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Research Article

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Anti-diabetic activity of *Sida cordifolia*

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Abstract

Diabetes mellitus (DM) is one of the major diseases affecting the quality life of population around the world. There is no complete medication that controls the DM and its complications, in fact maintaining good health conditions. The traditional medicine which is principally based on medicinal plants (MPs) provides treatment for different diseases including DM and its complications. Many reports provide the evidence that different MPs possess anti-diabetic activity (ADA) and still many TMs are unexplored about their ADA. So, the current study aimed to evaluate the ADA of *Sida cordifolia* on Alloxan-induced diabetic mellitus in WISTAR albino rats. The phytochemical analysis of the extracts of *S. cordifolia* reveals the presences of different phytochemical components like sterols, terpenoids, alkaloids, flavanoids etc. The ethanolic and aqueous extracts showed dose dependent anti-diabetic activity as standard drug Glibenclamide. The extracts significantly controlled the blood glucose level, body weight loss and alteration in different lipid metabolic enzymes. The result of the present study provides the scientific confirmation to the traditional usage of *S. cordifolia* and more research is going on to assess different pharmacological activities and isolation of bioactive molecules from it.

Key words: *Sida cordifolia*, Diabetes mellitus, Traditional medicine, Medicinal Plants, Alloxan.

1. Introduction

Diabetes mellitus (DM) is a chronic disorder characterized by impaired metabolism of glucose and other energy-yielding fuels, as well as the late development of vascular (involving small and large blood vessels) and neuropathic complications (Harris, 2004). Regardless of the cause, the disease is associated with a common hormonal defect, namely, insulin deficiency, which may be total, partial, or relative when viewed in the context of coexisting insulin resistance. There are estimated 177 million people worldwide sufferings from DM, almost five times more than the estimates ten years ago. This number may probably double by the 2030 and reports from the world health organization (WHO) indicate that DM is one of the major killers of our time, with people in south-east Asia and western pacific being most at risk (Bommer *et al.*, 2018). In recent years, India has witnessed a rapidly exploding epidemic of DM indeed India today leads the world with its largest number of diabetic subjects in any given country and 57.2 million people will suffer with DM by the year 2025 (one sixth of the world). Therefore, it has become necessary to look for an economical as well as therapeutically effective treatment for DM (Marín-Peñalver *et al.*, 2016).

The role of traditional medicines in the solution of health problems is invaluable on a global level. This is more striking when we consider the fact that approximately 80 % of the people around the world rely exclusively on traditional medicine for their health care needs 9 Jamshidi-Kia, 2018). India unquestionably occupies the topmost position in the use of herbal drugs since ancient times utilizing plant species in different formulations (Modak *et al.*, 2007; Choudhury *et al.*, 2017). Great majority of people in India have been depending on crude drugs for the treatment of various diseases as evidenced from well documented indigenous system of medicines, Ayurveda and Unani. Along with Indian there are many traditional medicines available such as Chinese, Korean, Iranian, African, Siddha traditional medicines (TMs) etc. All these TMs are basically depending on medicinal plants (Pang *et al.*, 2019). A lot of medicinal plants are still unexplored about their medicinal usages scientifically (Mohanraj *et al.*,

2018). In this point of view, the current research was carried to evaluate phytochemical constituents and anti-diabetic activity against alloxan induced diabetes.

Sida cordifolia is a tropical species found throughout the tropical and subtropical regions of India belongs to family Malvaceae. It has been using in certain respiratory disorders, including but not limited to asthma, nasal congestion and phthisis. Additionally, it has used in traditional indications in the treatment of dysentery, rheumatism, fever, and facial paralysis and other mental disorders (Franzotti *et al.,* 2000; Kushagra *et al.,* 2010; Kalaiarasan and Ahmed John, 2011).

2. Materials and Methods

2.1 Chemicals and Instruments

The solvents used in current study are analytical grade. The diagnostic kits were purchased from Coral clinical systems, Verna Goa, India. Shimadzu UV Spectrophotometer (model 1800), Incubator, Digital balance, Rotary flash evaporator (Superfit, Rotary Vaccum Digital Bath), Deep freezer, Albino rats (Wistar strain), accu check glucometer (one touch) was used to check glucose level.

2.2 Collection and extraction of plant material

Fresh whole plant of *Sida cordifolia* were collected from Western Ghats, Nilgiri district, Tamil Nadu and authenticated by field botanist, survey of medicinal plants & collection unit. The whole plant material was subjected to shade drying and material was further crushed to powder. The coarsely powdered plant material (500g) was packed in Soxhlet apparatus. The packed plant material extracted successively with Alcohol (Ethanol), Double distilled water and the extract where filtered and filtrate were concentrated by evaporation of solvent at room temperature, the residue were concentrated in the hot air oven, the final residue stored in desiccators.

2.3 Preliminary phytochemical analysis

The standard procedures were used to know the phytochemical constituents in prepared extract (Doss, 2009).

2.4 Experimental animals

Albino-Wister rats of either sex, weighing 150-200g were procured. The animals were acclimatized for seven days under laboratory conditions, all rats were kept at room temperature of 37°C in the animal house. The animals were fed with commercially available rat pelleted diet. Water was allowed *ad libitum* under strict hygienic conditions. Prior to the experiments, rats were fed with standard food for 1 week in order to adapt to the laboratory conditions. All the study was approved by institutional ethical committee ((Reg No:1987/PO/Re/S/17/CPCSEA).

2.5 Acute toxicity studies

Acute toxicity studies were performed for extracts according to the toxic classic method as per guidelines 423 prescribed by OECD, 2001 (OECD Guideline for testing of Chemicals, 2001). Female albino rats were used for acute toxicity study. The animals were kept fasting for overnight and provided with water only. These were divided into groups each containing three animals. Each of these groups was then administered with Ethanolic and aqueous extracts of *sida cordifolia* the dose of 5mg/kg b.w p.o., 50mg/kg b.w p.o., and 300mg/kg b.w p.o. The animals were observed continuously after administration of the first dose for 30 minutes and then periodically for first 24 hours with special attention during the first 4 hrs and thereafter daily, for a total of 14 days. The observations like sedation, convulsions, tremors, salivation, lethargy, death etc are systematically recorded with individual records of each animal. Since no mortality was seen at the dose levels 5 mg, 50mg, 300mg and the procedure was repeated with higher dose of 2000mg/kg b.w in fresh animals.

2.6 Alloxan induced diabetic model

Alloxan (2, 4, 5, 6-tetraoxypyrimidine; 2, 4, 5, 6-pyrimidinetetrone) is an oxygenated pyrimidine derivative, which selectively destroys insulin-producing cells in the pancreas when administered to rodents and many other animal species (Nakahara *et al.,* 2016). Hyperglycemia/diabetes were induced by single Intraperitonial injection of freshly prepared aqueous solution of alloxan monohydrate 120 mg/kg, to overnight fasted rats. After 72 h of alloxan

injection, the animals which did not developed hyperglycemia i.e. glucose level >200mg/dl, were rejected/replaced with new animals. Immediately after confirmation of diabetes (glucose level > 250 mg/dl), rats were classified into seven groups of six rats each as shown in Table 1. The blood samples were collected by the retro orbital plexus puncture method under mild ether anesthesia for the estimation of blood glucose level and body weight. Blood glucose levels and body weight were estimated on 1st, 7th, 14th and 21st day of the treatment. On the 21st day, blood samples were collected from overnight fasted rats by cardiac puncture under mild ether anesthesia for biochemical estimations. The blood samples were subjected to centrifugation to obtain serum. Serum was analyzed for serum triglycerides (TG), serum total cholesterol (TC), serum HDL-C, serum LDL–C and serum VLDL–C were estimated. The animals were sacrificed by overdose of ether and autopsied. Plant extracts and standard drugs were suspended in distilled water using sodium carboxy methyl cellulose (sodium CMC, 0.3%) and administered orally to the animals with the help of an intragastric catheter.

Table 1. Experimental design

Group	Treatment
Group I	Normal control (0.3% CMC.,0.5ml by oral route)
Group II	Diabetes induced control (Alloxan 120 mg/kg., i.p.)
Group III	Diabetes induced + Standard drug treated. (Standard drug: Glibenclamide 1mg/)
Group IV	Diabetes induced + Test drug treated Dose 200 mg/kg. (*Sida cordifolia* ethanolic extract).
Groups V	Diabetes induced +Test drug treated Dose 400 mg/kg. (*Sida cordifolia* ethanolic extract).
Group VI	Diabetes induced + Test drug treated Dose 200 mg/kg. (*Sida cordifolia* aqeous extract).
Group VII	Diabetes induced + Test drug treated Dose 400 mg/kg. (*Sida cordifolia* aqeous extract).

2.8 Statistical analysis

The data were expressed as mean ± standard error mean (SEM). The Significance of differences among the group was assessed using one way and multiple way analyses of variance (ANOVA). The test followed by Tukey-Kramer multiple comparison tests, the p values less than 0.001 were considered as significant.

3. Results and Discussion

The phytochemical analysis *Sida cordifolia* extracts were evaluated using different standard phytochemical test procedures and found the presence of phytochemicals in them. But, variation in the presence of different phytochemicals was observed in tested extracts (Table 2). The both extracts showed presence of sterols, terpenoids, glycosides, tannins, carbohydrates, alkaloids and phenols. The quinones are absent in both extracts, oils and flavanoids are present in ethanol extract absent aqueous extract, saponins are present in aqueous extract, absent in ethanol extract.

Table 2. Phytoconstituentsin different extracts of *Sida cordifolia*

Name of the Phytochemicals	Name of the extract	
	Ethanol	Aqueous
Phytosterols	+	+
Terpenoids	+	+
Glycosides	+	+
Saponins	-	+
Flavonoids	+	-
Tannins	+	+
Carbohydrates	+	+
Alkaloids	+	+
Amino acids	-	-
Oils	+	-
Quinones	-	-
Phenols	+	+

+= Present, – = Absent

After the preliminary phytochemical analysis, the extracts were tested to know about their toxicity. The selected plant extracts showed neither visible sign of toxicity nor mortality. The results clearly indicated non-toxicity of the extracts at a dose of 2000 mg/kg. From this, 1/20th 1/10th, and 1/5th and doses were selected for the experimental study. Hence there is no LD_{50} and all the extracts tested are considered safe and nontoxic.

The current investigation, anti-diabetic activity of S*ida cordifolia* was carried on alloxan induced diabetic albino rats. Intraperitoneal administration of alloxan (120 mg/kg of body weight) effectively induced DM in normal rats as reflected by glycosuria, hyperglycaemia, polyphagia, polydipsia and body

weight loss compared with normal rats.

The variations in body weight due to the alloxan were observed before the treatment and after the treatment. Alloxan diabetic control significantly reduced the body weight, then treatment with standard and plant extracts which gained significant weight. The ethanol and aqueous extract treated diabetic albino rats showed a significant dose dependent beneficial effect when compared with the reference drug glibenclamide (Fig 1).

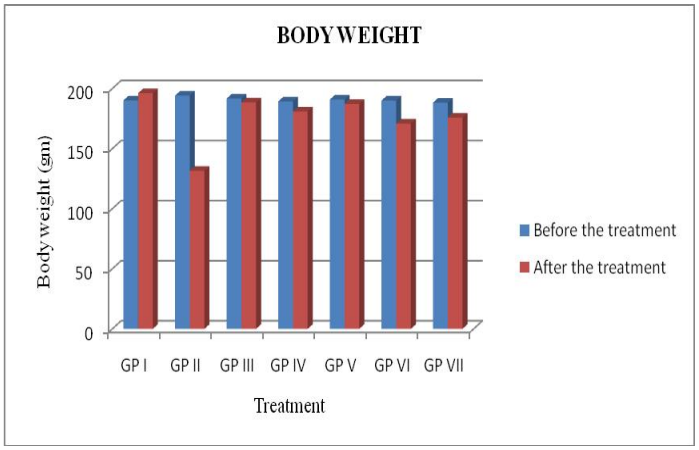

Fig 1. Effect of *Sida cordifolia* on body weight in alloxan treated diabetic rats.

The blood glucose levels (BG) of the animals which are treated with *S. cordifolia* (Groups IV, V, VI and VII) and the standard drug glibenclamide (Group-III), were observed on 1st, 7th, 14th, and 21st day. The diabetic rats which treated with *S. cordifolia* and glibenclamide showed a significant decrease in blood glucose level on 1st, 7th, 14th, and 21st day. On 21st day BG of Group-III decreases nearly too normal range. When compared with untreated group, the *S. cordifolia* at the dose of 200 and 400mg/kg significantly reduces the hyperglycemia (Fig 2).

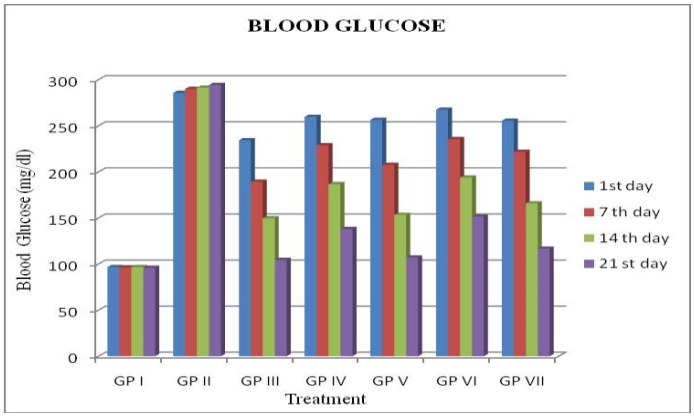

Fig 2. Effect of *Sida cordifolia* on blood glucose level in alloxan treated diabetic rats.

Diabetes mellitus is also associated with hyperlipidemia with profound alteration in the concentration and composition of lipid and changes in the concentrations of the lipid contribute to the development of vascular disease (Parhofer, 2015; Athyros *et al.*, 2018). Alloxan significantly increased TC, TG, LDL, and VLDL and decreases the HDL levels (Table 3 and Figs 3-7). The abnormally high concentration of serum lipids in DM is mainly due to an increase in the mobilization of free fatty acids from the peripheral fat depots, since insulin inhibits the hormone sensitive lipase (Erejuwa *et al.*, 2016; Farsani *et al.*, 2016). Excess of fatty acids in plasma produced by alloxan promotes the liver conversion of some fatty acids to phospholipids and cholesterol. These two substances, along with excess of TG formed in the liver, may be discharged into lipoproteins in the blood. Administration of *Sida cordifolia* to diabetic rats reversed all the above-mentioned changes and improved the HDL levels. The results of the present investigation clearly indicate that the *S. cordifolia* has a glucose lowering effect on alloxan-induced diabetic rats. It was also found to be highly effective in managing the complications associated with DM, such as body weight maintenance and hyperlipidaemia and prevents the defects in lipid metabolism. The observed hypolipidemic effect may be because of decreased cholesterogenesis and fatty acids. Significantly lowering the total cholesterol and raise in HDL Cholesterol is a very desirable biochemical status for prevention of atherosclerosis and ischemic conditions.

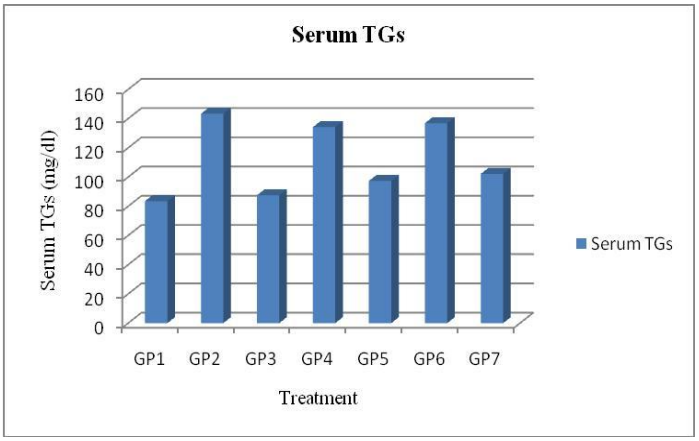

Fig 3. Effect on Serum TG level on alloxan treated diabetic rats.

Table 3. Effect of *Sida cordifolia* on lipid profile on alloxan induced diabetic albino rats.

Group	Biochemical parameters(mg/dl)				
	TG	TC	HDL	LDL	VLDL
GP I	83.5±1.54	132.15±4.36	55.33±2.83	32.16±1.70	18.83±1.30
GP II	143.33±1.85	269.16±5.02	34.66±1.60	62.66±1.58	40.83±1.01
GP III	87.5±2.64***	149.83±3.85***	47.16±1.16***	34.33±1.43***	22.16±0.90***
GP IV	134.16±1.44**	253.16±2.98**	38.83±1.01**	47.83±1.01**	35.16±1.16**
GP V	97.33±2.67***	169.16±2.56***	42.83±1.37***	36.66±1.202***	26.16±1.32***
GP VI	136.83±1.53*	255.16±2.63**	32.16±1.27**	54.5±0.99**	36.83±1.30**
GP VII	102.16±2.15***	173.16±2.25***	41.66±1.08***	40.83±1.10***	28.33±0.80***

Values are expressed as mean ± SEM (n=6); One-way ANOVA followed by Tukey-Kramer mulptiple test. Where, *represents significant at p<0.05, ** represents moderate significant at p< 0.01, *** presents highly significant at p<0.001.

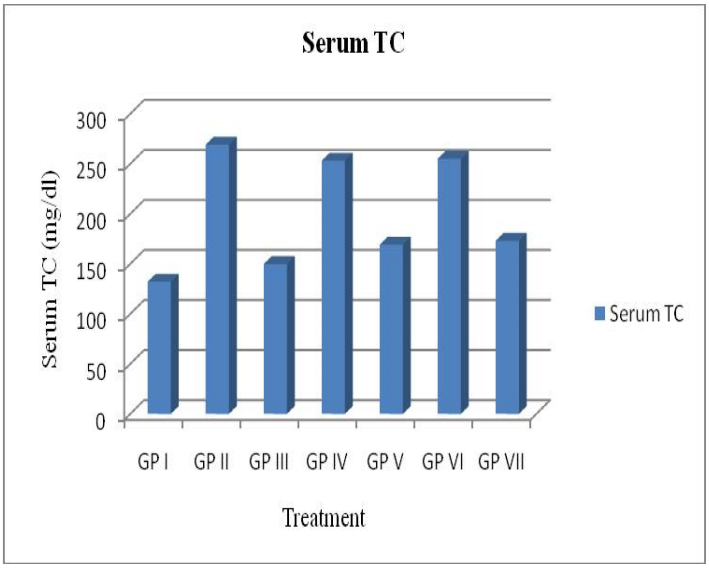

Fig 4. Effect on Serum TC level on alloxan treated diabetic rats.

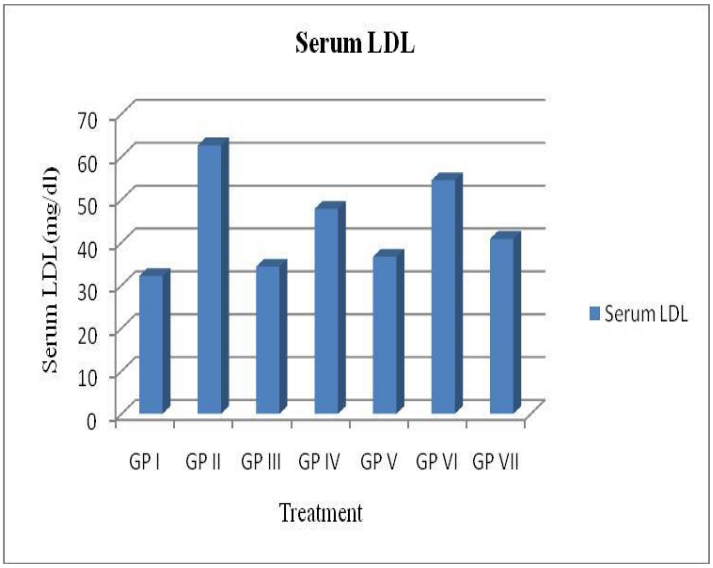

Fig 6. Effect on Serum LDL level on alloxan treated diabetic rats.

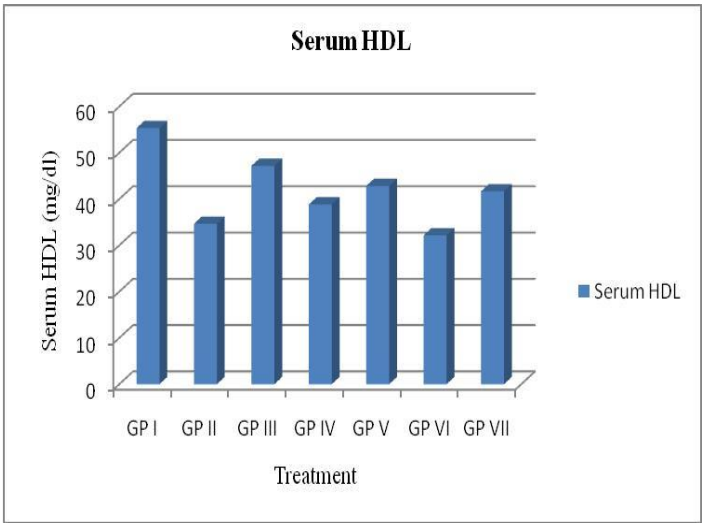

Fig 5. Effect on Serum HDL level on alloxan treated diabetic rats.

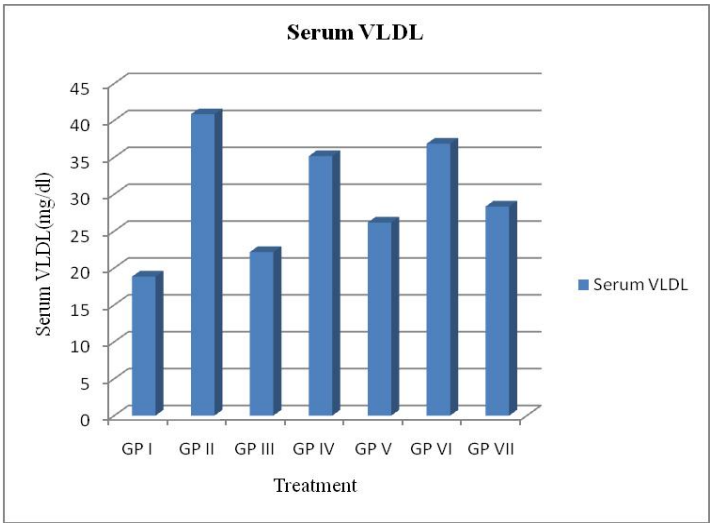

Fig 7. Effect on Serum VLDL level on Alloxan treated diabetic rats.

The ethanol and aqueous extracts of *S. cordifolia* was screened to explore the anti-diabetic activity because there have been no studies on it. However, in current study, presence of different phytochemical compounds in tested extracts and are possess hypoglycemic activity. The results of present study suggest that *Sida cordifolia* extracts possess significant reduction in increased BG, controls the loss of body weight due to DM and control the lipid metabolism complications such as TC, TG, LDL, and VLDL and HDL levels as standard drug Glibenclamide.

4. Conclusion

The results of current research conclude that *S. cordifolia* having significant bioactive phytochemical constituent which are protective agent against the development and progression of DM and possible related cardiovascular complications in DM.

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Conflict of Interest

None to declare.

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