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Research Article

IN VIVO ANTIDIABETIC POTENTIAL OF *CYCLEA PELTATA* IN STREPTOZOTOCIN-INDUCED-DIABETIC RATS

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ABSTRACT

Objective: Diabetes is one of the most common metabolic disorders in worldwide. Diabetes mellitus is a disorder of carbohydrate metabolism in which sugars in the body are not oxidized to produce energy due to lack of the pancreatic hormone, insulin. This study was undertaken to find out the antioxidant and antidiabetic potential of ethanolic root extract of *Cyclea peltata*.

Methods: The ethanolic root extract of *C. peltata* was administered to control and the experimental rats for 30 days. After the experimental period, the animals were sacrificed and the serum, tissue samples were used for the determination of blood glucose level, protein, urea, creatinine, liver marker enzymes, antioxidant enzymes, lipid profile, protein, lipid peroxidation and histopathological examination.

Results: The results of this study supports that the ethanolic root extract of *C. peltata* shows better antioxidant potential through which it exert antidiabetic potential. Histopathology results also support the protective effect of *C. peltata* against streptozotocin induced diabetes.

Conclusion: The results scientifically confirm that the *C. peltata* can be used to treat various disorders caused by free radicals and other chemical substances due to the presence of secondary metabolites that exert antioxidant and antidiabetic action.

Keywords: Antidiabetic, Antioxidants, *Cyclea peltata*, Lipid peroxidation.

INTRODUCTION

Diabetes is a chronic disorder linked with the metabolism of carbohydrate, protein and fat due to absolute or relative deficiency of insulin secretion with or without varying degree of insulin resistance [1]. It also associated with impaired glucose metabolism leads to ketoacidosis, which if untreated, can lead to fatal ketoacidosis [2,3]. It is a major disease characterized by derangement in carbohydrate, fat and protein metabolism [4]. This disease is categorized as metabolic disease and characterized by hyperglycemia that is an important factor in the development and progression of microvascular progressions [5]. Streptozotocin (STZ) treatment results in diabetes due to the destruction of beta-cells of the pancreas that secrete insulin [6].

Insulin therapy is the most common method used for the management of diabetes mellitus, but several drawbacks such as insulin resistance, anorexia nervosa, brain atrophy and fatty liver were reported [7]. Most of the hypoglycemic agents used in allopathic medicines are reported to have side-effects including hematological coma and disturbances in liver and kidney [8]. This has necessitated the exploration and screening of medicinal plants with acclaimed therapeutic efficacies in diabetes mellitus management [9].

Cyclea peltata (Menispermaceae) commonly known as Paatha that is a climbing shrub found throughout South and East India at altitudes of 900 m. The plant *C. peltata* is widely used in the treatment of cough, fever, kidney disorder, urinary disorder, and snake poisoning. Powdered roots of this plant used for the treatment of diabetes, toothache; decoction of the roots and leaves used for treating malaria and asthma. Tuberous roots of the plant are used in the treatment of jaundice, fever, stomach ache and asthma [10].

METHODS

Collection of plant material

The roots of *C. peltata* were procured from the Trichur, Kerala and was then identified by the Botanical Survey of India, Tamil Nadu Agricultural University (TNAU) campus, Coimbatore and authenticated by Dr. G.V.S. Moorthy (Voucher No: BSI/SRC/5/23/09-10/Tech-985).

Preparation of solvent extraction

The plant material was ground to a coarse powder and extracted using 95% ethanol. This ethanolic extract of *C. peltata* was used for the preliminary phytochemical screening and animal studies. About 50 g of powdered plant material was mixed with 250 ml of ethanol in a 500 ml conical flask and was placed in a shaker for 16 hrs. The solution was then extracted using a separating funnel and was concentrated by solvent evaporation using a rotary evaporator. The sample material was stored in an airtight container at 4°C and used for further experimental analysis.

Preparation of animals

Adult female albino rats weighing about 150-180 g were obtained from the animal house of Karpagam University, Coimbatore and were used for the study. Rats were housed in polycarbonate cages in a room with a 12 hrs day-night cycle, at constant temperature of 22°C and humidity of 45-64%. During the experimental study rats were fed on pellets (Gulmohur Rat Feed, Lipton India, Bengaluru) with free access to tap water. The rats received humane care according to the criteria outlined in Principles of Laboratory Animal Care, 1985. The study was approved by Institutional Animal Ethics Committee (IAEC) and the experiments were conducted according to the ethical norms and IAEC guidelines.

Induction of diabetes

Rats were rendered diabetic by a single intraperitonial injection of freshly prepared STZ (45 mg/kg body weight) in 0.1 M citrate buffer (pH 4.5) in the volume of 1 ml/kg body weight using sterile 25G needle. Diabetes was identified in rats by moderate polydipsia and marked polyuria. After 48 hrs of STZ administration, blood glucose levels were estimated in rats following overnight fasting. Rats with a blood glucose level ranging between 200 and 300 mg/dl were considered diabetic and used for the experiments.

Experimental pattern

The animals were divided into five groups of five animals each. Group I served as control animals given normal pelleted diet and 1.0 ml citrate buffer as vehicle, Group II rats served as diabetic rats, Group III rats were induced with diabetes and treated with standard drug glibenclamide (2 mg/kg body weight) through oral intragastric tube, Group IV animals were induced with diabetes and treated with ethanolic root extract of *C. peltata* (400 mg/kg body weight) and Group V control rats were treated with *C. peltata* only at a concentration of 400 mg/kg body weight. The extract was given daily through oral gastric tube for a period of 30 days.

Sacrification of animals

After experimental period, rats were sacrificed by cervical dislocation after giving chloroform in mild dose. Blood was collected, and the serum was separated by centrifugation at 20,000 rpm for 30 minutes. Liver and kidney were immediately dissected out, washed and stored in 0.9% ice-cold saline for various biochemical evaluations and tissues stored in 1% formalin were used for histopathological studies.

Biochemical estimations

In the present study, the antidiabetic activity was evaluated biochemically and histopathologically. The serum was used for the analysis of glucose by O-toluidine method [11], cholesterol, triglycerides (TGs), high-density lipoprotein (HDL) cholesterol was estimated by one step method using diagnostic reagent kit manufactured by Span Diagnostics Ltd., very-low-density lipoprotein (VLDL) was calculated by the formulae: VLDL (mg/dl) = TGs/5, LDL was calculated by the formulae: LDL (mg/dl) = Cholesterol−HDL−VLDL, total protein was estimated by Lowry method [12], urea was estimated by DAM method using diagnostic reagent kit manufactured by Span Diagnostics Ltd., creatinine was estimated by alkaline picrate method using a reagent kit intended for *in vitro* quantitative determination manufactured by Beacon Diagnostics Pvt. Ltd., serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase and alkaline phosphatase (ALP) was estimated by method using diagnostic kits manufactured by Span Diagnostics Ltd.

Tissue homogenate was used to analyze the enzymatic and non-enzymatic antioxidant and the parameters analyzed were superoxide dismutase [13], catalase [14], glutathione peroxidase (GPx) [15], glutathione-s-transferase (GST) [16], GSH [17], vitamin-C [18], basal lipid peroxidation [19], ascorbate induced lipid peroxidation and peroxide-induced lipid peroxidations were estimated according to the method given by Devasagayam and Tarachand [20].

Histopathological studies

The anti-diabetic activity was confirmed through histopathological studies on liver and kidney of rats. For histopathological study, liver and kidney from each animal was removed after dissection and preserved in 10% formalin. Sections of livers stained with hemotoxylin and eosin were observed microscopically for histopathological studies.

Statistical analysis

All the data were expressed as Mean±standard deviation of a number of experiments. Statistical significance was evaluated using one-way analysis of variance (ANOVA) using SPSS version 7.5 (SPSS, Cary, USA) and the individual comparisons were obtained by the Duncan's Multiple Range Test.

RESULTS AND DISCUSSION

Medicinal plants, the potential sources of bioactive agents are gaining adequacy worldwide. The ethnobotanical survey can bring out many different clues for the development of drugs by using medicinal plants to treat human diseases like diabetes. Safe, effective, and inexpensive remedies are gaining popularity equally among the people of both the urban and rural areas, especially in developing countries like India [21].

In Table 1, the elevation in blood glucose is because STZ enters the pancreatic β-cells via a glucose transporter 2 and results in the destruction of β-cells thereby causing an elevation in the glucose level [22]. The present study showed that *C. peltata* when given for 30 days significantly reduced elevated blood glucose level in STZ induced diabetic rats. The glucose level of experimental animals treated with *C. peltata* was brought back to near normal through the regulation of glucose uptake from the intestinal lumen, through the inhibition of carbohydrate digestion or absorption [23]. Thus increased utilization of glucose by the body may be responsible for antihyperglycemic activity of the extract.

Rats receiving extract of *C. peltata* showed the normalization of blood glucose level which shows that the extract prevent decreased insulin secretion by protecting cells against destruction caused by STZ or the extract may act by competing with STZ for glucose associated receptors on β-cell membranes. The acute hypoglycemic action of glibenclamide is the stimulation of the insulin release and the inhibition of glucagon secretion [24].

Table 2 shows the levels of TG, cholesterol, LDL and VLDL were increased along with a decrease in the HDL level on STZ administration. Insulin deficiency results in the failure that in turn activate the enzyme, lipoprotein lipases that hydrolyze TG thereby causing triglyceridemia [25]. Diabetes is also associated with hypercholesterolemia due to abnormal metabolism of lipids. The plasma lipid and lipoprotein profile is also elevated that pulls the diabetes to high risk of coronary heart disease, in diabetes mellitus [26]. The reversal of the abnormal lipid profile on treatment with the ethanolic root extract and the standard drug implies probable activation of the enzyme lipoprotein lipase by the extract and the gibenclamide. The *C. peltata* showed anti-hyperlipidemic effect that could play a protective role against the development of atherosclerosis and cardiovascular complications in diabetes mellitus [27].

The activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), ALP and serum markers of experimental animals were shown in Table 3. Activities of these enzymes were found to be significantly increased in diabetes-induced animals than in control animals. On the treatment with plant extract, the levels were significantly decreased in a dose-dependent manner showing a favorable change in groups treated with 400 mg/kg. Treatment with ethanolic extract alone did not show any significant difference when compared to normal control group. The elevated serum liver marker enzymes AST and ALT in diabetic induced rats can be attributed to the damage is associated in the histostructural integrity of the liver cells. Necrosis or membrane damage is associated with the release of these enzymes into the circulation [28]. The ethanolic extract of *C. peltata* brought the levels of AST and ALT to normal. This suggests the possibility that *C. peltata* is able to normalize the hepatocytes, so as to cause accelerated regeneration of parenchyma cells, thus providing fortification against membrane fragility and decreases the leakage of these marker enzymes [29].

The levels of urea and creatinine were significantly increased in Group II diabetic induced animals. Significant elevations in serum urea and creatinine levels indicate impaired renal function of diabetic animals. Kidney maintains optimum chemical composition of body fluid by acidification of urine and removal of metabolic wastes such as urea, uric acid, creatinine, and ions. During renal diseases, the concentration of these metabolites is increased in blood [30]. Ethanolic extract of *C. peltata* lowered the serum urea and creatinine levels by enhancing the renal functions that are generally impaired in diabetic rats. The extract can increase the level of protein in plasma; it shows that there is a pathological reverse reaction after secondary complications of diabetes mellitus.

Reduced level of non-enzymatic antioxidants observed in liver and kidneys in STZ induced diabetic rats when compared to control rats (Table 4) could be due to increased oxidative stress. The decreased level of ascorbic acid in diabetic rats may be due to either increased

Table 1: Concentration of blood glucose in mg/dl at various stages of study

Particulars blood glucose (mg/dl)	Control (Group I)	Diabetic control (Group II)	Diabetic+glibenclamide treated (Group III)	Diabetic+*C. peltata* (Group IV)	*C. peltata* alone treated (Group V)
0th day	109.5±0.178^{aNS}	295.2±0.268^{b***}	302.43±0.273^{c***}	291.5±0.322^{d***}	104.36±0.186^{eNS}
15th day	108.5±0.268^{aNS}	395.23±0.136^{b***}	246.9±0.268^{c***}	265.36±0.39^{d***}	105.2.6±0.87^{eNS}
30th day	107.5±0.314^{aNS}	494.63±0.508^{b***}	114.4±0.409^{c***}	127.13±0.287^{d***}	108±0.178^{eNS}

Values are expressed as mean±standard deviation, values are taken as a mean of five individual experiments, a: 0th day compared with 15th day, b: 15th day compared with 30th day, c: 0th day compared with 30th day, ***Significance at p=0.01, **Significance at p=0.05, NS: Not significant, *C. peltata: Cyclea peltata*

Table 2: Changes in levels of lipid and lipoprotein profiles in serum of experimental animals

Particulars (mg/dl)	Control (Group I)	Diabetic control (Group II)	Diabetic+glibenclamide treated (Group III)	Diabetic+*C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
Cholesterol	111.62±0.312^{a}	211.65±0.296^{b}	117.77±0.183^{c}	114.65±0.280^{d}	111.52±0.280^{a}
TGs	94.5±0.389^{a}	190.3±0.544^{b}	89.6±0.322^{c}	86.72±0.271^{d}	91.67±0.286^{e}
HDL	23.10±0.423^{a}	10.48±0.405^{b}	24.36±0.361^{c}	22.6±0.409^{d}	22.52±0.448^{a}
VLDL	19.16±0.434^{a}	37.87±0.132^{b}	17.71±0.302^{cd}	17.37±0.398^{d}	18.33±0.356^{e}
LDL	69.60±0.318^{a}	150.73±0.225^{b}	74.6±0.536^{c}	74.83±0.186^{cd}	69.53±0.450^{a}

Values are expressed as mean±SD. Values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-e) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, TGs: Triglycerides, HDL: High-density lipoprotein, VLDL: Very-low-density lipoprotein, LDL: Low-density lipoprotein

Table 3: Changes in levels of urea, creatinine, SGOT, SGPT and total protein in serum of experimental animals

Particulars	Control (Group I)	Diabetic control (Group II)	Diabetic+glibenclamide treated (Group III)	Diabetic+*C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
Urea (mg/dl)	22.23±0.255^{a}	40.44±0.322^{b}	24.41±0.22^{c}	25.2±0.409^{d}	21.13±0.441^{e}
Creatinine(mg/dl)	0.76±0.02^{a}	2.51±0.027^{b}	0.71±0.027^{c}	0.64±0.049^{d}	0.78±0.0017^{a}
SGOT (IU/L)	118.73±0.225^{a}	275.1±0.409^{b}	205.66±0.314^{c}	199.63±0.492^{d}	117.66±0.372^{a}
SGPT (IU/L)	84.66±0.314^{a}	181.63±0.314^{b}	81.76±0.287^{c}	86.62±0.315^{d}	85.52±0.384^{a}
ALP (IU/L)	258.69±0.292^{a}	379.57±0.404^{b}	298±0.089^{c}	295.2±0.389^{d}	265.26±0.492^{e}
Protein (g/dl)	6.97±0.328^{a}	3.16±0.314^{b}	6.80±0.013^{a}	5.81±0.421^{c}	7.48±0.326^{a}

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-e) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase

Table 4: Levels of non-enzymatic antioxidants in liver and kidney of experimental animals

Particulars	Control (Group I)	Diabetic control (Group II)	Diabetic+glibenclamide treated (Group III)	Diabetic+*C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
Vitamin C (mg/g of protein)					
Liver	1.54±0.023^{a}	0.706±0.013^{b}	1.43±0.040^{c}	1.36±0.037^{d}	1.52±0.027^{a}
Kidney	1.41±0.023^{a}	0.53±0.046^{b}	1.22±0.027^{c}	1.19±0.036^{c}	1.37±0.031^{a}
GSH (µg/mg protein)					
Liver	50.27±0.289^{a}	31.22±0.042^{b}	45.79±0.150^{c}	45.25±0.276^{d}	49.66±0.264^{a}
Kidney	49.26±0.205^{a}	23.83±0.186^{b}	47.30±0.318^{c}	43.46±0.480^{d}	48.86±0.301^{a}

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-d) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, GSH: Glutathione, *C. peltata: Cyclea peltata*

utilization of antioxidant defense system against increased reactive oxygen species or to a decrease in GSH level since GSH is required for the recycling of ascorbic acid [31]. Hyperglycemia can increase oxidative stress and change the redox potential of GSH. Administration of extract and glibenclamide increases the content of vitamin-C and GSH in liver and kidney of diabetic rats, which may be due to the less production of reactive oxygen species.

In Tables 5 and 6 show the effect of ethanolic extract of *C. peltata*. The results showed that the activity of catalase, superoxide dismutase, GPx, GST and polyphenol oxidase were decreased significantly in STZ induced diabetic group compared with the normal control group of liver and kidney. GSH, super oxide dismutase and catalase protect the cell constituents from oxidative damage. Oxidative stress may lead to a reduction in GSH or inactivation of superoxide dismutase and catalase [32,33]. Ethanolic extract of *C. peltata* treated diabetic rats shown a significant increase in the antioxidant enzyme activities and reversed them to their near normal levels. The same phenomenon was seen in the results of glibenclamide treated groups. Normal rats treated with ethanolic extract of *C. peltata* showed the same effect as that of control rats, and there was no significant change.

Lipid peroxidation is a free radical-mediated process leading to oxidative decline of polyunsaturated lipids. Under normal physiological conditions, low concentrations of lipid peroxides are found in plasma and tissues. Oxygen derived free radicals were generated in excess amount in response to various process that could be cytotoxic to several tissues. Most of the tissue damage is mediated by the free radicals by attacking membranes through peroxidation of polyunsaturated fatty acids. The effect of the ethanolic extract of *C. peltata* on the liver and kidney lipid peroxidation is given in Tables 7 and 8. The elevated levels of basal lipid peroxidation, ascorbate induced lipid peroxidation and peroxide-induced lipid peroxidation in STZ induced diabetic rats was reduced significantly to near normal levels upon treatment with

Table 5: Levels of enzymatic antioxidants in liver of experimental animals

Particulars	Control (Group I)	Diabetic control (Group II)	Diabetic+ glibenclamide treated (Group III)	Diabetic+ *C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
GPx (µg of GSH/mg of protein)	26.83±0.269[a]	10.9±0.358[b]	23.60±0.502[c]	20.36±0.450[d]	26.96±0.372[a]
Superoxide dismutase (units/g tissue)	6.54±0.031[a]	3.82±0.265[b]	5.52±0.362[c]	5.49±0.32[c]	6.35±0.083[a]
Catalase (µmoles of H_2O_2 utilized/min/mg/protein)	66.96±0.353[a]	39.72±0.45[b]	62.84±0.281[c]	61.54±0.507[d]	66.13±0.190[a]
GST (µmoles of CDNB conjugate formed/mg of protein)	8.37±0.136[a]	4.34±0.120[b]	7.78±0.161[c]	7.18±0.229[d]	8.14±0.314[a]
Polyphenol oxidase (mg/g of fresh tissue)	23.74±0.210[a]	15±0.447[b]	21.23±0.261[c]	19.52±0.357[d]	23.40±0.330[a]

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-d) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, GPx: Glutathione peroxidase, GST: Glutathione-s-transferase, CDNB: Chloro-2,4 dinitrobenzene, *C. peltata: Cyclea peltata*, GSH: Glutathione

Table 6: Levels of enzymatic antioxidants in kidney of experimental animals

Particulars	Control (Group I)	Diabetic control (Group II)	Diabetic+ glibenclamide treated (Group III)	Diabetic+ *C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
GPx (µg of GSH/mg of protein)	36.08±0.143[a]	14.8±0.236[b]	32.21±0.415[c]	29.74±0.239[d]	35.3±0.216[a]
Superoxide dismutase (units/mg of protein)	1.73±0.037[a]	0.94±0.040[b]	1.60±0.037[c]	1.53±0.049[cd]	1.68±0.044[a]
GST (µmoles of CDNB conjugate formed/mg of protein)	6.51±0.022[a]	2.76±0.040[b]	5.46±0.361[c]	5.44±0.049[c]	5.93±0.225[ac]
Catalase (µmoles of H_2O_2 utilized/min/mg/protein)	28.87±0.140[a]	16.82±0.257[b]	25.52±0.304[c]	23.01±0.107[d]	28.09±0.259[a]
Polyphenol oxidase (mg/g of fresh tissue)	20.13±0.192[a]	10.90±0.362[b]	17.88±0.306[c]	16.75±0.337[d]	19.77±0.445[a]

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-d) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, GPx: Glutathione peroxidase, GST: Glutathione-s-transferase, CDNB: Chloro-2,4 dinitrobenzene, *C. peltata: Cyclea peltata*, GSH: Glutathione

Table 7: Levels of lipid peroxidation in liver of experimental animals

Particulars (percentage of inhibition)	Control (Group I)	Diabetic control (Group II)	Diabetic+ glibenclamide treated (Group III)	Diabetic+ *C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
Basal lipid peroxidation	13±0.322[a]	29.43±0.273[b]	15.38±0.223[c]	16.26±0.345[d]	13.14±0.283[a]
Ascorbate induced lipid peroxidation	15.1±0.183[a]	36.29±0.337[b]	19.58±0.37[c]	21.23±0.195[c]	15.19±0.16[a]
Peroxide induced lipid peroxidation	10.90±0.167[a]	26.4±0.250[b]	14.29±0.147[c]	15.21±0.296[d]	10.59±0.152[a]

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, values not sharing a common superscript letter (a-d) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, *C. peltata: Cyclea peltata*

Table 8: Levels of lipid peroxidation in kidney of experimental animals

Particulars (% of inhibition)	Control (Group I)	Diabetic control (Group II)	Diabetic+ glibenclamide treated (Group III)	Diabetic+ *C. peltata* treated (Group IV)	*C. peltata* alone treated (Group V)
Lipid peroxidation	9.43±0.328[a]	24.37±0.189[b]	11.90±0.362[c]	13.27±0.201[d]	9.34±0.252[a]
Ascorbate induced lipid peroxidation	12.18±0.141[a]	30.41±0.317[b]	15.43±0.454 [c]	16.53±0.416[d]	12.12±0.443[a]
Peroxide induced lipid peroxidation	8.59±0.462[a]	22.37±0.418[b]	11.37±0.490[c]	12.36±0.307[d]	8.32±0.448[a]

Values are expressed as mean±SD, values are taken as a mean of five individuals' experiments, Values not sharing a common superscript letter (a-d) differ significantly (DMRT), SD: Standard deviation, DMRT: Duncan's multiple range test, *C. peltata: Cyclea peltata*

C. peltata extract and the same results obtained in standard drug glibenclamide. The plant extract alone treated rats did not show any significant change. The increased susceptibility of the tissues of the diabetic animals may be due to the activation of the lipid peroxidation system. The possible source of oxidative stress in diabetes that mediates shifts in redox balance resulting from altered carbohydrate and lipid metabolism, which in turn cause increased generation of reactive oxygen species [34].

Histopathology of the liver (Fig. 1) in the control liver tissue section shows sinusoidal cards of hepatocytes with central vein and portal tracts. The portal tracts show portal triad with portal vein, hepatic artery and bile duct, whereas the diabetic rat liver tissue section shows distortion in the arrangement of cells around the central vein, periportal fatty infiltration with focal necrosis of hepatocytes. Diabetic rats with *C. peltata* extract (400 mg/kg body weight) treated brought back the cellular arrangement around the central vein and reduced necrosis. In diabetic animals treated with glibenclamide, liver sections maintained lobular architecture, mild sinusoidal dilation, and congestion. The control rats treated with plant extract of *C. peltata* alone showed normal histological structure.

Histopathology of the kidney (Fig. 2) in control animals shows normal histology. In diabetic control animals, the kidney section showed severe tubular epithelial atrophy. In diabetic animal treated with glibenclamide, the kidney sections maintained mild tubular epithelial atrophy. Kidney of diabetic animal treated with ethanolic extract of *C. peltata* showed mild tubular atrophy. The normal animal treated with plant extract of *C. peltata* alone showed normal histological structure.

CONCLUSION

The result of this study shows that oral administration of the ethanolic of *C. peltata* reduces blood glucose, serum lipids which could be due

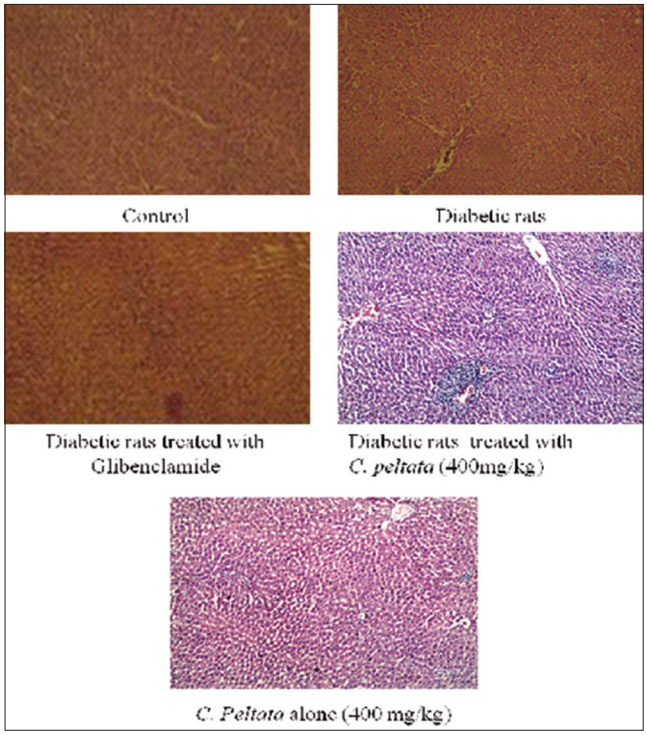

Fig. 1: Histopathology of liver

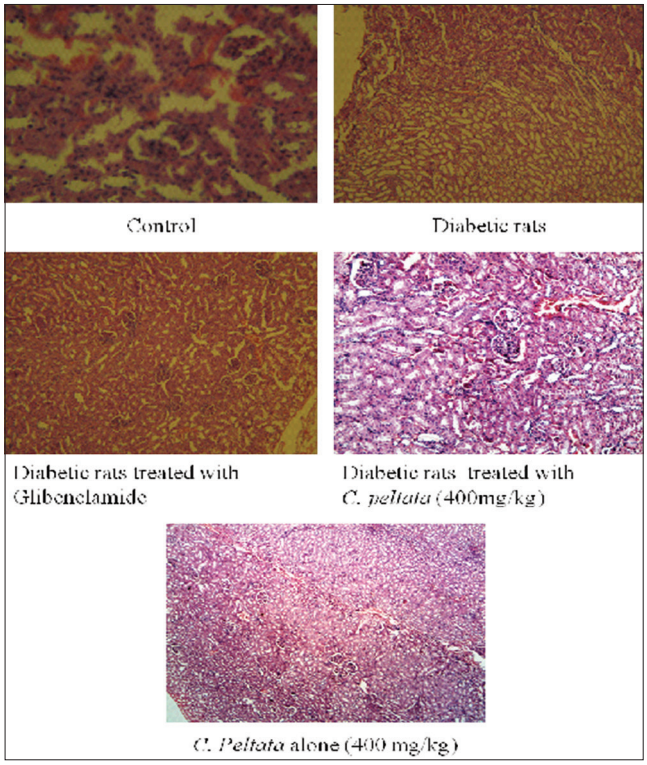

Fig. 2: Histopathology of kidney

to improvement in insulin secretion by recovery of pancreatic β-cells and the antioxidant system of *C. peltata* prevents diabetic complications from lipid peroxidation in experimental diabetic rats. Presence of alkaloids and flavonoids of *C. peltata* have also been found to be beneficial in controlling diabetes and many other diseases as evident from this study. It is, therefore, concluded from the data that *C. peltata* extract possess antidiabetic activity, and it may prove to be effective for the management of diabetes.

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