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PHYTOCHEMICAL AND PHARMACOLOGICAL EVALUATION OF ETHANOLIC EXTRACT OF THE *ARTOCARPUS HIRSUTUS* LAM. LEAVES

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ABSTRACT: *Artocarpus hirsutus* Lam. is a common plant with a variety of folk medicinal value. The present study was conducted to evaluate the phytochemical and pharmacological properties of the ethanolic extract of *Artocarpus hirsutus*. The screening for various phytochemicals was conducted by using various standard procedures. Acute toxicity of the extract was determined by using OECD guidelines 423. The antidiabetic activity of the plant was evaluated by using the streptozotocin-induced diabetic model in Wistar albino rats. The histopathology of the pancreatic tissue was also performed. The antioxidant activity of the extract was also performed by using the liver homogenate of the animal. Statistical analysis was performed by using one way ANOVA followed by Dunnet's test. The phytochemical screening of extract leads to the detection of various secondary metabolites like alkaloids, flavonoids, saponins, terpenoids, *etc*. No mortality was observed during acute toxicity studies up to the dose of 2000 mg/kg. The effect of the extract on parameters like body weight, fasting blood glucose level, SGOT, SGPT, ALP, bilirubin, total protein, urea, creatinine shows a significant variation. The histopathological examination of the pancreatic tissue shows marked regeneration of tissue. The enzymatic and nonenzymatic antioxidant parameters were determined and compared. These findings indicate that the ethanolic extract of *A. hirsutus* leaves have various phytopharmacological activities needed for pharmacological activity and thus it would be useful to isolate and characterize the compounds responsible for these bioactivities in the future.

INTRODUCTION: Diabetes is a common chronic noninfective metabolic disorder with micro and macrovascular complications [1] which results in significant morbidity and mortality. It is considered as one of the five leading causes of death in the world.

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The diabetes incidence has been increased worldwide. According to the International Diabetes Federation, the number expects to hit 380 million by 2025. [2]

Treatment for diabetes includes various categories of drugs like sulphonylureas, biguanides, thiazolidinediones, *etc*. with various mechanisms like enhancement of insulin action at target tissues, stimulation of endogenous insulin secretion, reduction in insulin demand, *etc*. Direct insulin along with physical activity was considered as the best therapy for diabetes. Despite its positive effects, the unwanted burden of these medicines is

its side effects like diarrhea, dyspepsia, nausea, edema, dizziness, myocardial infarction, *etc*. The plant is an exemplary source of medicine that has been derived directly or indirectly. About 800 plants with antidiabetic potential have been reported. The hypoglycemic activity of above said plants might be due to their ability to restore the pancreatic tissue function by causing an increased insulin secretion and inhibiting the absorption of intestinal glucose and facilitating their metabolites in insulin-dependent process [3, 4, 5, 6].

Oxidative stress develops inside the cells of our body as a result of an imbalance between reactive oxygen species production and its detoxifying capacity of the biological system. A reducing environment is preserved within the cells, and thus reducing state is maintained *via* enzymes by a constant input of metabolic energy. Any alteration in redox potential cause damage to living cells by production of free radicals and peroxides which destroy the proteins, lipids and DNA fragments of the cells and this event may lead to numerous diseases like parkinsonism, atherosclerosis, diabetes, nephrotoxicity, *etc*. The cells are equipped with different antioxidant enzymes which play a vital role in free radical scavenging and cell membrane protection [7, 8].

Antioxidants are substance lowers the oxidative stress by suppressing or arresting the free radical generation and detoxify by upregulation of enzymes and its actions [9]. Most of the medicinal plants are the source of antioxidants which improve the defense mechanism of the body. Various plant remedies for diabetes were described in the ancient system of Indian medicine [10, 11]. The major plants reported with antioxidant and antidiabetic properties are *Tinospora cordifolia*, *Annona squamosa*, *Calendula officinalis*, *Allivum sativum*, *Beta vulgaris etc*. [12, 13]

Artocarpus hirsutus is a perennial tree belonging to family Moraceae which is a tall evergreen tree found in Western Ghats of India. Artocarpus means evergreen tree which is grown in the tropical area and hirsutus means prickly, hairy resembling the morphological feature of the fruit of the plant. It grows well at an altitude of 1000 m from sea level with an annual rainfall of 1500 mm and above. The wood is used as timber for making wooden boat and furniture. The whole plant is of medicinal importance. Traditionally tribal peoples use this plant to treat many diseases like ulcers, wounds; joint pains, *etc*. [14] The GC-MS analysis of the *Artocarpus hirsutus* shows the presence of various bioactive components with valuable biological activities. The major chemical constituents reported are 2-Furancarboxaldehyde 5-methyl- Propyl-phosphonic dichloride, 2-Methylbutyraldehyde, 5-Hydroxymethylfurfural 3, 3-Dimethylbutan-2-yl methylphosphonofluoridate, butanal, n-Hexadecanoic acid, 2-Methyl-3-propyloxirane, and N-Pentadecane 2, 6-dimethoxy-4-vinyl phenol, *etc*.

Phytochemicals present in this plant contain various natural components like alkaloids, flavonoids, terpenoids, phenolic compounds. The flavonoids present in this plant possess antidiabetic and antioxidant activity. The plant has been reported to have antioxidant, hepatoprotective, antiulcer, diuretic, antimicrobial properties *etc*. Research on this plant is still unexplored and therefore in this study the antioxidant and antidiabetic activity of the plant *Artocarpus hirsutus* was investigated [15].

MATERIALS AND METHODS:

Plant Material: *Artocarpus hirsutus* plant leaves were collected in Kerala in December 2014. The plant was taxonomically identified and authenticated by Mr. G. V. S. Murthy, Scientist F and Head of Office, Botanical Survey of India, Tamil Nadu Agricultural University Campus, Coimbatore bearing the reference number BSI/SRC/5/23/2015/Tech.1345.

Preparation of the Crude Extract: The leaves of *Artocarpus hirsutus* were dried under shade and then pulverized with a mechanical grinder. The powder plant material was passed through sieve no. 40 and stored in an airtight container under refrigeration for further use. The powdered plant material was extracted with 90% alcohol using Soxhlet apparatus [16].

Phytochemical Screening: Various phytochemical tests were performed to identify the presence of phytoconstituents like alkaloids, glycosides, terpenoids, flavonoids, tannins, phenolic compounds in the extracts.

Acute Toxicity Study: The Acute toxicity study of the ethanolic extract of the *Artocarpus hirsutus* was performed in Swiss albino mice (20-25 g) according to Organization for Economic Cooperation and Development (OECD) guidelines no. 423. The study was conducted after obtaining approval from Institutional Ethics Committee approval for the animal experiment (IAEC No: NCP/IAEC/NO: 04/2014-2015). The plant extract was administered at the dose of 5, 50 300, 2000 mg/kg to the overnight fasted mice according to their body weight [17]. After administration of the extract, the animals were observed continuously for 14 days for its general behavior and mortality. Based on the results of toxicity tests the LD_{50} was selected as 200 and 400 mg/kg., p.o.

Chemicals Used: Streptozotocin the diabetic inducing drug was obtained from Sisco Research Laboratories Pvt. Ltd., Mumbai, India and the standard drug glibenclamide was obtained from the local pharmacy shop. All other reagents and chemicals used were of analytical grade.

Animals and Diabetes Induction: Male Wistar albino rats of 170-250 g weight were obtained from Nandha College of Pharmacy, Erode. The rats were housed under standard laboratory conditions of 23 ± 2 ºC with 12 h light and dark cycle in a polypropylene cage with free access to water and standard chow diet. The acclimatized animals were checked for initial blood glucose level and injected with a single dose of streptozotocin (60 mg/kg) by intraperitoneal route in distilled water.

After 7 days of rats with fasting plasma glucose level of 250 mg/dl or above to be included in the study. Streptozotocin induces diabetes in laboratory animals through the damage and death of endocrine pancreatic *β*-cells [18]. The test compound and the standard drugs were dissolved in water administered orally with the help of orogastric cannula.

Experimental Design: Diabetic rats were randomly divided into five groups of six animals in each group.

Group I: Normal control (distilled water 10 ml/kg p.o.)

Group II: Negative control (streptozotocin 60 mg/kg i.p)

Group III: Positive control (Streptozotocin + Glibenclamide 10 mg/kg p.o).

Group IV: Test I (Streptozotocin + EAAH 200 mg/kg p.o).

Group V: Test II (Streptozotocin + EAAH 400 mg/kg p.o).

Evaluation of Parameters:

General Parameters: Antihyperglycemic activity in the diabetic rats was assessed by measuring the fall in blood glucose level [19]. Blood samples were collected from the tip of the tail vein on 0^{th}, 7^{th}, 14^{th}, 21^{st} and 28^{th} days from the tail vein by snipping off the tip of the tail and the blood glucose were checked by using glucometer (a One Touch simple access, Johnson & Johnson). Change in body weight was measured during the experimental period. At the end of the study, animals were sacrificed under light ether anesthesia, followed by cervical dislocation the pancreas was removed and sent to a lab for histopathological examination.

Estimation of Biochemical Parameters in Serum: After the completion of experiment the blood samples were collected through the retro-orbital puncture of eye of animal under mild ether anesthesia in Eppendorf''s tube (1 ml) containing 50 µl of anticoagulant (10% trisodium citrate) and serum was separated by centrifuging at 3000 rpm for 15 min. The biochemical parameters like HDL, LDL, total cholesterol, triglycerides, and phospho-lipids were determined by using commercial kit available.

Preparation of Homogenate: Liver was removed from the animal and kept in the 0.2M; pH 6.6 phosphate buffer by using the homogenizer liver and the obtained homogenate was subjected to centrifugation process at 3000 rpm for 10 min. The obtained supernatant was used for the following tests.

Estimation of Protein Content: Protein content of the tissue homogenate was assayed by the method described (Lowry OH,). The blue color developed by the reduction of phosphomolybdic phospo-tungstic components in the Folin-Ciocolteau reagent by the amino acid tyrosine and tryptophan present in the protein plus the color developed by the biuret reaction of the protein with the alkaline cupric tartarate are measured by the Lowry's

method [20]. Then 0.5 ml of Folin reagent was added and incubated at room temperature in the dark for 30 min. The absorbance was measured at 660 nm. Protein content was expressed as μg/mg of protein.

Estimation of Malondialdehyde (MDA): Malondialdehyde an index of lipid peroxidation was evidenced by the formation of thiobarbituric acid reactive substances (TBARS) and hydro-peroxides (HP) were measured [21]. About 0.1 ml of liver homogenate (Tris HCl buffer, PH 7.4) was treated with 2 ml (1:1:1 ratio) of TBA-TCA-HCl reagent (Thiobarbituric acid 0.37%, 0.25N HCl and 15% TCA) and placed in a water bath for 15 min, cooled and centrifuged at 1000 rpm at room temperature for 10 min. The absorbance of the clear supernatant was measured against a reference blank at 535 nm. The values are expressed as units/mg protein.

Determination of Anti-oxidants:

Estimation of Superoxide Dismutase (SOD): SOD estimation was done by auto-oxidation of hydroxylamine at pH 10.2 which was accompanied by a reduction of NBT and the nitrite produced in the presence of EDTA was detected calorimetrically [22]. One enzymatic unit of SOD is the amount in the form of proteins present in 10% liver homogenate required to inhibit the reduction of 24 mM NBT by 50% and is expressed as units per milligram of protein.

Estimation of Catalase (CAT): Catalase activity was determined by the decomposition of H2O2 at 240 nm in the assay mixture containing phosphate buffer [23]. One international unit of catalase utilized is equal to the amount that catalyzes the decomposition of 1 mM H_2O_2 /min/mg of protein at 37 ºC. Catalase activity was calculated by using the millimolar extinction coefficient of 0.07 and expressed as micromole/minute/ milligram of protein.

Estimation of Peroxidase (Px): Peroxidase estimation was based on periodide formation which can be determined spectrophotometrically at 353 nm and is directly proportional to the peroxidase concentration in the reaction mixture containing approximate amounts of H_2O_2 and enzyme [24]. The peroxidase activity of one unit is defined as the change in absorbance per minute and expressed as units per milligram of protein.

Estimation of Glutathione Peroxidase (GPx): Glutathione peroxidase activity was measured with the reaction mixture consisting of 0.2 ml of 0.4M phosphate buffer pH 7.0, 0.1 ml of 10 mM sodium azide, 0.1 ml of 0.2 mM hydrogen peroxide, 0.2 ml of glutathione and 0.2 ml of supernatant. The contents were incubated at 37 ºC for 10 min. The reaction was arrested by the addition of 0.4 ml 10% TCA, and the absorbance was measured at 340 nm.

Estimation of Glutathione Reductase (GSSH): The enzyme activity was determined spectrophotometrically by a decrease in absorbance of NADPH at 340 nm. The reaction mixture contained 2.1 ml of 0.25mM potassium phosphate buffer pH 7.6, 0.1 ml of 0.001 M NADPH, 0.2 ml of 0.0165 M oxidized glutathione and 0.1 ml (10 mg/mL) of bovine serum albumin (BSA). The reaction was started by addition of 0.02 ml of liver homogenate with mixing, and the decrease in the absorbance at 340 nm was measured for 3 min against a blank. Glutathione reductase activity was expressed as moles NADPH oxidized/min/mg at 30 ºC [25].

Estimation of Reduced Glutathione (GSH): This was estimated by using dithiobisnitro-benzoate as a substrate. The yellow color developed and read immediately at an absorbance of 412 nm and expressed as μM GSH/g protein [26].

Statistical Analysis: Statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests using graph pad prism trial version. P-values <0.05 were considered significant.

RESULTS:

Phytochemical Screening: Phytochemical screening of the leaves of *Artocarpus hirsutus* shows the presence of alkaloids, flavonoids, saponins and terpenoids and absence of glycosides, tannins, and steroids.

Effect of EEAH on Body Weight: Administration of streptozotocin (60 mg/kg) to the experimental animal shows a significant (P<0.05) decrease in body weight in the diabetic group which may be due to excessive breakdown of tissue protein, muscle wasting, dehydration and catabolism of fats. On treating with glibenclamide and the extract,

doses show significant (P<0.01) increase in body weight when compared to vehicle-treated STZ rats.

TABLE 1: PHYTOCHEMICAL SCREENING OF ETHANOLIC EXTRACT OF LEAVES OF *A. HIRSUTUS*

Phytochemicals	Plant extract
Alkaloids	+
Flavonoids	+
Saponins	+
Terpenoids	+
Tannins	-
Glycosides	-
Steroids	-

(+) Presence of constituents, (−) Absence of constituents

Effect of EEAH on Blood Glucose Level: The blood glucose levels are measured in normal and experimental rats in initial and at the 7, 14, 21 and 28 days of treatment.

Streptozotocin-induced diabetic rats showed significant (P<0.01) increase in the levels of blood sugar as compared to normal rats. Oral administration of ethanolic extracts of EEAH (200 and 400 mg/kg) shows a significant decrease (P<0.05), (P<0.01) in blood sugar levels when compared to vehicle control group.

TABLE 2: EFFECT OF *ARTOCARPUS HIRSUTUS* ON BODY WEIGHT CHANGES IN CONTROL AND EXPERIMENTAL RATS

Groups	Body weight of animals on the first day (g)	Body weight of animals on 28thday (g)	Bodyweight a difference (g)
Normal control	162.3 ± 4.8	174.6 ± 3.2	12.3
Negative control	171.8 ± 6.1	182.3 ± 5.6	10.5^{a}
Positive control	168.3 ± 5.2	180.2 ± 4.9	11.9^{b}
EEAH 200 mg/kg	168.3 ± 5.2	180.2 ± 4.9	10.8^{b}
EEAH 400 mg/kg	168.3 ± 5.2	180.2 ± 4.9	11.2^{b}

The values are expressed as mean ± SEM; n=6 in each group. a P<0.01, when compared to normal control, b P<0.01, when compared to negative control.

TABLE 3: EFFECT OF EEAH ON BLOOD GLUCOSE LEVEL OF THE EXPERIMENTAL ANIMAL

Groups	7th day	14th day	21st day	28th day
Normal control	86.5 ± 3.2	88.9 ± 4.2	84.3 ± 3.8	85.9 ± 5.8
Negative control	239.5 ± 9.6^{a}	255.8 ± 17.9^{a}	272.5 ± 13.2^{a}	251.7 ± 3.4^{a}
Positive control	216.8 ± 11.9^{c}	184.3 ± 9.5^{c}	157.3 ± 10.3^{c}	112.7 ± 6.6^{c}
EEAH 200 mg/kg	231.6 ± 7.8^{b}	201.2 ± 10.4^{c}	183.1 ± 11.6^{c}	172.1 ± 5.3^{c}
EEAH 400 mg/kg	225.2 ± 5.4^{c}	196.4 ± 8.6^{c}	190.6 ± 14.7^{c}	134.6 ± 7.8^{c}

Values are mean ± SEM; n=6 in each group. a P <0.01 when compared to normal control, b P<0.05, c P<0.01, when compared to negative control.

Effect of EEAH on Liver Parameters: The serum levels of liver enzymes like SGOT, SGPT, ALT, urea, creatinine are found to increase in the streptozotocin-induced diabetic rats. But on treatment with the standard glibenclamide, the value of these enzymes found reduced. On treatment with an ethanolic extract of *Artocarpus hirsutus* the level of the enzyme reduced to a marked level significantly (P<0.01) to 400 mg extract when compared to vehicle control. The value of total proteins was found to decrease in streptozotocin-induced diabetic group (II) on comparing with normal control. On treatment with glibenclamide, the protein levels found to increase significantly (P<0.01). Similarly, the treatment with the ethanolic extract improves the level of protein in the test group (IV and V).

Effect of EEAH on Lipid Parameters: The levels of cholesterol, triglycerides, LDL and VLDL tend to increase in streptozotocin-induced diabetic animals. The level reaches its maximum in the negative control group. But the condition was overcome in glibenclamide, and the extract treated animals. The effect of the decrease in lipid parameters was found to be significant (P<0.01) in the extract treated animals. In the case of HDL, the value decreases in the negative control (II) on comparing to normal control. This effect was reversed in glibenclamide, and the extract treated animals. This increase in HDL level was found to be significant (P<0.01).

Effect of EEAH on Liver Protein, MDA and LH: The liver protein, MDA and LH levels increases in the streptozotocin-induced diabetic rats. The level reaches its maximum in the negative control group. This level tend to decrease in glibenclamide, and the extract treated animals. The decrease in the levels of liver protein, MDA and LH were found to be significant (P<0.01).

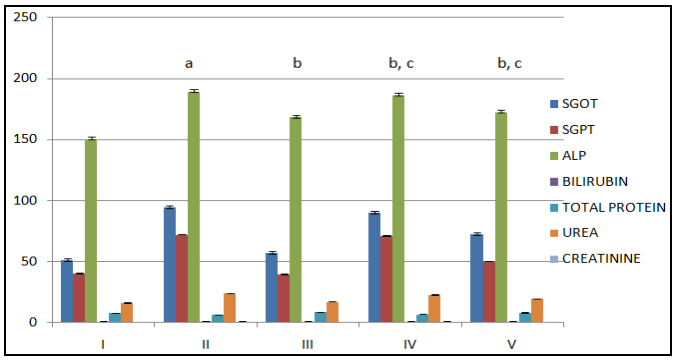

FIG. 1: EFFECT OF EEAH ON LIVER PARAMETERS. The values are expressed as mean± SEM; n=6 animals in each group. a P<0.01 when compared to normal control, b P<0.01, c P<0.05when compared to negative control

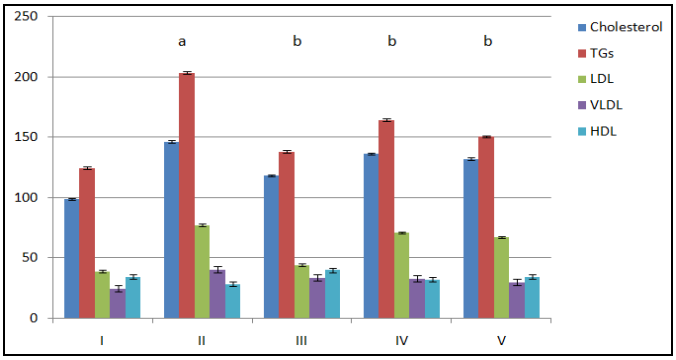

FIG. 2: EFFECT OF EEAH ON LIPID PARAMETERS. Values were expressed as mean ± SEM; n = 6 animals in each group. a P< 0.01when compared to normal control, b P< 0.01 when compared to negative control

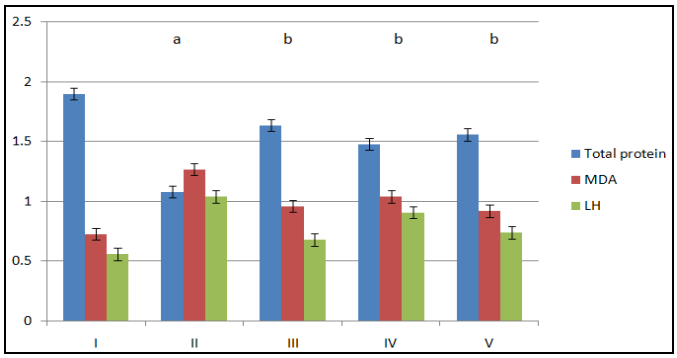

FIG. 3: EFFECT OF EEAH ON LIVER PROTEIN, MDA AND LH. Values are mean ± SEM; n=6 animals in each group. a P <0.01 when compared to normal control, b P<0.01 when compared to negative control

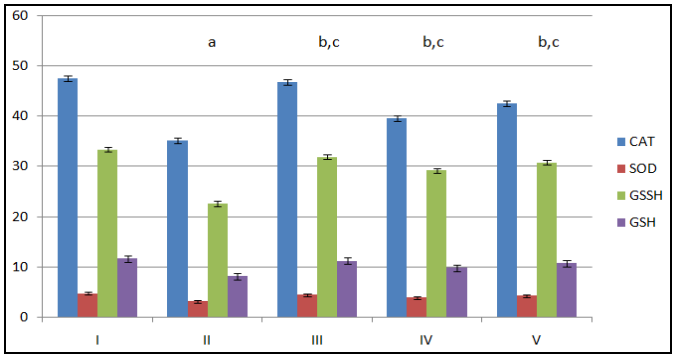

FIG. 4: EFFECT OF EEAH ON ANTIOXIDANT ENZYMES. Values are mean ± SEM; n=6 animals in each group. a P <0.01 when compared to normal control, b P<0.01, c P<0.05, when compared to negative control

Effect of EEAH on Antioxidant Enzymes: The level of catalase, reduced glutathione, and the glutathione levels were found to increase due to streptozotocin treatment in negative control when compared to normal control. This gets reversed significantly (P<0.01) on glibenclamide and the ethanolic leaf extract treatment). The level of SOD found to be decreased in the negative control.

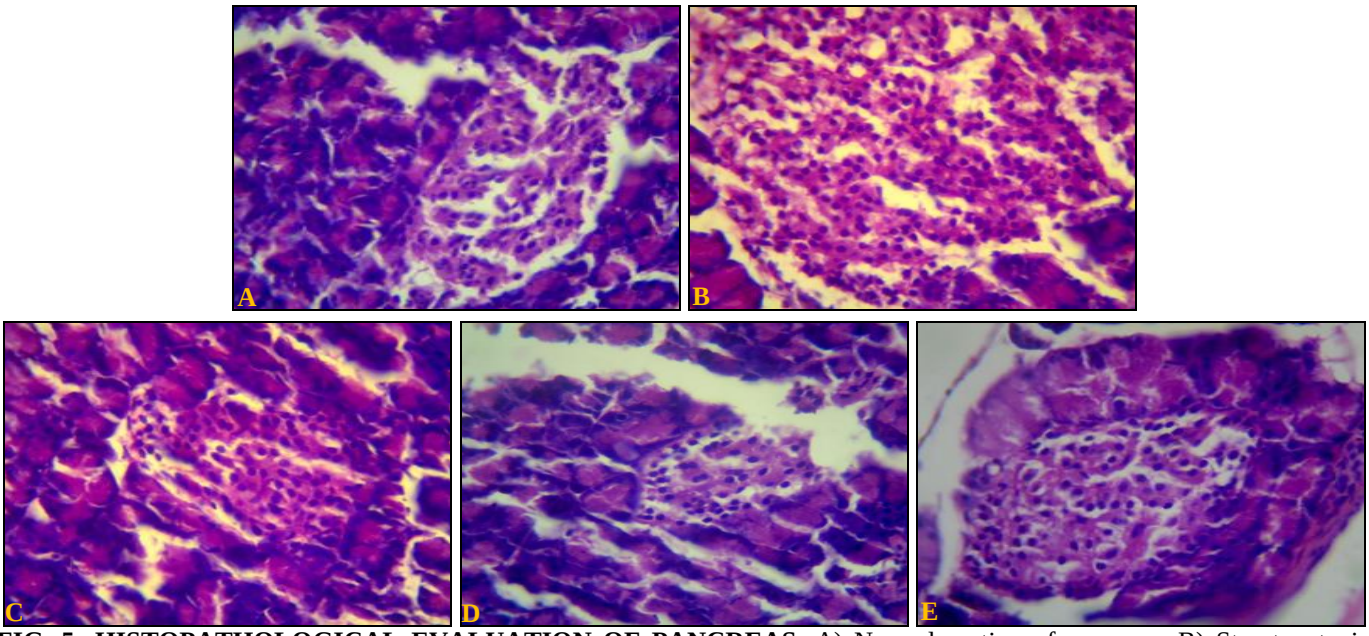

FIG. 5: HISTOPATHOLOGICAL EVALUATION OF PANCREAS. A) Normal section of pancreas, B) Streptozotocin treated pancreas, C) Streptozotocin (60 mg/kg) + Glibenclamide (10 mg/kg), D) Streptozotocin (60 mg/kg) + EEAH (200 mg/kg), E) Streptozotocin (60 mg/kg) + EEAH (400 mg/kg).

But on treatment with standard drug and the ethanolic leaf extract the levels were found to increase significantly (P<0.01).

SUMMARY AND DISCUSSION: The present deals with the exploration of pharmacological and phytochemical screening of *Artocarpus hirsutus* lam belonging to the family Moraceae. The preliminary phytochemicals screening shows the presence of alkaloids, terpenoids, flavanoids, and saponins. It was reported that the flavonoids frequently found in plants possess hypoglycaemic activity. The acute study of the plant extract was done using mice up to 2000 mg/kg of extract and no mortality was observed for 24 h. Thus the dose was identified as per OECD 423 guidelines. STZ is well known for its selective pancreatic islet *β*-cells cytotoxicity. It interferes with cellular metabolic oxidative mechanisms. Intraperitoneal administration of STZ effectively induced diabetes in normal rats, as observed by hyperglycemia. STZ (60 mg/kg, i.p.) was used to induced diabetes. Rats with blood glucose levels of above 200mg/dL were considered to be diabetic and used for the study [27, 28].

Induction of diabetes with STZ is associated with the characteristic loss of body weight which is due to increased muscle wasting in diabetes. In this study, the extract significantly prevented loss of body weight in diabetic rats when compared with diabetic control rats. Diabetic rats treated with the ethanolic extract showed an increase in body weight as compared to the diabetic control which may be due to its protective effect in controlling muscle wasting, *i.e*. reversal of gluconeogenesis. The improvements of these parameters could be attributed to the hypoglycemic properties of the plant [29, 30].

In blood glucose level there is a drastic increase in blood glucose due to insulin deficiency because of beta cell destruction. The elevated glucose level in blood was reversed by treatment with the ethanolic extract. This may be possibly due to the effect of flavonoids in the extract which acts on peripheral tissues, either by promoting glucose uptake and metabolism or by inhibiting hepatic gluconeogenesis [31].

The most common lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia. Administration of the extract decreases hypertriglyceridemia and hypercholesterolemia significantly (P<0.01). The observed hypolipidemic effect may be due to decreased cholesterologenesis and fatty acid synthesis [32, 33]. The extract significantly improved HDL cholesterol level. Oxidative stress in diabetes mellitus shows the reduction in the antioxidant levels and glycation of proteins, enzyme inactivation and alteration in structure, functions of collagen in the basement membrane.

Liver enzymes like SGOT, SGPT, and bilirubin levels were increased in diabetic rats which is responsible for the liver damage (marker enzyme). The elevated serum level of these enzymes was significantly reduced by ethanolic extract treatment. Diabetic complications such as increased gluconeogenesis and ketogenesis may be due to an elevation of the enzymes. The restoration of transaminases to their normal levels due to treatment with extract indicates the revival of insulin secretion. The extract also improves the renal functions in diabetic rats by reducing serum urea and creatinine [34, 35].

MDA is considered as an essential indicator of lipid peroxidation which is found to be increased in STZ-induced diabetic rats which may be due to lipid peroxidation. Rat treated with ethanolic extract shows the protection against lipid peroxidation characterized by a significant decrease in MDA level [36]. The oxidative stress is considered as an important biochemical parameter for diabetes. The antioxidant enzyme superoxide dismutase (SOD) is considered the first line of defensive enzymes against free radicals.

In the present study, there is a significant decrease in activity of superoxide dismutase (SOD) with a significant increase in malondialdehyde (MDA) concentration in STZ-induced diabetic rats and it was observed that treatment with the ethanolic extract significantly increases SOD in STZ-induced diabetic rats and significantly decreased MDA levels. This shows that the ethanolic extract of *Artocarpus hirsutus* leaves can reduce reactive free radicals that might lessen oxidative damage and this might be due to the rich presence of flavonoids which have antioxidant property [37, 38].

Flavonoids can exert their antioxidant activity by various mechanisms, *e.g.*, by scavenging or quenching free radicals, by chelating metal ions, or by inhibiting enzymatic systems responsible for free radical generation [39]. Catalase is present in almost all the mammalian cells and protects the cell from oxidative damage by H_2O_2 and hydroxyl radical. The enzyme GSSH catalyzes the conversion of oxidized glutathione (GSSG) to reduced glutathione (GSH), thereby maintaining a constant level of GSH [40]. GPx has a major role in degrading the levels of H_2O_2 in cells. Reduced glutathione (GSH) an intracellular reductant plays a significant role in catalysis, metabolism, and transport. The normal cells contain a high concentration of GSH, which scavenges the toxic reactive oxygen species.

Treatment with streptozotocin significantly decreased the activities of enzymatic and nonenzymatic antioxidants as compared with the control group. However, the groups supplemented with the *Artocarpus hirsutus* leaf extract produced a significant ($P<0.01$) increase in the level of antioxidant enzymes which is almost similar to glibenclamide treated group. The histopathological evaluation of the pancreatic beta cells represents the destructive action of streptozotocin. The groups treated with glibenclamide, ethanolic *Artocarpus hirsutus* extract (200 mg/kg, 400 mg/kg) shows the regeneration of the beta cells of islets cells of pancreas. This shows the protective action of the extract of *Artocarpus hirsutus* on beta cells of the pancreas.

CONCLUSION: The present study shows the ameliorative properties of *Artocarpus hirsutus* extract against STZ induced diabetes in rats. Further, the principal constituents that are responsible for the activity were to be identified and analyzed also for the activity.

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CONFLICT OF INTEREST: Nil

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