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Research

Evaluation of Antidiabetic Activity of *Corchorus trilocularis* Linn Plant Extract

Shaista Omer[1,3], Suryadevara Vidyadhara[2*] and Doppalapudi Sandeep[2]

[1]*Research Scholar, Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur, Andhra Pradesh, India – 522510*

[2*]*Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chandramoulipuram, Chowdavaram, Guntur, Andhra Pradesh, India – 522019*

3Department of Pharmacology, MMJG College of Pharmacy, Haveri, Karnataka, India - 581110

Abstract: Diabetes is a major health issue that has been faced by the majority of the population in the world. Extensive research is being carried out towards development of an antidiabetic component. The aim of the present research was to determine the antidiabetic activity of *Corchorus trilocularis* Linn plant belonging to the Tiliaceae family. The objectives were to evaluate various serum and pancreatic parameters related to evaluation of diabetes. The whole plant was extracted using various solvents. Phytochemical screening was done for the extracts. Antidiabetic activity was determined using Streptozotocin (STZ) induced diabetes model in rats using 200 mg/kg and 400 mg/kg doses of various extracts. Biochemical components like glycosylated hemoglobin (HbA1c), glutathione, creatine kinase (CK) and lactate dehydrogenase (LDH) were estimated for the collected blood samples from rats. The pancreatic tissue was homogenized and the result was subjected for estimation of TBARS (thiobarbituric acid-reactive substances), catalase, superoxide dismutase (SOD) and glutathione (GSH). Phytochemical screening showed presence of carbohydrates, glycosides, alkaloids, triterpenes, phytosterols, tannins, flavonoids, saponins, mucilage and steroids. The chloroform extract at 400 mg/kg dose significantly lowered the levels of HbA1c and restored blood GSH levels. The levels of CK and LDH were increased in diabetic rats. The treatment with chloroform extract (400 mg/kg) for 21 days significantly reduced the levels of CK when compared to diabetic rats. Extent of TBARS formed was significantly higher ($p<0.001$) in STZ treated group. In chloroform extract (400 mg/kg) treated groups, TBARS levels have significantly decreased ($p<0.001$). Diabetic rats treated with chloroform extract (400 mg/kg) showed significant increase ($p<0.01$) in levels of SOD. GSH activity was reduced in pancreatic tissue of diabetic rats, compared to normal animals. These levels were significantly ($p<0.01$, $p<0.001$) increased with chloroform extracts (200 mg/kg and 400 mg/kg) treatment. Thus the present study showed the antidiabetic potency of *Corchorus trilocularis* Linn plant.

Keywords: Diabetes, Streptozotocin, Glibenclamide, Wistar Rats, HbA1c, Glutathione

***Corresponding Author**

Suryadevara Vidyadhara , Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chandramoulipuram, Chowdavaram, Guntur, Andhra Pradesh, India – 522019

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1. INTRODUCTION

Herbal medicines are now-a-days playing a significant job in the treatment of different ailments in human beings and animals.[1] They represent highly low cost valuable medicinal agents which can be utilized in the treatment of various ailments in individuals. Promising bioactive constituents can be developed for many problems of health on the basis of scientific education offered on studying a virtuous account of medicinal plant number.[2] Diabetes mellitus is a carbohydrate metabolic disorder in which an increase in blood glucose level was observed. It is a major health issue in most people.[3]It occurs due to several reasons like inability to produce required amount of insulin by pancreas or inability to show response by the body cells to the insulin produced. The predominant type of diabetes is type 2 which occurs due to insulin resistance mostly in adults. It can be controlled by using oral hypoglycemic agents like Metformin, Glibenclamide, Acarbose etc.[4] and also can be controlled by lifestyle modifications. But these agents have more side effects.[5] As there is a need to reduce the side effects and at the same time to attain better efficacy, the research has been shifted towards development of a natural compound for the treatment and control of diabetes.[6] The current research could fulfill this need. Many natural remedies have also been in use for the treatment of diabetes.[7]One of such plants is *Corchorus trilocularis* which belongs to the family Tiliaceae. It is commonly called wild jute. The entire plant is utilized in the curing diseases of the abdominal viscera by the rural populations in India. It is rich in various phytochemical constituents which made it one of the natural sources in treatment of several ailments. Past studies have shown the presence of phytochemical components like flavonoids, terpenoids, diterpenes and vitamin E.[8] The leaves are employed in the treatment of gripe and nausea. In addition anti-pyretic, anti-inflammatory and analgesic activities of the plant have been documented by the early researchers.[9] *Corchorus* was also known to possess antiulcer and antidiabetic properties based on the literature survey. But these properties haven't been evaluated in the earlier studies. The lack of such research findings pertaining to antidiabetic efficacy has evoked the current study. The novelty of the present work lies in the establishment of antidiabetic potency of *Corchorus trilocularis* Linn along with biochemical estimations. By performing this study, a novel natural derivative in treatment of diabetes could be established from *Corchorus trilocularis* Linn. Diabetes in wistar rats can be induced by methods like Alloxan induced diabetes and Streptozotocin (STZ) induced diabetes. Among those, STZ induced diabetes is widely employed due to its ease of study.[10] Streptozotocin is toxic to the β cells of pancreas which secretes insulin.[11] The main aim of the present research is to determine the antidiabetic property of *Corchorus trilocularis* Linn plant extract along with estimation of various biochemical parameters. This could be a boon for the patients suffering with diabetes in future.

2. MATERIALS AND METHODS

2.1. *Plant Material*

A fresh entire plant of *Corchorus trilocularis* (Linn) was collected from Dharwad, Karnataka. The taxonomic identification of the plant and authentication was done by Prof. I.C. Prabhu, Department of Pharmacognosy, S.C.S. College of Pharmacy, Harapanahalli. The collected plant specimen was tagged and deposited in the college herbarium.

2.2. *Preparation of Extracts of Corchorus trilocularis*

The entire plant of *Corchorus trilocularis* was shade dried, powdered and subjected to soxhlet extraction process after defatting by petroleum ether. The extraction was done using various solvents like chloroform, ethyl acetate, ethanol, petroleum ether, methanol and water. At the end, the extracts were evaporated on water bath to obtain crude.[12] After cooling, the condensed extracts were weighed and stored in air-tight containers at 4 ºC till further investigation.

2.3. *Phytochemical Analysis*

Preliminary phytochemical screening was performed for the extracts of *Corchorus trilocularis* to detect the presence of various constituents responsible for the pharmacological activity.[13] The results were given in table 2.

2.4. *Experimental Animals*

Healthy adult rats (Wistar strain) weighing 150 to 200 g were procured and housed in polypropylene cages, maintained under standardized conditions i.e., 12:12 hour light/dark cycle at 25 ± 2ºC with paddy husk bedding. They were provided with standard pellet food and had free access to purified drinking water. The guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India were followed and prior approval was sought from Institutional Animal Ethics Committee (IAEC) for conducting the study (SETCP/IAEC/2008-2009/037).

2.5. *Determination of Acute Toxicity*

The animals were subjected to acute toxicity studies based on OECD guideline 2001. The animals were subjected to fasting during the night preceding the administration of the drug. Different extracts as single dose (2000 mg/kg) of the body weight was given orally (3 animals). The animals were observed for a period of 24 hours for any changes in their behavior or/and hypersensitivity reactions etc. In addition, any mortality in the animals was observed for 2 weeks.[13]

2.6. *Preparation of Doses*

Based on the results from acute toxicity studies, the doses to be tested were calculated. The extracts were suspended in tween 80.1%w/v.

2.7. *Evaluation of Antidiabetic activity*

2.7.1. *Induction of Diabetes using Streptozotocin*

40 mg/kg i.p Streptozotocin as a single dose in citrate buffer (pH 4.5) is administered to albino rats after 18 hours of fasting. The animals had access to food and water after injection. The animals were provided with water (5 % glucose) facility all through night to defy the hypoglycemic effect. Blood glucose concentration was estimated after 3 days employing glucometer to confirm the hyperglycemia. Animals with 250 mg/dl of glucose were selected for further study.[14]

2.7.2. *Experimental Protocol*

The selected animals (albino rats) were randomly categorized into 15 groups with 6 animals in each group, to assess the antidiabetic activity of *Corchorus trilocularis* extracts. The treatment protocol was indicated in table 1

Table 1: Treatment Protocol for Evaluation of Antidiabetic activity of Corchorus trilocularis

Group No	Treatment	Dose
1	Normal Control	Saline
2	Diabetic control	STZ – 40mg/kg
3	Pet. Ether extract	200 mg/kg
4	Pet. Ether extract	400 mg/kg
5	Chloroform extract	200 mg/kg
6	Chloroform extract	400 mg/kg
7	Ethyl acetate extract	200 mg/kg
8	Ethyl acetate extract	400 mg/kg
9	Ethanolic extract	200 mg/kg
10	Ethanolic extract	400 mg/kg
11	Methanolic extract	200 mg/kg
12	Methanolic extract	400 mg/kg
13	Aqueous extract	200 mg/kg
14	Aqueous extract	400 mg/kg
15	Glibenclamide	5mg/kg

The standard drug and test extracts are orally given at 2 doses for 21 days.[15]

2.7.3. *Blood Collection and Biochemical estimations in Serum*

The fasting blood samples were collected from all the animal groups on the 22nd day from the tail vein and the blood glucose concentration was recorded using glucometer. Glutathione levels and glycosylated hemoglobin (HbA1C) of the samples were estimated. Specific marker enzymes like creatine kinase (CK) and lactate dehydrogenase (LDH) were also analysed.[16] In diabetes, streptozotocin-induced oxidative stress is also a predictor of cardiac damage. Elevated serum CK and LDH levels were considered as markers for oxidative stress-induced cardiac damage since these are specific cardiac marker enzymes.[17] The results obtained were indicated in table 3.

2.7.4. *Biochemical estimation in Pancreatic Tissue*

The group of animals which showed better effect in blood parameters were sacrificed and the pancreas is collected carefully. Using ice cold saline, the tissue was washed, minced and placed in 0.15 M ice-cold potassium chloride solution. 10 % homogenate was prepared for estimation of TBARS (thiobarbituric acid reactive substances) and superoxide dismutase estimation (SOD). 10 % of the homogenate is prepared in 0.02 M EDTA for estimation of glutathione and catalase estimation with Teflon homogenizer. Elevation in TBARS values with decline of endogenous antioxidants levels is an indication of oxidative stress.[18] The results were indicated in table 4.

2.7.5. *Oral Glucose Tolerance Test*

The animal groups showing best antidiabetic activity were subjected to a glucose tolerance test. 4 groups of animals were taken, among which one group is normal control, another is standard and remaining two groups include the extracts of *Corchorus trilocularis* which showed best antidiabetic activity. Just before the administration and after 30 min of administration of the samples to normoglycemic rats, the blood glucose levels were determined. Then the rats were given 2 g/kg of glucose p.o and the blood glucose levels were estimated at time intervals of 120, 150 and 270 min. Blood was collected from the tail tip and using glucose oxidase –peroxidase (GOD-POD) method, the blood glucose levels were estimated.[19] The results obtained were given in table 5.

3. STATISTICAL ANALYSIS

The results obtained in the study were statistically evaluated using Graph Pad Prism 5.0 software. The mean value is accompanied by the standard error of mean (mean ± SEM). The results were analyzed using one-way ANOVA with dunnett's multiple comparison test and the parameter showing a probability value (p) of less than 0.05 was considered as significant statistically.

4. RESULTS AND DISCUSSION

The present study was performed to prepare extracts of *Corchorus trilocularis* plant using various solvents and to evaluate its antidiabetic property. Among all the extracts prepared, the extract derived using ethanol showed the highest yield of 11.28 %w/w. All the extracts were subjected to phytochemical and pharmacological screening.

4.1. Phytochemical Screening

The phytochemical investigation results of various extracts of *Corchorus trilocularis* were indicated in table 2. Previous research revealed that, the phytochemical constituents that are present in the extracts of *Corchorus trilocularis* like phenols, alkaloids, glycosides, carbohydrates, flavonoids, steroids, tannins, triterpenes and saponins have been

responsible for the antidiabetic activity. Alkaloids tend to show antidiabetic activity by their free radical scavenging action.[20] Carbohydrates regulate secretion of insulin and help in proper digestion and absorption of glucose. Glycosides control the amount of insulin to be produced and synthesis of glycogen. Flavonoids show antidiabetic effect by free radical scavenging and controlling insulin synthesis.[21] Saponins cause regeneration of pancreatic β cells and free radical scavenging which imparts antidiabetic effect. Steroids restore insulin levels. Tannins cause free radical scavenging and thus show antidiabetic effect.[22]

Table 2: Phytochemical Screening of Extracts of Corchorus trilocularis

Phytochemical Constituents	Plant Extract of *Corchorus trilocularis*				
	Petroleum Ether	Chloroform	Ethyl Acetate	Ethanol	Water
Carbohydrates	–	–	–	–	+
Glycosides	–	+	+	+	+
Alkaloids	+	+	+	+	+
Triterpenes	+	+	+	+	+
Phytosterols	+	+	+	+	+
Proteins	–	–	–	–	–
Fixed oils	–	–	–	–	–
Tannins	–	+	+	+	–
Flavonoids	–	–	+	+	+
Saponins	–	–	–	–	+
Mucilage	+	+	+	+	+
Steroids	–	–	+	+	+

+ indicates Presence; – indicates Absence

4.2. *Determination of Acute Toxicity and Preparation of Doses*

Even at the highest dose of 2000 mg/kg, no toxic effects were seen in wistar rats. Taking this into consideration, the doses for the study were calculated as $1/10^{th}$ and $1/5^{th}$ of the maximum tested dose, i.e200 and 400 mg/kg of *Corchorus trilocularis* extract.

4.3. *Evaluation of Antidiabetic Activity*

4.3.1. Effect of Corchorus trilocularis extracts on various Serum Parameters

The dose of streptozotocin significantly elevated the levels of glycosylated haemoglobin (HbA1c) in group 2 diabetic control rats. STZ induced diabetes through destruction of pancreatic β cells. There is a decrease in body weight of the animals too. This might be due to irregularity in the metabolic pathways of glucose as observed in the past research.[23] Of all the extracts, the chloroform extract showed better results. The results were indicated in table 3. After treatment with chloroform extract of *Corchorus trilocularis*, the level of glycosylated haemoglobin was significantly lowered in both doses. The levels of blood glutathione in diabetic rats (group 2) were significantly lowered ($p<0.001$) when compared with those in normal control rats of group 1. Similar results were obtained with other natural treatments too.[24] Treatment with chloroform extract (200 mg/kg and 400mg/kg) for 21 days significantly restored the blood glutathione (GSH) levels compared to group 2 rats. Glibenclamide treatment showed a highly significant ($p<0.01$) increase in blood GSH levels when compared to group 2. Petroleum ether, ethanolic and methanolic extracts had moderately significant effects in treated groups. This is in par with the other similar studies.[25] This is attributed to the effect of plant extract with free radical scavenging and in turn protection of GSH.[26]

Table 3:Effect of Corchorus trilocularis extracts on various Serum Parameters

Group No	Treatment	Serum Parameters (Mean ± S.E.M)			
		HbA1c (%)	GSH (mg/dl)	Creatine Kinase (CK) (IU/L)	Serum LDH (IU/L)
1	Normal Control	5.12 ± 0.22	3.19 ± 0.15	69.14 ± 2.88	190.12± 5.40
2	Diabetic control	15.33±0.42***	1.10 ± 0.10*	153.32 ± 3.91**	311.44±8.11***
3	Pet. Ether extract (200 mg/kg)	13.58 ± 0.24	1.82 ± 0.32*	145.48 ± 1.90*	298.71±10.67*
4	Pet. Ether extract (400 mg/kg)	12.34± 0.11*	1.85 ± 0.22*	140.28 ± 0.75**	272.21±9.40**
5	Chloroform extract (200 mg/kg)	9.22± 0.14**	1.97 ± 0.21**	132.18 ± 0.65**	262.31±8.23**
6	Chloroform extract (400 mg/kg)	7.34±0.17***	2.30± 0.26***	121.18± 0.64***	253.21±8.30***
7	Ethyl acetate extract (200 mg/kg)	13.23 ± 0.32	1.15 ± 0.20	150.32 ± 3.61	307.34± 8.15
8	Ethyl acetate extract (400 mg/kg)	12.22± 0.32*	1.20 ± 0.30	148.12 ± 3.83*	305.14± 7.32
9	Ethanolic extract (200 mg/kg)	9.40± 0.11**	1.37 ± 0.25*	138.13 ± 0.69*	268.32±8.11**
10	Ethanolic extract (400 mg/kg)	9.00± 0.16**	1.87 ± 0.29**	130.16 ± 0.54**	260.21±7.60**
11	Methanolic extract (200 mg/kg)	9.21± 0.10**	1.64± 0.20*	134.43 ±0.44*	270.77± 7.08**
12	Methanolic extract (400 mg/kg)	8.92± 0.12**	1.83± 0.18**	129.68±0.51*	261.38 ± 7.91**
13	Aqueous extract (200 mg/kg)	14.22 ± 0.41	1.34 ± 0.15	147.12 ± 3.78	305.54± 7.17
14	Aqueous extract (400 mg/kg)	13.20 ± 0.52	1.45 ± 0.19	145.22 ± 3.61	298.64± 7.15
15	Glibenclamide(5 mg/kg)	6.17±0.43***	3.79± 0.22***	89.62 ± 2.67***	233.76±9.34***

Mean ± Standard Error of Mean for six animals; *p<0.05, **p<0.01, ***p<0.001 compared with diabetic control vs treated groups

Furthermore, the levels of CK and LDH were significantly increased in group 2 diabetic rats. Past studies have shown that there is a marked increase in the levels of CK and LDH during diabetes which is an indication of tissue damage.[27] However, the test extract treatment for 21 days significantly reduced the levels of CK ($p<0.01$ with 200 mg/kg and 400 mg/kg) when compared to diabetic rats. Administration of chloroform, petroleum ether and ethanolic extracts moderately reduced ($p<0.01$) the serum LDH levels in both doses when compared to pathogenic diabetic control rats and results were compared with Glibenclamide treatment. The phytochemical constituents present in the plant extract impart the antidiabetic activity. This is in par with the recent studies on antidiabetic activity.[28, 29]

4.3.2. Effect of Corchorus trilocularis extracts on various Pancreatic Tissue Parameters

The chloroform extract of *Corchorus trilocularis* showed better antidiabetic effect on blood parameters. So, this extract treated animals were selected and pancreas were isolated to estimate lipid peroxides, catalase, superoxide dismutase and glutathione levels.

Table 4: Effect of Corchorus trilocularis extracts on Pancreatic Tissue Parameters

Group No	Treatment	Serum Parameters (Mean ± S.E.M)			
		TBARS (nmol MDA/mg protein)	CAT (nmol H_2O_2 consumed/ min/mg protein)	SOD (IU/mg protein)	GSH (min/mg protein)
1	Control	0.489± 0.037	4.33± 0.089	3.59± 0.069	52.4±0.945
2	Diabetic control	4.921±0.562***	0.79± 0.020***	0.262±0.025***	11.58±1.034***
3	Chloroform extract(200 mg/kg)	2.853±0.451*	2.10± 0.132**	3.44±0.272**	40.24±1.446***
4	Chloroform extract(400 mg/kg)	0.893±0.013***	2.92± 0.079**	3.68±0.093***	43.52±1.123***
5	Glibenclamide(5 mg/kg)	1.223±0.041***	3.39± 0.156***	3.78±0.087***	44.65±1.656***

Mean ± Standard Error of Mean for six animals;
****p<0.05, **p<0.01, ***p<0.001 compared with diabetic control vs treated groups.***

All the extracts had significant effects on antioxidant enzymes. The results were shown in table 4. Extent of TBARS formed was significantly higher ($p<0.001$) in STZ treated group. In both groups of chloroform extract (200 mg/kg and 400 mg/kg) treatment, level of TBARS decreased significantly ($p<0.001$). TBARS were an indication for oxidative stress. Decreased levels of TBARS after treatment with extract showed its effect against diabetes. This can be compared with the previous research.[30] Significant reduction ($p<0.001$) in the activity of SOD in pancreas of diabetic animals (group 2) was observed in comparison to normal rats. Diabetic rats treated with chloroform extract (200 mg/kg and 400 mg/kg) showed significant increase ($p<0.01$) in the level of SOD. As SOD also involves in the metabolism of hydrogen peroxide, increased levels of SOD indicates better antioxidant effect which is indicated in the past experimentation.[31]Total glutathione (GSH) activity was reduced significantly in pancreatic tissue of diabetic rats as compared to normal control animals. The levels were significantly ($p<0.01$, $p<0.001$) increased with chloroform extract (200 mg/kg and 400 mg/kg). These results suggested the antidiabetic activity of *Corchorus trilocularis* plant extracts. This potential is due to the phytochemical constituents present in the extracts. Plants having similar extracts have shown the same result.[32] Antioxidant enzymes make free radicals less harmful or ineffective. GSH is one of the antioxidant substances that prevent oxidative stress. Increase in superoxide dismutase levels also helps in control of superoxide that helps in prevention of degeneration of pancreatic cells.[33] The same has been proved in the recent research work too.[34]

4.3.1. Oral Glucose Tolerance Test

The results of the oral glucose tolerance test were indicated in table 5.

Table 5: Effect of Corchorus trilocularis extracts on Oral Glucose Tolerance

Group No	*Treatment*	*Blood Glucose Levels (mg/dl) (Mean±S.E.M)*					
		0 min	***30 min***	***60 min***	***120 min***	***150 min***	***270min***
1	Control	72.33±4.44	72.69±3.08	74.07±4.22	164.71±3.66	116.58±2.99	76.69±4.42
2	Standard Glibenclamide (5mg/kg)	74.09±3.43	63.75±4.05**	53.48±3.37**	137.96±4.01**	86.82±4.31**	72.24±4.61**
3	Chloroform extract(200 mg/kg)	72.98±3.68	68.92±4.57**	65.58±4.49**	148.21±5.08**	101.47±5.21**	75.31±4.06**
4	Chloroform extract(400 mg/kg)	73.65±4.55	65.86±2.97**	58.27±3.32**	142.05±5.66**	90.63±4.32**	75.20±3.98**

Mean ± Standard Error of Mean for six animals;**p<0.01 compared with normal control vs treated groups.

The chloroform extract of *Chorchorus trilocularis at a dose* of 400 mg/kg showed a highly significant glucose tolerance effect related to the standard drug Glibenclamide. This effect might be not dependent on the release of insulin.[35]

5. CONCLUSION

The present study succeeded in developing a novel natural derivative with antidiabetic property. From the above results, it was concluded that chloroform extract of *Corchorus*

trilocularis at a dose of 400mg/kg showed promising antidiabetic effect on serum and hepatic parameters among all the extracts. A dose dependent effect was observed in all extracts. The obtained results were statistically significant ($p<0.01$). Serum parameters like TBARS, SOD, CAT and GSH should be typically controlled in diabetes. *Corchorus trilocularis* restored the levels of these parameters near to standard agent. It even passed the oral glucose tolerance test. All these effects of *Corchorus* might be attributed to its phytochemical composition. Further research is needed to be done on the isolation of specific phytochemical components that are responsible for imparting the antidiabetic effect.

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7. AUTHORS CONTRIBUTION

Dr. Suryadevara Vidyadhara has designed , supervised the process and reviewed the manuscript. Shaista Omer has carried out the experiments, analyzed the results and contributed in preparation and revision of manuscript. Dr. Doppalapudi Sandeep has contributed in preparation and revision of manuscript. The authors have read and approved the final version of the manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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