HYPOGLYCEMICACTIVITY OF *SIDA VERONICA EFOLIA*INALLOX AN INDUCED DIABETICRATS

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ABSTRACT
Medical science still faces difficulties in developing side-effect-free medications for diabetes management. This has increased the need for safe and effective natural remedies that may lower blood sugar levels. The purpose of this study is to determine whether or not an *Ethyl Acetate Extract* of *Sida veronicaefolia* leaves reduces blood sugar levels in alloxan-induced diabetic albino rats. *Sida veronicaefolia* Ethyl Acetate extract activity was compared to that of the *metformin* (*250 mg*/kg p.o.) standard antidiabetic medication. Normal rats were given oral dosages of an Ethyl Acetate extract of *Sida veronicaefolia* leaf. At a dosage of 200 mg/kg, the Ethyl Acetate extract was significantly ($p<0.05$) hypoglycemic. Leaves extracted with ethyl acetate from the *Sida veronicaefolia* plant have anti-diabetic effects on a par with those shown in diabetic control mice. *Sida veronicaefolia*leaves extract in ethyl acetate has been shown to have potent and non-toxic anti-diabetic properties.

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INTRODUCTION
Herbs have recently gained popularity as both healthful dietary options and potential new medicinal ingredients. Despite limited understanding of the mechanisms by which herbal medicines derived from plant extracts work, they are increasingly being used to treat a wide range of clinical diseases, such as liver disease**[1]**, ischemia, perfusion injury, atherosclerosis, acute hypertension, hemorrhagic shock, diabetes mellitus, and cancer. Herbal treatments for diabetes mellitus have a long history of usage in Indian culture**[2]**.

Over 800 plants with possible anti-diabetic activity are included in the ethnobotanical data**[3]**.

Sida veronicaefolia is used in Ayurveda, Sidha, and Unani, and is also popular among rural, mostly tribal people in India (Orissa, Chhattisgarh, and Bihar) for the treatment of a wide range of illnesses. The leaves are used to make a juice that is utilized as a diuretic, laxative, diaphoretic, laxative, diaphoretic, and laxative**[4- 6]**. The spleen may also be enlarged with the help of leaves. This study set out to determine how well anEthyl acetate extract of *Sida veronicaefolia* leaves performed against diabetes brought on by the chemical alloxan in rats.

MATERIALSANDMETHODS
Animals
Albino wistar male rats weighing 150-200g was used for the present study. They were maintained in the animal house of School of pharmacy, Sunrise University, Alwar, for experimental purpose. The animals weremaintained under controlled conditions of temperature (23 ± 2C),humidity (50 ± 5%) and 12-h light-dark cycles. All the animals wereacclimatized for seven days before the study. The animals were randomized into experimental and control groups and housed individually in sanitized

polypropylene cages containing sterilepaddy husk as bedding. They had free access to standard pellets asbasaldietandwateradlibitum.Animalswerehabituate dtolaboratory conditions for 48 hours prior to experimental protocol tominimize if any of non-specific stress. All the studies conducted wereapproved by the Institutional Animal Ethical Committee (IAEC) of School of pharmacy, Sunrise University, Alwar,. According to prescribed guidelines of CPCSEA, Government o f India.

PlantMaterial

Leaves of the plant *Sida veronicaefolia* were obtained and identified from authentic sources. The leaves of the *Sidaveronicaefolia* were collected from Alwar and authenticated by Rajasthan University, Jaipur. The collected leaves were dried in shade, crushed to coarse powder and used for further studies.

Preparationofextract

150gmsleavespowderswereextractedwith400mlofE thyl Acetatefor18hrsby hot continuous extraction method. The Ethyl Acetate extract wasfilteredandpartitionedbyusingpetroleumethert oremoveimpurities .The solvent was evaporated under reduced pressure anddried in vacuum. The dried extract of *Sida veronicaefolia*thus obtained was used for the assessment of hypoglycemic activity.The extracts were subjected to preliminary qualitative tests **[7-8]** to identify the various phyto constituents present in leaves.

Acute Toxicity Studies

The Ethyl Acetate extractof*Sida veronicaefolia* leaves was found to be safe for further biological studies as no toxic effect and lethality was observed up to 10000 mg/ kg per oral in rat. Only the consumption offood was increased by 20% in the dose of 1000 and 2000 mg/kgduring 4h but remainingnormalafterwards.

Hypoglycemicactivityinnormalrats

Twenty-four albino rats weighing 150-200g were fasted for 18h andwere divided into four groups of six animals in each. The groupsincluded**i) (vehicle control)** received5%gumacaciainnormalsaline.

ii) (EAESV) received 550mg/kg, p.o.ofEthyl Acetate extract.

iii) (Standard) received *Metformin* (0.5 mg/kg p.o. 10%w/v, 1ml/200 g rat).

One milliliter of blood from the tail of each ratwas collected at '0' hour. At two hours of treatment, blood sampleswere collected again fromthetreated animals andblood glucosewasestimatedbyglucose estimated method**[9]**.

Alloxaninduceddiabetes

To induce hyperglycemia, alloxan monohydrate (150 mg/kg i.p.) was dissolved in NS and administered i.p. after the animals had fasted for 18 hours. The animals were given regular pellets and water ad libitum after alloxan was given to them for an hour. While the patient was only sedated somewhat, the blood sugar level was checked using an Accu Check advantage II glucose kit. BGL (BGLs) over 150mg/dl were used to determine which surviving *rodents* will be included in the research. Metformin (250 mg/kg) was administered to animals in Group II, whereas alloxan (as a control) was given to those in Group III. BGL (BGL) were measured at 1, 3, and 12 days after Groups IV received *Sida veronicaefolia* (550 mg/kg).

Effects of *Sida veronicaefolia* on Biochemical Parameters chemicallyInducedDiabetes

Changes in body weight, blood LP, and blood sugar levels were used to evaluate the efficacy of the herbal preparation in both normal and diabetic *rodents*. The last step was choosing One animal will be offered from each group. under diethyl ether anaesthesia, followed by the isolation of liver and kidney tissues for biochemical and histological analysis.

Results and Discussion

The leaves of the *Sida veronicaefolia* plant were identified, collected, and verified for this study. After being crushed into a coarse powder, the leaves were dried in the shade. All of the recommended plants had their medicinal powders extracted using petroleum ether and Ethyl Acetate. After vacuum concentration, all of the extracts were dried, weighed, and placed in desiccators for safekeeping.

Acutetoxicity Study

At predetermined periods, we checked up on the animals. No deaths occurred in any of the cases within the first 24 hours. Changes in the somatic motor activity and behavioral pattern, as well as the skin, fur, eyes, mucous membranes, respiratory, autonomous, and central nervous systems, have been observed. Convulsions and tremors were closely monitored as well. Toxicology tests were performed in accordance with OECD guidelines. Up to 5000 mg/kg of the *Sida veronicaefolia* was not associated with any adverse events or fatalities. Therefore, a

dose of 550 mg/kg was used for the study.

Hypoglycemicactivityinnormalrats

The*Sida veronicaefolia*Ethyl Acetate extract showed hypoglycemic activity by reducing blood glucose level significantly. It is also much effective when compare with the standard drug *Met form in*. It reduces blood glucose level after seven days at the 550mg/kg in rats compare with standard drug. We found that Ethyl Acetate extract of plant *Sida veronicaefolia* leaves is more effective in reducing the blood glucose level compare to thestandarddrug (*Metformin*).

The hypoglycemic activity of Ethyl Acetate extract of *Sida veronicaefolia* leaves in normal (nondiabetic) rats is shown in Table.1 The extract, at a dose of 550mg/kg, p.o.significantlylowered the blood, at 2h. However, the activity of the standard drug,*metformin* (*250 mg*/kg/day), was more pronounced (P<0.001).

Sida veronicaefolia impact* on Alloxan induced diabetic *rodents

Reactive oxygen species (ROS) play a role in the action mechanism of alloxan. Increased intracellular calcium due to free radical dismutation accelerates the death of pancreatic beta cells. Reactive oxygen species (ROS) are generated in a cyclic reaction that includes dialuric acid as a reduction product of alloxan (Winterbourn and Munday, 1989; Winterbourn*et al.,* 1989).

Elevated levels of glucose, triglycerides in the plasma, and total cholesterol are all hallmarks of the kind of diabetes generated in *rodents* by the drug alloxan (Dhandapani*et al.,* 2002). On the other hand, animals given either Ethyl Acetateextractof***Sida veronicaefolia*** or metformin showed reduced triglyceride and cholesterol levels and normal BGL. These results showed that the Lipid Profiles of diabetic *rodents* might be improved with the help ofEthyl Acetateextractof***Sida veronicaefolia***. Alloxan causes *rodents* to lose weight (Chougale*et al.,* 2007), which has been seen. The decreased visceral fat seen in diabetic *rodents* givenEthyl Acetateextractof***Sida veronicaefolia*** may be a result of the rodents' decreased overall body mass.

The hypoglycemic impact of Ethyl Acetateextractof***Sida veronicaefolia*** was partially responsible for preventing the body weight loss observed in this animal (*Table 2* and *Figure 1*). After 21 days, the Blood Glucose Level of the *rodents* treated with Ethyl Acetateextractof*Sida veronicaefolia* and metformin had decreased significantly (P > 0.01). Both groups BGL were similar to those of the healthy control animals (*Table 3* and *Figure 2*).

Treatment with Ethyl Acetateextractof*Sida veronicaefolia* and metformin resulted in a significant (P>0.01) decrease in serum total cholesterol and Triglyceride level, returning it to within normal range (*Table 4* and *Figure 3*). Total cholesterol in diabetics was 127.64 ±11.67, and triglycerides were 97.36±7.45. After being given Ethyl Acetateextractof***Sida veronicaefolia***, the mean and standard deviation dropped to 130.60±11.38 and 102.87±8.64, respectively. The values were reduced to the same extent as the control group.

Antioxidant indicators improved significantly after treatment with**Ethyl Acetateextractof***Sida veronicaefolia* and standard metformin (*Table 5* and *Figure 4*). Animals given **Ethyl Acetateextractof***Sida veronicaefolia* likely experienced less Alloxan-induced hyperglycemia since the specific plants contained in the *Sida veronicaefolia* had free radical scavenging properties.

Table1:HypoglycemicactivityofEthyl Acetateextractof*Sida veronicaefolia*leavesinnormal rats

Groups	Fasting	2hafterTreatment
Control(2%gumacacia)	78.05±0.03	**75.73±0.05**
Ethyl Acetateextractof*Sida veronicaefolia*(550mg/kg)	70.76±0.08	**56.43±0.03****
Std*Metformin*(250mg/Kg)	**69.76±0.25**	**41.45±0.04****

Valuesaremg(%), mean±SD, n=6ineachgroup,*p<0.01,**p<0.001ascomparetorespective control.

***Table 2*:Effectof Ethyl Acetateextractof*Sida veronicaefolia*onBody weight ofAlloxaninduceddiabetic*rodents*.**

Groups(n=6)	BW(gms)indifferentdays

	Day0	**Day7**	**Day14**	Day21
Control	180.40±12.73	181.67±17.34	181.34±14.23	**183.21±16.34**
DiabeticControl	195.28±17.28	201.23±18.26	205.93±18.06	**205.43±18.73**
Diabetictreatedwithstandard drug*Metformin*	176.53±13.67	179.64±14.61	178.67±14.31	**178.07±14.81**
Treated withEthyl Acetateextractof *Sida veronicaefolia*	**179.26±15.08**	**182.42±14.28**	**180.76±16.24**	**180.24±16.76**

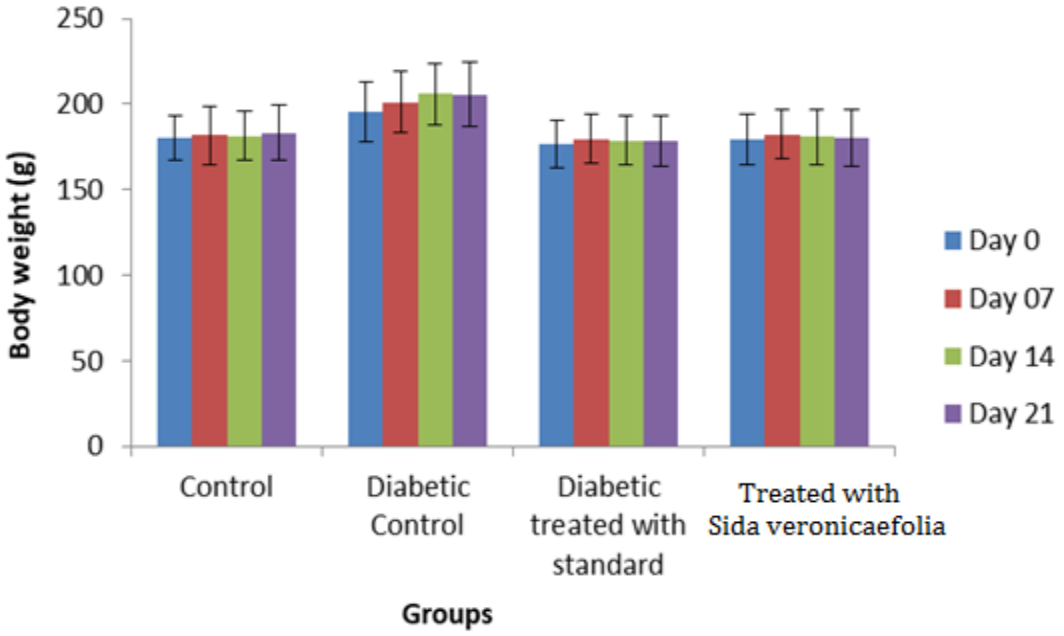

***Figure 1*: *Sida veronicaefolia*impact onbodyweight ofAlloxaninduceddiabeticrodents**

Table 3*:**Ethyl AcetateextractofSidaveronicaefolia*i m p a c t onbloodglucoseofAlloxaninduceddiabetic*rodents***

Groups(n=6)	Blood glucoselevel	
	Day0	Day21
Control	138.29±5.83	**137.43±7.68**
DiabeticControl	341.28±25.19	**338.25±28.19**

Diabetictreatedwithstandard (*Metformin)*	324.58±24.89	**142.39±12.36**
TreatedwithEthyl Acetateextractof*Sida veronicaefolia*	**317.53±26.40**	**140.46±15.28**

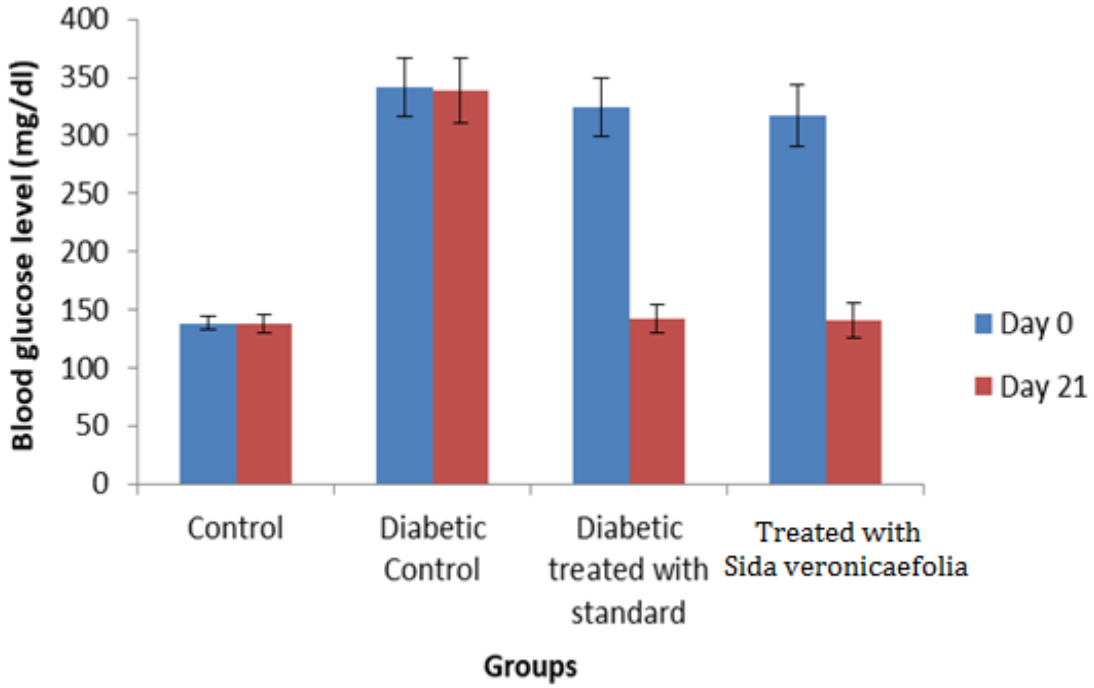

***Figure 2*:EffectofEthyl AcetateextractofSida *veronicaefolia*onbloodglucoseofAlloxaninduceddiabeticrodents.**

Table 4*:Effectof**Ethyl AcetateextractofSida veronicaefolia*onLipid ProfileofAlloxaninduceddiabetic*rodents***

Groups(n=6)	LP onDay21	
	Total Cholesterol (TC)(mg/dL)	**Triglyceride(TG)(mg/dL)**
Control	127.61±11.66	**97.37±7.46**
DiabeticControl	216.83±19.33	**217.65±19.74**
Diabetictreatedwithstandard*(Metformin)*	134.22±11.47	**112.38±9.35**
Treatedwith Ethyl Acetateextractof*Sida veronicaefolia*	**130.64±11.39**	**102.88±8.65**

Mean Values± SD; *P>0.01

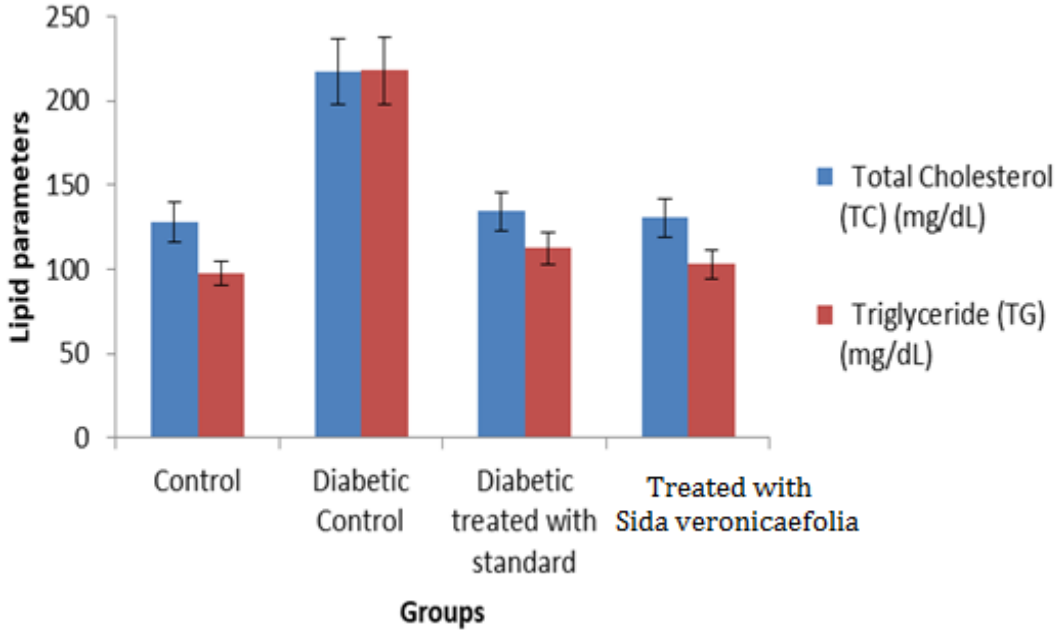

***Figure 3*:*Impact*of Ethyl AcetateextractofSida *veronicaefolia*onLPofAlloxaninduceddiabeticrodents.**

Table 5*:Effect of**Ethyl Acetateextractof*Sida veronicaefoliaon enzymes and non-enzymatic levels of tissues inAlloxan-induced diabetic rodents**

Groups	Enzymaticandnon-enzymaticassay		
	SOD(µg/50mgtissue)	**CAT(µmol/50mgtissue)**	GSH(µmol/50 mgtissue)
Control	42.06±3.81	37.18±2.48	**54.26±4.15**
DiabeticControl	22.35±1.96	21.85±1.85	**24.68±2.85**
Diabetictreatedwithstandard*(Metformin)*	40.53±3.25	35.63±2.45	**53.68±3.46**
Treated with Ethyl Acetateextractof*Sida veronicaefolia*	**41.27±3.61**	**34.25±2.96**	**50.62±4.24**

n=6albino*rodents*pergroup,Meanvalue±S.D.*P<0.01,whencomparedeachtreatedgroup with control group

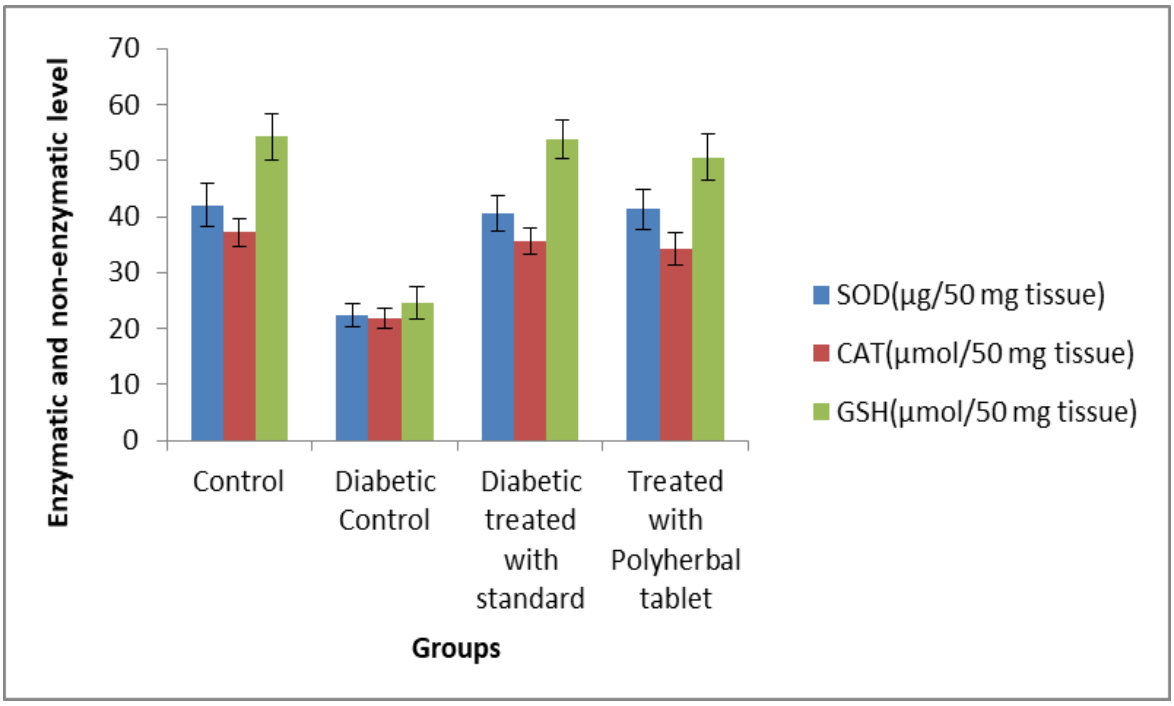

***Figure 4*:Alloxan-induced diabetes in rodents: on enzymes and non-enzymatic levels of tissues**

StatisticalAnalysis

Resultsareexpressedasmean±SD.Thedifferencesbetweenexperimentalgroupswerecomparedbyone-wayAnalysisofVariance (ANOVA) followed by Bonferroni's test. The results were considered statistically significant when P<0.05.

DISCUSSION

The Ethyl Acetate extract of *Sida veronicaefolia* leaves exhibited antidiabetic property. The antidiabetic effect of ethyl acetate extract of leaves of *Sida veronicaefolia*at the dose of 500mg/kg is evens lightly lower than *met formin*250mg/kg. Our results are supporting its use as folklore medicine forthe treatment of diabetes. Plants may act on blood glucose through different mechanisms, some of them may have in sulin-like substances and some may inhibit insulinase activity**[15,16]**. Stimulationof β-cells to produce more insulinand others may increase β-cellsinthe pancreas by activatingregenerationofpancreatic cells**[17]**.

The mechanism of alloxan diabetes has been the subject of manyinvestigations and it is now generally accepted that free radicals areselectively involved in the initiation of the damage that ultimatelyleadstoβcellsdeath**.**Therefore,thepancreasi sespeciallysusceptibletotheactionofalloxaninducedfreeradicaldamage.Many substances have been shown to ameliorate the diabetogenicityof alloxan in animals, which protect by reacting with free radicalsformed from alloxan during its interaction with β cells, or preventradical formation**[18]**. ThepresentfindingindicatesthatadministrationofEthyl AcetateextractofSida *veronicaefolia*confirms the possibility that the major function of the extract is ontheprotectionofvitaltissuesincludingthepancreas,therebyreducing the causation of diabetes in these animals**[19]**. Therefore,protective effect ofEthyl AcetateextractofSida *veronicaefolia*extract on BGLofalloxaninduceddiabeticratscouldbeattributeddirectlytoscavengingactivityandformoreextenttothereg enerativepropertiesoftheextract.

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