rats after treatment with PLF of Ai compared with DC rats.

Histopathology

Examined the liver of the NC rats, the liver tissue shown normal cytoarchitecture without any pathological changes in central vein and hepatocytes. The group of rats which received STZ induces the complication including degenerative changes (severe damage) in liver tissue with an evidence of congestion. The PLF-treated rats have not shown any pathological alterations in the hepatocyte and central vein of the liver. The treatment of diabetic rats with PLF of Ai confined that it has a potential antidiabetic property with an evidence of regeneration of liver tissue in diabetic rats. The standard glibenclamide treated group animals have also protected the liver from STZ intoxication [Figure 5].

DISCUSSION

Polyphenols are commonly found in both edible and nonedible plants have many biological properties such as anti-lipid peroxidation and antioxidant activities. Crude extracts of vegetables, herbs, fruits, cereals, and other sources are having also rich in phenol content. Due to their protective nature from oxidative stress, conditions are increasing interest in pharmacy for treating various radical-associated diseases.[26] In this study, we separated and quantified the phenolic compounds of Ai, which revealed that it has rich in phenolic compounds [Figure 1]. Further, phenolic profile analysis in HR-LC-MS explored a huge number of OH group-contained polyphenols. These phenolic data support that the Ai might act as a strong antioxidant and anti-lipid peroxidation agent.[19]

Polyphenols, bioactive substances, are the reducing agents that can able to diminish the oxidative stress by their radical-scavenging

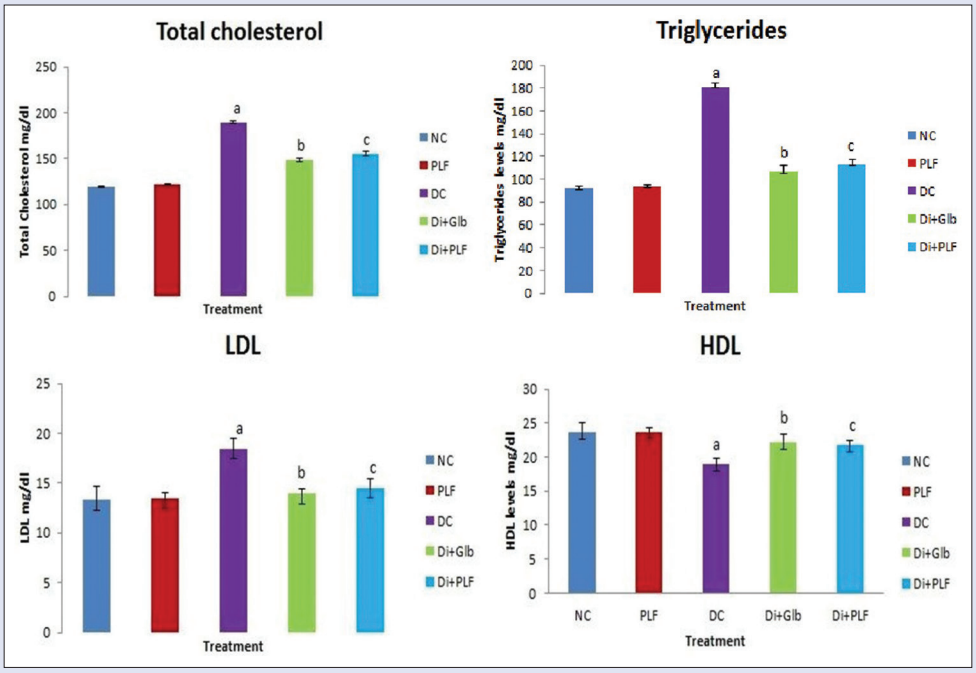

Figure 4: Effect of PLF on LDL, HDL, total cholesterol, and triglyceride levels in plasma under diabetic condition. The groups which not have the same alphabet letter are significant ($P < 0.01$) to the control and those groups have not alphabet letter are not significant to the control. Values are means ± SD for six rats per group

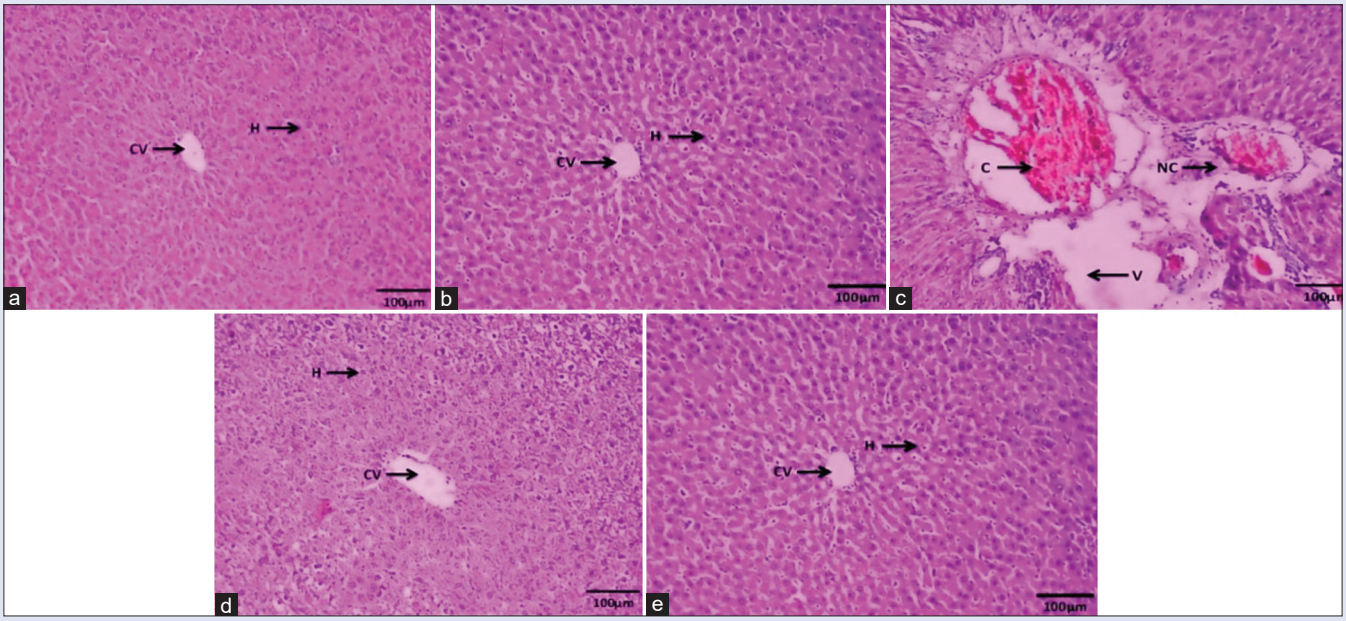

Figure 5: Photomicrograph sections of livers stained with H and E and microscopic magnification (×10). (a) Cytoarchitecture of liver tissue with normal hepatocytes (H) and Central vein (CV). (b) Normal cytoarchitecture maintained by polyphenol treatment. (c) Degenerative changes in central vein having congestion (c), vacuolization and necrotic changes (NC), (d) Regenerative changes in glibenclamide-treated liver tissue (H) and central vein, (e) Regenerative changes in polyphenolic fraction treatment in liver tissue (H) and central vein like normal control

character.[19] The previous experimental and epidemiological evidences have been suggested that dietary polyphenols play a role in ameliorating atherosclerosis and anti-inflammatory activity.[27,28] However, several epidemiological reports have been demonstrated that lack of insulin or insulin resistance under STZ-induced intoxication in experimental animals induced the hyperglycemia and hyperlipidaemia meanwhile it has also effect the liver function.[29-31] In order to that, controlling of glucose levels in plasma was the main concern in diabetes management to restrict the further development of diabetic complications.[30,32] Therefore, the available diabetic agents were shown hypoglycemic effects; meanwhile, the usages of these agents were restricted due to several considerable side effects.[33]

In the present study, Ai leaves of PLF showed 67 different polyphenols, bioactive compounds. Among those, 26 phenolic compounds showed [Table 1] different biological activities. Our reports clearly demonstrated that treatment with Ai leaves of PLF at dose 100 mg/kg showed hypoglycemic, hypolipidemic, and hepatoprotective activity under diabetic condition by decreased the glucose, lipid profiles, and liver biomarkers in plasma.

In the present study, we found the body weight of rats were persistent reduction under STZ intoxication when compared with the NC rats. Diabetes is associated with body weight loss, caused by elevated muscle wasting and decrement of tissue proteins.[34] However, treatment with PLF of Ai attenuated the reduction of body weight in diabetic rats compared with DC rats, perhaps attributable to an increase in insulin secretion and glycemic control. Similar kinds of effect, i.e., body weight gain, were reported previously under diabetic conditions when treated with plants and especially their polyphenol-rich fractions.[35]

The persistent chronic high glucose level in the blood was a sign of diabetes, which was found in the present study in STZ-induced diabetic rats when compared with normal rats.[36] In diabetes management, reduction of the blood glucose level is the primary therapeutic goal.[30] However, treatment with PLF of Ai considerably reduced the blood glucose levels in diabetic rats compared with DC rats conceivably due to potentiating of insulin secretion from existing β-cells in the pancreas or may enhance the conversion of blood glucose to glycogen by the liver.[37] Thus, the PLF of Ai potentially had shown hypoglycemic activity under diabetic condition.

Improvement of insulin secretion and insulin sensitivity of the tissue was the main strategy in diabetes treatment in consequence of insulin levels declined due to malfunction of the pancreas.[38] From the obtained results, plasma insulin levels were significantly decreased in diabetic rats compared with normal rats, while plasma insulin levels of diabetic rats considerably enhanced when treated with PLF of Ai by virtue of its hyperinsulin activity to lift the insulin secretion by stimulation or regeneration of β-cells in the pancreas.[39]

Several earlier reports have demonstrated that diabetes was associated with liver damage, caused by elevation of liver biomarkers such as AST, ALT, GGT, bilirubin, and ALP in plasma.[6] Hyperglycemia and overinsulinization are believed to be metabolic preconditions in liver disease. However, plasma enzyme activities can be used as useful biomarkers for monitoring the cytotoxicity of xenobiotics including STZ.[31] In our study, STZ induces hepatic tissue damage which is one of the typical changes in diabetes as evidenced by elevation of plasma AST, ALT, GGT, bilirubin, and ALP levels in diabetic rats compared with NC rats. Conversely, treatment of the diabetic rats with PLF of Ai caused a reduction in the levels of AST, ALT, GGT, bilirubin, and ALP in plasma compared with the DC rats. In accordance with this report, previous studies have also been confirmed that polyphenols of antioxidant activity protect the liver from oxidative injury initiated by hyperglycemia under diabetic condition.[34,40] Thus, PLF of Ai administration to the diabetic group of rats significantly declined liver biomarkers suggesting its hepatoprotective nature in diabetic condition.

In diabetes, liver dysfunction was associated with hyperlipidaemia hyperglycemia.[41] Therefore, hyperglycemia accelerates the accumulation of free fatty acid conversion into TGs in the liver.[42] As a result, it increased the LDL and decreased the HDL in plasma immensely accelerate the micro- and macro vascular diabetic complications.[43] In our study, similar consequences were observed in diabetic rats which shown increased plasma TC, TG, and LDL levels and decreased HDL levels when treated the diabetic rats with PLF, plasma TC, TGs, and LDL levels significantly decreased and increased HDL levels were found may be due to control the glucose levels in the blood by virtue of its hypoglycemic activity which in turn to regulate the lipid metabolism in the liver.[44]

Further studies are essential to isolate the polyphenols bioactive compounds and evaluate the antidiabetic activity at molecular level in the prevention of diabetes. Thus, our results clearly demonstrated that PLF of Ai could be able to retrieve the lipid profile to normal level under diabetic condition by asset of its hypoglycemic and hypolipidemic activity.

CONCLUSION

The overall outcomes of the current study indicate that PLF of Ai has remarkable hypoglycemic, hypolipidemic, and hepatoprotective activities in STZ-induced diabetic rats. These properties seem to be due to the presence of bioactive compounds. Hence, the fraction can be used as an herbal drug to treat diabetes. Further studies are essential to isolate the polyphenols bioactive compounds and evaluate the antidiabetic activity at molecular level in the prevention of diabetes.

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Conflicts of interest

There are no conflicts of interest.

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