

# Antidiabetic Aptitude of *Cordia sebestena* and its Outcome on Biochemical Parameters, Serum Electrolytes, and Hematological Markers

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## ABSTRACT

**Objective:** The present study investigated the antidiabetic outcome of ethanolic extract of *Cordia sebestena* fruit (EECSF) in streptozotocin (STZ)-induced diabetogenic rodents and evaluated its consequence to improve the level of biochemical parameters, serum electrolytes level, and hematological indices along with its impact on body weight. **Materials and Methods:** The albino rodents were selected to observe oral glucose tolerance test by oral intake of aqueous glucose solution (4 g/kg, body weight) in normal rodents and assessment of blood glucose level after administration of EECSF at 100 and 200 mg/kg and standard drug glibenclamide at 0.6 mg/kg, body weight. Antidiabetic activity was estimated in the chronic biological model by STZ (65 mg/kg/i.p.)-induced diabetes in rodents escorted by the determination of blood glucose. Further pharmacological research was carried out to explore the effect of EECSF on body weight, variations in biochemical parameters including aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, and total protein, transformations in serum electrolytes such as Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, and Ca<sup>2+</sup> along with estimation of hematological indices such as red blood cells, white blood cells, hemoglobin, lymphocytes, neutrophils, eosinophils, and monocytes. **Results:** It was discovered that EECSF significantly lowered the blood glucose level of diabetic rodents along with enhancement in body weight. Correspondingly, EECSF significantly ameliorated the biochemical parameters, serum electrolytes, and hematological indices. **Conclusion:** The results demonstrated the antidiabetic potential of EECSF in STZ-induced diabetes in rodents, and it could be selected to benefit from diabetes and its affiliated complexities inclusive of anemia, diabetic nephropathy, retinopathy, neuropathy, and hepatitis.

**Key words:** Anemia, antidiabetic, *Cordia sebestena*, Glucose, Streptozotocin

## INTRODUCTION

Diabetes is a metabolic disorder which evolves from imperfect insulin action and secretion.<sup>1</sup> In congruence with the International Diabetes Federation, diabetes is among the utmost gigantic health hassles. The planetary preponderance of hyperglycemic patients is hypothesized to augment from 415 million in 2015 to 642 million by 2040, symbolizing the escalation of 35.5% in the next 25 years.<sup>2</sup> Diabetes inaugurates multiple organ ruination including eyes, kidneys, liver, heart, and blood vessels.<sup>3</sup> Conventionally, blood investigation is one of the screening proceedings to authenticate general health. Glucose, cholesterol, calcium, total protein, alkaline phosphates, uric acid, sodium, potassium, and chloride levels are indicative values for diabetes mellitus<sup>4</sup> and its associated diseases such as coronary artery disease, dyslipidemia,<sup>5</sup> diabetic nephropathy,<sup>6</sup> chronic hepatopathy, and liver disease.<sup>7</sup> Innumerable plants are affluent source of antidiabetic consequence and have been practiced in

traditional folk medicine for inverting hyperglycemia,<sup>8</sup> and innumerable plant derived antidiabetic drugs have obtained authorization from WHO.<sup>9</sup>

*Cordia sebestena* (L.) (*Boraginaceae*) is universally recognized as Geiger tree. It comprises furthermore 300 species allocated extensively in East Africa, Mexico, West Indies, Central America, Sri Lanka, India, and Nigeria. Ethnomedicinally, the leaves are used as emollient and in the treatment of bronchitis, cough, fever, and influenza. The plant leaves showed antidiabetic and antibacterial activity. Sebestenoids A–D have been isolated from the fruits of *C. sebestena* and represented activity against Alzheimer's disease by inhibiting aspartic protease.<sup>10,11</sup> The current research proposed antidiabetic potential of ethanolic extract of *C. sebestena* fruit (EECSF) employing streptozotocin (STZ) executed diabetes in rodents along with its influence on biochemical parameters, serum electrolytes level, and hematological markers.

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## MATERIALS AND METHODS

### Chemicals

All the chemicals used were of LR grade, purchased from Qualigens Fine Chemicals, Mumbai, India.

### Fruit collection and authentication

The fresh and matured fruits were collected from the roadside garden of College of Pharmacy, University of Sharjah, Sharjah, United Arab Emirates. Prof. Sudhansu Ranjan Swain, Director, Department of Pharmacognosy, Moradabad Educational Trust, Group of Institutions, Faculty of Pharmacy, Moradabad, Uttar Pradesh, India, attained identification and authentication.

### Fruit extraction

The freshly collected fruits (500 g) of *C. sebestena* were dried and powdered at room temperature (24°C–28°C). The powdered plant material was macerated with petroleum ether; the marc was exhaustively extracted with ethanol for 3 days. The extract was dried by rotator evaporator (Buchi, U.S.A) under reduced pressure and procured in desiccator and the extract achieved was subjected to biological exploration.

### Animals

Albino rodents (150–200 g) of either sex were nominated for pharmacological study. The animals were settled under standard environmental surroundings and provided with food and water *ad libitum*. The animals were put on starving for 12 h before the investigation, and study protocols were in conformity with proceedings authorized by the institutional animal ethics committee of Moradabad Educational Trust, Group of Institutions, Faculty of Pharmacy, Moradabad, Uttar Pradesh, India

### Acute toxicity study

The acute toxicity of EECSF was evaluated at doses of 5, 50, 300, 500, and 2000 mg/kg, as per the OECD 423 guideline, and dose of 2000 mg/kg represented toxic indications. Therefore, in agreement with OECD guideline 423, it is expressed as a LD<sub>50</sub> cutoff value. Doses, 100 and 200 mg/kg, bodyweight were preferred for pharmacological inspection by fixed-dose methods.<sup>12</sup>

### Assembling of animals for antidiabetic studies

Experimental rodents were categorized into five groups ( $n = 6$ ). Group-I (normal control) was administered with distilled water (0.5 mL/kg, body weight, p.o.). Group-II (diabetic control) was administered with 5% Tween, p.o., Group-III permitted 0.6 mg/kg, body weight of glibenclamide p.o., and Group IV–V permitted 100 mg/kg and 200 mg/kg, body weight, p.o., of EECSF, respectively.

### Antidiabetic studies

#### Oral glucose tolerance test in normal rodents

The normal rodents were fasted overnight to inspect oral glucose tolerance test and were divided into four groups ( $n = 6$ ). Group-I (normal control) was provided with distilled water orally, Group-II (positive control) was provided with glucose (4 g/kg) body weight. Group-III was administered with glibenclamide (10 mg/kg, body weight, p.o.). Group-IV and V were treated with 100 and 200 mg/kg, body weight, p.o., of EECSF, respectively, 30 min before the oral administration of glucose (2 g/kg) body weight. Blood was collected from the tail at 0, 30, 60, and 90 min intervals for estimation of glucose level.

#### Experimental inception of diabetes

Albino rodents (150–200 g) body weights were selected for the biological activity. Food was terminated 18 h before administration of STZ. STZ 65

mg/kg, body weight in ice-cold sodium citrate buffer (0.01 mol/L and pH 4.4) was injected intraperitoneally. Diabetes was affirmed by estimating fasting glucose level on the 2<sup>nd</sup> day postadministration of STZ and rodents with glucose level elevated than 200 mg/dL were assigned as diabetogenic.<sup>13</sup>

### Biological study on streptozotocin-induced diabetic rodents

The biological study was performed on animal groups by providing EECSF and standard drug for 21 days sequentially. The animals were fasted 18 h before processing for study and blood glucose levels were estimated on (considered as 0 day reading) 7, 14, and 21 days. The impact of EECSF at dose of 100 and 200 mg/kg along with glibenclamide at dose of 0.6 mg/kg, on body weight was estimated on 7<sup>th</sup>, 14<sup>th</sup>, and 21<sup>st</sup> day.

### Assessment of body weight

The body weight of the animals was measured at 0 day and every 7<sup>th</sup> day for the period of 21 days.

### Blood collection and estimation of biochemical parameters

On 21<sup>st</sup> day, rodents were starved overnight and sacrificed by cervical decapitation and blood was assembled. For serum samples, blood was coagulated followed by centrifugation at 3000 rpm for 20 min at 4°C to separate serum. Sera were divided in aliquots and maintained at –80°C for biochemical assay. Fasting serum glucose level was estimated by glucose oxidase-peroxidase method employing kit of Randox Laboratories Ltd, U.K. Aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase (ALT, AST, and ALP) were assessed using standard kits supplied by Teco Diagnostics, U.S.A. Total bilirubin (TB) in the serum was estimated using commercial kit supplied by Human Diagnostics, Germany, and total protein (TP) was evaluated by method designed by Lowry *et al.*<sup>14</sup>

#### Estimation of serum electrolytes

To assess the effect of diabetes on serum electrolytes, Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, and Ca<sup>2+</sup> were estimated.<sup>15</sup>

#### Estimation of hematological indices

Red blood cells (RBCs), white blood cells (WBCs), hemoglobin (Hb), lymphocytes, neutrophils, eosinophils, and monocytes were estimated employing hematology analyzer SB21, New Delhi, India.

### Statistical analysis

The data achieved were investigated to statistical analysis using one-way analysis of variance followed by Newman–Keuls test employing Graph-Pad Prism version 5.01, Graph-Pad software, San Deigo, California, U.S.A. The values were represented as mean ± standard error of the mean for six rodents.

## RESULTS

### Ethanollic extract of *Cordia sebestena* fruit dose election

LD<sub>50</sub> was estimated following the OECD guidelines to fix the dose for pharmacological screening. In this study, it was contemplated that up to a maximum dose of 2000 mg/kg body weight, there were no alterations in normal behavioral format and no prodromal of toxicity and mortality were observed. The pharmacological assessment was accomplished at doses of 100 and 200 mg/kg body weight.

### Oral glucose tolerance test in normal rodents

The significant demotion in blood glucose level ( $145.2 \pm 0.85$  and  $84.3 \pm 0.4$ ;  $P < 0.01$  and  $0.05$ ) was perceived for ethanolic extract (100 mg/kg) at 60 and 90 min as compared to the animals in positive control group ( $148.2 \pm 0.9$  and  $138.0 \pm 0.56$ ). The same extract at 200 mg/kg has more significantly reduced the blood glucose level to  $81.5 \pm 0.7$ ,  $P < 0.05$  at 90 min compared to positive control group. Glibenclamide demonstrated its potent hypoglycemic effect by downgrading the elevated glucose level to almost normal level ( $92.5 \pm 0.54$  and  $82.6 \pm 0.5$ ;  $P < 0.05$ ) compared to positive control group at 60 and 90 min, respectively. The results are represented in Table 1.

### Biological study on streptozotocin-induced diabetic rodents

The biological study was executed for 21 days on STZ-induced diabetic rodents, and its results are tabulated in Table 2. EECSF at dose of 200 mg/kg indicated minimization of 33.16% and 32.39% in blood glucose level on the 14<sup>th</sup> day and 21<sup>st</sup> day ( $P < 0.001$ ), respectively. It was also explored that glibenclamide reduced 40.12% and 53.93% in blood glucose level on the 14<sup>th</sup> and 21<sup>st</sup> day ( $P < 0.001$ ).

### Consequence of ethanolic extract of *Cordia sebestena* fruit on body weight in diabetic rodents

The body weight of rodents at different time intermissions during the study is entitled in Table 3. The percentage change in body weight of rodents for all groups was computed. Group-I (-ve control) revealed elevation of 3.7% in body weight. Group-II (+ve control) expressed reduction of 10.3% in body weight. Group-III, IV, and V represented 2.85%, 0.41%, and 1.89% enhancement in body weight. Hence, it is affirmed that EECSF is effectual in restricting weight loss due to diabetes.

### Outcome of ethanolic extract of *Cordia sebestena* fruit on biochemical parameters

The level of ALP, ALT, AST, and TB was intensified in Group-II (+ve control) by 80.5%, 115.79%, 104.58%, and 262.5% although TP level was downturn by 39.04% compared to Group-I (-ve control) rodents. EECSF at 100 and 200 mg/kg dose subsided the level of ALP by 5.41%, 19.76%; ALT by 10.09%, 27.03%; AST by 20.72%, 29.76%; and TB by 10.34%, 34.48%, whereas TP level was ascended by 35.4%, 19.79%, respectively. However, glibenclamide declined ALP by 34.99%, ALT by 49.05%, AST by 45.06%, and TB by 58.62% and increased TP level by 1.82% as

**Table 1: Consequence of ethanolic extract of *Cordia sebestena* fruit on oral glucose tolerance test in normal rodents**

Groups	Blood glucose level (mg/dL)			
	0 min	30 min	60 min	90 min
Group-I (negative control)	82.3±0.45	84.0±0.35	82.0±0.9	81.3±0.7
Group-II (positive control)	84.3±0.5	122.0±0.9	148.2±0.9	138.0±0.56
Group-III	83.6±0.6*	94.8±0.9***	92.5±0.54***	82.6±0.5***
Group-IV	83.0±0.4***	119.6±0.5***	145.2±0.85**	84.3±0.4***
Group-V	81.7±0.3**	101.5±0.4*	131.5±0.6*	81.5±0.7***

Values are mean±SEM; n=6; \* $P < 0.001$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.05$  compared with positive control. SEM: Standard error of mean

**Table 2: Consequence of ethanolic extract of *Cordia sebestena* fruit on blood glucose levels in streptozotocin-induced diabetes in rodents**

Groups	Blood glucose level (mg/dL)			
	0 Day	7 Days	14 Days	21 Days
Group-I (negative control)	85.5±2.5	85.4±3.21	88.60±2.6	89.5±2.1
Group-II (positive control)	220.4±3.2	261.5±3.4	283.1±3.1	265.5±3.2
Group-III	201.4±3.4*	168.6±2.8***	169.5±3.5*	122.3±3.4*
Group-IV	217.6±4.2 (NS)	246.5±4.3**	221.6±3.6*	201.5±3.1*
Group-V	206.5±3.7***	198.6±3.4***	189.2±3.4*	179.5±3.4*

Values are mean±SEM; n=6; \* $P < 0.001$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.05$  compared with positive control. SEM: Standard error of mean; NS: Nonsignificant

**Table 3: Consequence of ethanolic extract of *Cordia sebestena* fruit on body weight in streptozotocin-induced diabetes in rodents**

Groups	Body weight (g)			
	0 day	7 days	14 days	21 days
Group-I (negative control)	171.6±0.6	173.3±0.4	178.3±0.8	178.2±0.6
Group-II (positive control)	167.3±0.8	165.2±0.7	155.6±0.6	151.6±0.3
Group-III	170.3±0.9***	175.3±0.9***	176.6±0.7***	175.3±0.7***
Group-IV	169.6±0.6**	167.2±0.7*	161.3±0.6***	170.3±0.4***
Group-V	171.3±0.5*	172.3±0.5***	171.5±0.5***	174.6±0.3***

Values are mean±SEM; n=6; \* $P < 0.001$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.05$  compared with positive control. SEM: Standard error of mean

**Table 4: Consequence of ethanolic extract of *Cordia sebestena* fruit on serum enzymes and biochemical parameters in streptozotocin-induced diabetes in rodents**

Groups	ALP (IU/L)	ALT (IU/L)	AST (IU/L)	TB (mg/dL)	TP (g/L)
Group-I (negative control)	95.7±2.1	78.50±2.0	124.3±2.4	0.8±0.01	6.3±0.01
Group-II (positive control)	172.75±2.4	169.4±2.1	254.3±2.6	2.9±0.08	3.84±0.03
Group-III	112.30±1.3*	86.30±2.6*	139.7±3.2*	1.2±0.06*	3.91±0.06*
Group-IV	163.4±2.1**	152.3±2.5*	201.6±2.9*	2.6±0.04**	5.2±0.08*
Group-V	138.6±2.1*	123.6±2.7*	178.6±3.2*	1.9±0.03*	4.6±0.07*

Values are mean±SEM; n=6; \*P<0.001; \*\*P<0.01; P<0.05 compared with positive control. SEM: Standard error of mean; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TB: Total bilirubin; TP: Total protein

**Table 5: Consequence of ethanolic extract of *Cordia sebestena* fruit on serum electrolytes concentrations in streptozotocin-induced diabetes in rodents**

Groups	Na <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Ca <sup>2+</sup> (mEq/L)
Group-I (negative control)	148.3±1.2	4.7±0.01	23.5±0.01	7.1±0.03
Group-II (positive control)	123.5±2.1	6.9±0.02	19.5±0.03	9.5±0.09
Group-III	142.6±2.2*	5.2±0.06***	22.6±0.05*	7.98±0.03*
Group-IV	132.5±2.1*	6.7±0.06**	20.4±0.06*	8.84±0.03*
Group-V	139.5±2.8*	5.4±0.08*	21.2±0.07*	8.1±0.07*

Values are mean±SEM; n=6; \*P<0.001; \*\*P<0.01; \*\*\*P<0.05 compared with positive control. SEM: Standard error mean

**Table 6: Consequence of ethanolic extract of *Cordia sebestena* fruit on hematological indices in streptozotocin-induced diabetes in rodents**

Hematological indices	Groups				
	Group-I (negative control)	Group-II (positive control)	Group-III	Group-IV	Group-V
RBC (×10 <sup>6</sup> /μL)	7.19±0.03	4.35±0.05	6.9±0.05*	4.57±0.03**	6.4±0.07*
WBC (×10 <sup>3</sup> /μL)	14.5±0.21	10.25±0.2	11.87±0.6*	13.2±0.8**	14.60±0.7*
Hb (g/dL)	13.1±0.02	9.8±0.03	12.3±0.04*	10.10±0.06*	11.89±0.05*
Lymphocytes (%)	23.5±0.6	35.6±0.7	22.6±0.7*	33.4±0.2**	21.6±0.2*
Neutrophils (%)	46.3±0.6	54.90±0.9	47.6±0.7*	50.4±0.6***	49.5±0.3**
Eosinophils (%)	2.36±0.02	4.1±0.03	2.98±0.04*	3.9±0.04**	3.01±0.07*
Monocytes (%)	4.19±0.03	6.89±0.05	4.96±0.08*	6.04±0.06*	5.2±0.07*

Values are mean±SEM; n=6; \*P<0.001; \*\*P<0.01; \*\*\*P<0.05 compared with positive control. RBC: Red blood cell; SEM: Standard error mean; Hb: Hemoglobin; WBC: White blood cell

compared to Group-II (+ve control) rodents. The results are tabulated in Table 4.

### Prominence of ethanolic extract of *Cordia sebestena* fruit on serum electrolytes

The results in Table 5 signified the variations in serum electrolytes level of diabetic rodents treated for 21 days with EECSF 100 and 200 mg/kg and glibenclamide 0.6 mg/kg, body weight. The concentrations of all the estimated electrolytes were diminished in Group-II rodents except for Cl<sup>-</sup> as compared to Group-I. The treatment with EECSF at 100 mg/kg significantly (P < 0.001) ameliorated altered concentrations of all the estimated electrolytes. EECSF at 200 mg/kg and glibenclamide significantly (P < 0.001) maintained the levels of electrolytes to conventional framework.

### Precedence of ethanolic extract of *Cordia sebestena* fruit on hematological indices

The results in Table 6 explicated that the significant reduction in the levels of RBC and Hb was noticed in Group-II rodents, whereas the levels of WBC, lymphocytes, neutrophils, eosinophils, and monocytes were inflated. EECSF at 200 mg/kg significantly elevated the levels of RBC and Hb to approximately mainstream range and the elevated levels of WBC, lymphocytes, neutrophils, eosinophils, and monocytes were significantly reduced and maintained to near-normal.

## DISCUSSION

The emergence of diabetes and liver disease is augmenting around the globe. The alliance between diabetes and liver disease is influential to diabetologist, hepatologist, and physicians. There are multiple hepatic diseases integrated to diabetes such as nonalcoholic fatty liver disease,

cholelithiasis, cholecystitis, hepatitis, cirrhosis, and hemochromatosis and other liver diseases.<sup>16</sup> A prodigious extension in the consumption of herbal medicaments has been inspected in the past 30 years. The World Health Organization determined that 80% of the world population living in developing countries depends on herbal medicinal products.<sup>9,17</sup> Hence, the present study was proposed to estimate the antidiabetic outcome of *C. sebestena* fruit extract.

Pancreatic  $\beta$ -cells via the glucose transporter 2 acquire STZ where it results in necrosis by DNA interruption. Finally, pancreatic  $\beta$ -cell necrosis results in depredation in insulin release, causing elevation in blood glucose level.<sup>2</sup> To inspect the antidiabetic outcome of EECSE, the biological study was performed for 21 days and the outcome affirmed that EECSE accommodates antidiabetic potential in dose-dependent manner. The significant antidiabetic outcome was observed at a dose of 200 mg/kg of EECSE as compared to glibenclamide-treated rodents.

Diabetes intensifies hepatic glucose constriction. It is evidenced that diabetes promotes serum activity levels of liver enzymes such as ALT, AST, and ALP. All these enzymes are present in multiple organs of the human body however are prominent in liver; elevated levels of these liver marker enzymes are noticed in hepatitis, cirrhosis, jaundice, and other hepatic dysfunctions. Similarly, bilirubin is an excretory product of hem, which is produced from oxidation of biliverdin and is among the key factors to estimate the liver function. Liver is responsible for conjugation of bilirubin with glucuronic acid to produce water-soluble derivative acceptable for excretion through bile, and extension in bilirubin level is an evidence of liver dysfunction. Similarly, declination in total protein levels may accord to impediment of oxidative phosphorylation process that result in depletion of protein absorption, reduction in protein synthesis, and an elevation in catabolic process. All these indicators reflected the hepatocytes disfigurement in STZ-induced diabetic rodents.<sup>3,18-21</sup> To investigate the outcome of EECSE on liver function distortion associated with diabetes, serum assessment of ALT, AST, ALP, bilirubin, and TP was accomplished and results expressed that EECSE at 200 mg/kg remarkably reforms the levels to normal parameter in diabetic rodents representing hepatoprotective efficacy of EECSE.

Electrolytes in the serum are crucial in metabolic activities, systematic operation of cells and enzymes, and concentration gradient.<sup>2</sup> Alterations in their concentrations designate development of various diseases. Diabetic patients may experience disorganization of water, and electrolytes balance evolved from insulin inadequacy, hyperglycemia, and hyperktonemia.<sup>22</sup> Diabetes mellitus causes hyperglycemia, finally resulted in cell dehydration and movement of  $K^+$  ions into extracellular fluid (ECF). This process intensified the activity of parietal cells of distal and cortical collecting tubules, resulting in increased renal excretion of  $K^+$ . However, glycosuria discovered in diabetes leads to excretion of abundant water,  $Na^+$ , and  $K^+$  in urine. Hence, it is evidenced that electrolytes and water loss associated with diabetes would result in loss of ECF, resulting in loss of  $Na^+$  and  $K^+$  concentration.<sup>23</sup> The function of  $Na^+/K^+$ -ATPase,  $Ca^{2+}/Mg^{2+}$ -ATPase,  $Na^+/Ca^{2+}$  exchanger, and  $Ca^{2+}$  pump established in cell membrane, mitochondria, and endoplasmic reticulum has been diminished in hyperglycemia. It was also observed that diabetic ketoacidosis initiated promotion in the level of  $Cl^-$  due to serum glucose generation via gluconeogenesis, glycogenolysis, ketogenesis, and ketoacidosis, resulting in blood acidification causing acid-base imbalance in body. Therefore, to balance it,  $Cl^-$  level is increased in the body.<sup>24-26</sup> However, in the present study, it was discovered that EECSE at 100 and 200 mg/kg amended the electrolyte imbalance significantly by increasing the diminished levels of  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$  and reducing the level of  $Cl^-$  in treated rodents.

Diabetes developed changes in multiple hematological parameters and immune system. However, toxicological studies discovered alterations in

hematological indices after ingestion of medicinal plant extract or drugs. Hence, assessment of hematological indices is a vital tool in detecting deleterious effect of synthetic drugs and plant extracts.<sup>27</sup> The depletion in RBC count is frequently affiliated to anemia, and its presence in diabetes can be affiliated with various factors such as glomerular filtration rate, urinary albumin excretion rate, and HbA1c levels.<sup>28</sup> Anemia in diabetes is because of increased nonenzymatic glycosylation of RBC membrane protein, which correlates with hyperglycemia and oxidation of glycosylated membrane protein and hyperglycemia resulted in an increase in the development of lipid peroxidases leading to hemolysis.<sup>29</sup> WBCs are accountable for body defense against infections and it is familiar that reduced level of WBC in diabetes resulted in suppressed immune system.<sup>30,31</sup>

In the current study, it was discovered that diabetic rodents represented unsettled blood indices. It was observed that animals in diabetic control group represented declined RBC and Hb levels as compared to normal and treated animals. The treatment with EECSE reconstructed the levels of RBC and its related indices, proclaiming that EECSE possessed few phytoconstituents that could elevate RBC and Hb. Moreover, EECSE at 100 and 200 mg/kg ameliorated WBC count, lymphocytes, neutrophils, eosinophils, and monocytes levels, therefore contributing to its immunomodulatory effect.

## CONCLUSION

The conclusion of the current research study is that *C. sebestena* fruit exhibited antidiabetic potential and maintained the level of various serum enzymes and biochemical parameters such as ALP, ALT, AST, TB, and TP which are altered in diabetes. The fruit extract maintained the level of serum electrolytes and hematological indices to normal in diabetic animals. Therefore, it can be recommended that *C. sebestena* fruit not only maintains normal blood glucose level rather has appreciable effect on various parameters that are disturbed in diabetes.

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## CONFLICTS OF INTEREST

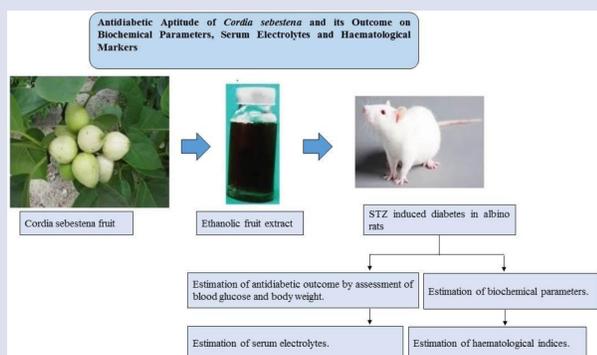
The authors declare no conflict of interest.

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## GRAPHICAL ABSTRACT



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## SUMMARY

- The antidiabetic effect of *Cordia sebestena* fruit was investigated against streptozotocin-induced diabetes in rats. The study also includes the effect of fruit extract on the levels of biochemical parameters, serum electrolytes, and hematological markers in diabetic rats.

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