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***Research Article** (Open Access)*

TINOSPORA CORDIFOLIA ATTENUATES HYPERGLYCEMIA AND PANCREATIC OXIDATIVE STRESS IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT
Diabetes mellitus (DM) is a widely spread multifactorial disorder with multiple etiology characterized by hyperglycemia, increased oxidative stress, impaired carbohydrate, fat, and protein metabolism. Continuous increase in the incidence and associated mortality needs serious attention and concern. Shifting approach towards phytotherapy has drawn the attention of the entire research community because it modulates diabetes multidimensionally. The present investigation involves an herbal approach to regulate diabetes in which ethanolic extract of *Tinospora cordifolia* (250mg/kg.b.wt) stem was and Diabetogenic material was Alloxan (100 mg/kg.b.wt). Wistar rats were divided into five groups each containing five rats. Extract of *Tinospora cordifolia* (250mg/kg.b.wt) stem was administered for 30 days with interval of 10 days. After each interval rats were sacrificed and the sample was collected for Biochemistry parameters of blood, and an anti-oxidative assay of pancreatic tissues. Research reveals hypoglycemic, as well as anti-oxidative nature of the *Tinospora cordifolia* extract. Deregulated parameters (Glucose, Insulin, amylase, lipase, ALT, AST, serum electrolytes, Differential WBC counts, SOD, GPx, GST, Catalase, GSH, and Total Thiol) were restored to normalization with extract treatment after 30 days. Results were statistically significant and recommend as a potential candidate in preventing and treating diabetes, hyperglycemia and oxidative stress-mediated complications. However, a multidisciplinary collaborative study is required on a large number of sample sizes for the clinical purpose of the development of novel drugs.

***Keywords*:** *Diabetes, Alloxan, Hyperglycemia, Oxidative stress, Pancreas, Tinospora cordifolia*

INTRODUCTION
Diabetes mellitus (DM) is a widely spread multifactorial disorder characterized by increased blood glucose resulting from absence, reduced, or impaired insulin secretion. It is a disorder of multiple etiologies characterized by hyperglycemia, increased oxidative stress, impaired carbohydrate, fat, and protein metabolism. Continuous increase in the incidence and associated mortality needs serious attention and concern (Salehi *et al.,* 2019). Inadequate regulation of the blood sugar imposes serious consequences for health like macrovascular, microvascular, ketoacidosis, hyperosmolality, and lastly to multiorgan failure. Urgent need to diagnose and the suitable hypoglycemic agent is required to stop at earliest to stop its further proliferation.

Intake of excess nutrients rich stuffs enriched in carbohydrates, and fatty substances above permissible limit leads to overstimulation of beta cells, are assumed to be an important patron to decreased insulin secretion in Diabetes (Gerber *et al.,* 2017). Pancreatic beta cells are one of the most metabolically active tissues in the human body, and they are highly dependent on oxidative metabolism for the synthesis of adenosine triphosphate (ATP), at enhanced glucose concentrations. β- Cell in the pancreas is 1-2% of the entire pancreatic volume and receives 15% of the total pancreatic blood supply reflects the extensive engagement of the cells in metabolic activity. Oxidative metabolism for the synthesis of ATP generates excess reactive oxygen species (ROS) which are an unavoidable by-product of mitochondrial respiration during glucose stimulation.

An imbalance may render beta cells highly susceptible to damage induced by either oxidative stress or oxygen deprivation (Jansson *et al.,* 2002). The exocrine and endocrine part of pancreas is highly coordinated, and malfunction of endocrine also subjects to altered exocrine activity and vice-versa (Altay *et al.,* 2019). Earlier studies have concluded that stress caused due to Reactive oxygen species could be recognized as key mediator of intra-acinar event and systematic inflammatory response in the exocrine function of pancreas pertaining to acute pancreatitis (Singh *et al.,* 2016). A study among diabetics revealed that diabetic individual had a greater level of pancreatic fibrosis and evidence of chronic pancreatitis than controls (Braganza *et al.,* 2011).

In the present study Alloxan was used as create experimental diabetic model in rats due of its selective the destruction of pancreatic β cell because of its free radical production upon decomposition. Action of Alloxan toxicity is exhibited by its rapid uptake through GLUT2 transmembrane protein. After entry of Alloxan to pancreatic β-cells its reduction occur to dialuric acid which is further oxidized to its pre-existing state i.e., Alloxan completing redox cycle followed with formation of various reactive oxygen species (ROS) and super oxides results in the formation of different radicals are involved in the necrosis of the beta cell through various pathways (Bromme *et al.,* 2005).

Sensible treatment of diabetes with widely available pharmaceuticals targets specific pathways to regulate diabetes complications leaving various side effects behind. However, diabetes is a multifactorial disorder, in such case multiple target site drugs should be probed in to practice with less cost and negligible side effects. Shifting approach towards phytotherapy could lead to treat diabetes multidimensionally

Tinospora cordifolia is also one of them which possesses hypoglycemic property as well it has huge anti-oxidative properties that modulate the complexity and severity of diabetes mellitus. It is a large extensively spreading glabrous, perennial, deciduous plant having a succulent stem with papery bark belongs to the Menispermaceae family widely distributed in the Indian subcontinent (Dhama *et al.,* 2017).

MATERIALS AND METHODS

For the present research work healthy wistar rats (*Rattus norvegicus*) of weight ranging from 180-200 gm were selected and provided ambient physical and physiological condition as per the standard protocol and all the experimental protocol was carried based on the guideline adopted by Mahavir Cancer Sansthan ethical comittee, Phulwarisariff Patna.

Feeding of rats

The laboratory rats were fed on laboratory prepared enriched bread constitutes wheat flour, jaggery, powdered milk and gram flour. For providing vitamin supplement they were fed with carrot, sprouted gram and sprouted moong bean.

Plant materials: Stem of *Tinospora cordifolia*

Preparation of ethanolic extract: The dried plant materials i.e., stem of *Tinospora cordifolia* blended to fine powder and then soaked with absolute ethanol and kept in dark to avoid from light for 48 hours in order to get the secondary metabolites dissolved in to the solvent. After 48 hours extract was filtered till the clear material appeared. The solvent containing secondary metabolite of both the plant was mounted on the vaccuma rotary evaporator at 40^0C. The extract was kept on the vaccuma rotary till the thick paste was not appeared devoid of any solvent material. The thick paste colloidal was was lyophillysed in lyophyliser (Labconco, USA). The lyophilized plant extract were stored in deep freezer at $^{-}80^0$ C until further test.

Experimental Design: Male healthy rats were utilized for the experimental work divided into five groups namely.

Group I - Normal control
Group II – Diabetic control (DM) (Alloxan treated 100mg/kg.b.wt)
Group III - DM + 10 Days *Tinospora cordifolia* extract (TCE) fed (250mg/kg.b.wt).
Group IV - DM + 20 Days *Tinospora cordifolia* extract (TCE) fed ((250mg/kg.b.wt).
Group V - DM + 30 Days *Tinospora cordifolia* extract (TCE) fed ((250mg/kg.b.wt).

Except normal, all the rats were made diabetic and only those rats were considered for the experimental group which persisted diabetic condition (glucose >250mg/dl) after 10-12 days of Alloxan induction. After subsequent interval of the time different types of sample were collected for various tests.

Induction of diabetes: Diabetes was induced by repeated dose of Alloxan monohydrate 100 mg/kg. b.wt in cold citrate buffer bearing pH 4.5.

Sample collection: After the treatment of the extract for 10, 20, and 30 days respectively the tissues collected were for anti-oxidant quantification. For anti-oxidant analysis the tissue sample were subjected to preparation of post mitochondrial supernatant (PMS).

Biochemical estimation

Biochemical estimation includes plasma glucose (Glucose oxidase/peroxidase method by using systronic UV, Visible Spectrophotometer 119, India) (Trinder P., 1999), Serum insulin by ELISA (Robonik, Readwell Touch™, Automatic ELISA plate analyser, India), serum amylase (Direct Substrate Method) (IFCC, 1999)], serum lipase (Turbidometric U.V. Method) (Rizzotti *et al.*, 1985)], Alanine aminotransferase (ALT) Reitman and Frankel method and Aspartate aminitransferases (AST) Modified IFCC method and, serum electrolyte by flame photometry (Systronic 128, Ahmedabad, India).

Hematology estimation

Hematology estimation include Total RBC by using hayem's fluid, Total WBC, Hemoglobin (Cyanmethemoglobin method) (David *et al.*, 1935), and differential count using polychromic solution containing Gention violet and Eosin manually by smear preparation.

Antioxidant enzyme estimation

Antioxidant parameters were carried out by the published standard literature like Estimation of Catalase was done by (Sinha, 1972), estimation of total reduced Glutathione (GSH) (Boyne *et al.*, 1972), estimation of Glutathione Peroxiase (Rostruck *et al.*, 1979), estimation of Glutathione-s-transferase by (Habig *et al.*, 1974), and quantification of Superoxide dismutase (SOD) was done by (Marklund *et al.*, 1974).

Statistical Analysis

Statistical analysis was done using Prism graph pad. Data are represented as mean ±SD. Differences between groups were assessed using one way analysis of variance (ANOVA) followed by Tukey multiple range test, compared with entire column. Level of significance were expressed as, [a] indicates $P < 0.001$, [b] $P< 0.01$, [c] $P <0.05$, and [d] $P >0.05$ non- significant.

RESULTS AND DISCUSSION

Present study was designed to probe the efficacy of the ethanolic extract of *Tinospora cordifolia* stem in the Diabetic rats. The Diabetic rats received 250 mg/kg.b.wt of the extract. Olive oil was used as carrier of the extract. The study brought towards the significant result in the alleviation of glucose, Insulin, Pancreatic enzymes, and anti-oxidative stress of the pancreatic tissues. Beside these serum electrolyte and some hematological parameters were also considered in the present study.

Table I. Concentration of Glucose and Insulin in different groups

	Glucose (mg/dl)	Insulin (µIU/ml)
Normal Control	97.80±5.63 [a]	8.22±0.58 [a]
Diabetic Control	328.0±18.23 [a]	2.37±0..48 [a]
Diabetic + 30 Days TCE	290.8±16.02 [b]	3.4±0.61 [d]
Diabetic + 30 Days TCE	254.0±18.51 [a]	4.40±0.57 [a]
Diabetic + 30 Days TCE	177.0±14.40 [a]	6.15±0.81 [a]

Values are expressed as mean±SD (Standard Deviation); [a]indicates $P < 0.001$, [b] $P< 0.01$, [c] $P <0.05$, and [d] $P >0.05$ non- significant. one-way ANOVA was performed followed by Tukey multiple range test, compared with entire column

Table II. Concentration of serum amylase, lipase, ALT, and AST in different groups

	Amylase (U/L)	Lipase (U/L)	ALT (U/L)	AST (U/L)
Normal Control	87.80±10.33 [a]	41.01±9.62 [a]	36.0±3.31[a]	37.80±5.65[a]
Diabetic Control	361.0±23.02 [a]	177.0±11.51 [a]	118.4±10.74[a]	123.4±10.74[a]
Diabetic + 10 Days TCE	321.0±23.02 [c]	131.0±16.73 [a]	92.20±12.81[b]	101.8±10.66[a]
Diabetic + 20 Days TCE	231.0±15.97 [a]	111.4±11.50 [a]	73.80±65.3[a]	80.50±9.68[b]
Diabetic + 30 Days TCE	156.0±23.82 [b]	81.60±12.05 [b]	51.0±6.51[c]	58.00±5.7[c]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table III. Enzyme activityof Superoxide, Glutathione, and Catalase in different groups.

	Superoxide Dismutase (SOD) (U/ml)	Glutathione Peroxidase (GPx) (nmol/NADPH oxidized/min)	Catalase (CAT) (mU/mg protein)
Normal Control	9.51±0.90 [a]	5.63±0.52 [a]	9.27±1.21 [a]
Diabetic Control	4.25±0.45 [a]	1.78±0.39 [a]	2.42±0.43 [a]
Diabetic + 30 Days TCE	5.22±0.42 [b]	2.85±0.54 [b]	3.76±0.55 [a]
Diabetic + 30 Days TCE	6.60±0.46 [a]	3.85±0.29 [a]	5.67±0.70 [a]
Diabetic + 30 Days TCE	7.96±0.44 [b]	4.53±0.36 [a]	7.45±0.51 [b]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table IV. Enzyme activity of Glutathione peroxidase, Glutathione s transferase, and Total thiol in different groups.

	Glutathione (GSH) (mg/mL)	Glutathione s transferase µmol of GSH consumed/mg protein/min	Total Thiol (nmol/NADPH oxidized/min)
Normal Control	17.30±1.85 [a]	1.92±0.13 [a]	5.16±0.69 [a]
Diabetic Control	7.67±0.66 [a]	0.80±0.07 [a]	1.31±0.21 [a]
Diabetic + 30 Days TCE	9.30±1.72 [d]	0.93±0.04 [d]	2.49±0.36 [b]
Diabetic + 30 Days TCE	12.70±1.20 [a]	1.27±0.13 [a]	3.55±0.28 [a]
Diabetic + 30 Days TCE	15.64±1.15 [a]	1.66±0.13 [a]	4.65±0.55 [a]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table V. Concentration of serum electrolyte (Serum Sodium and Potassium) in different groups.

	Sodium (mmol/L)	Potassium (mmol/L)
Normal Control	142.2±3.19 [a]	4.08±0.3 [a]
Diabetic Control	131.0±2.23 [a]	5.28±0.19 [a]
Diabetic + 30 Days TCE	135.0±2.55 [d]	4.9±0.15[d]
Diabetic + 30 Days TCE	138.2±2.8 [b]	4.72±0.07 [b]
Diabetic + 30 Days TCE	141.0±2.0 [a]	4.19±0.10 [a]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. one-way ANOVA was performed followed by Tukey multiple range test, compared with entire column

Table VI. Fluctuation of hematologic parameters (RBC, Hb, and WBC, and Lymophocyte) in different groups.

	Total Erythrocyte (million/mm3)	Hemoglobin (mg/dl)	Total Leucocyte (thousand/mm3)	Lymphocyte (%)
Normal Control	5.9±0.20 [a]	14.95±0.28 [a]	6.48±0.16 [a]	45.0±4.12 [a]
Diabetic Control	4.35±0.28 [a]	12.38±0.24 [a]	8.24±0.23 [a]	58.0±2.55 [a]
Diabetic + 30 Days TCE	4.5±0.27 [a]	13.35±0.35 [a]	7.96±0.28 [a]	56.0±2.45 [a]
Diabetic + 30 Days TCE	4.83±0.20 [a]	13.52±0.31 [a]	7.69±0.36 [a]	51.80±1.79 [b]
Diabetic + 30 Days TCE	5.18±0.19 [c]	14.12±0.21 [b]	7.33±1.7 [c]	48.40±1.7 [d]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. one-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table VII. Fluctuation of differential count of WBC (Neutrophil, Eosinophil, Basophil, Annd Monocyte) in different groups groups.

	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)
Normal Control	51.40±2.40 [a]	1.0±0.70 [a]	0.50±0.54 [d]	0.83±0.40 [d]
Diabetic Control	42.20±1.92 [a]	1.80±0.83 [a]	0.50±0.54 [d]	0.50±0.54 [d]
Diabetic + 30 Days TCE	42.40±2.30 [a]	3.8±0.83 [d]	0.83±0.75 [d]	0.66±0.51 [d]
Diabetic + 30 Days TCE	48.60±2.41 [d]	4.40±0.89 [d]	0.33±0.55 [d]	1.0±0.63 [d]
Diabetic + 30 Days TCE	50.60±1.67 d	4.0±0.70 [d]	0.66±0.51 [d]	0.83±0.75 [d]

Values are expressed as mean±SD (Standard Deviation); [a]indicates P < 0.001, [b] P< 0.01, [c] P <0.05, and [d] P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Effect of Tinospora cordifolia (TCE) 250 mg/kg.b.wt on fasting plasma glucose and serum insulin.

Insulin increases glucose uptake in muscles and fat and inhibits hepatic glucose production, thus serving as the primary regulator of the blood glucose level (Schwartsburd P, 2018). Diabetic rats registered 3.35 ($p<0.001$) times increased in fasting plasma glucose in comparison to normal control but after treatment with the extract for 30 days the increased margin reduced to 1.80 times ($p<0.001$). In case of insulin concentration the diabetic subjects were nearly 4 times ($p<0.001$) increased but with the dose

administration increase in the Insulin concentration was noticed and the margin was 1.34 ($p<0.001$) (Table I) times the normal Insulin level. These results confirm the hypoglycemic and β-cell regenerative properties of the extract and hence it could be developed into potential oral hypoglycemic drug with lesser side effects (Rajlaxmi *et al.*, 2016).

Effect of Tinospora cordifolia (TCE) 250 mg/kg.b.wt on pancreatic enzymes Serum amylase and lipase.

In the present investigation there was 4.1 times ($p<0.001$) serum amylase and 4.31 times ($p<0.001$) serum lipase increased level were noticed which indicates the condition of acute pancreatic inflammation as per The revised Atlanta Classification [20] , but as the dose prolonged the concentration of increased enzymes were reduced to 1.7 times ($p<0.01$) in amylase and 1.97 times ($p<0.01$) in lipase. The extract was found to inhibit the amylase and lipase level or the level was decreased due to decreased oxidative stress after 30 days of extract administration (Chongale *et al.*, 2009, Sharma *et al.*, 2015)**.** Liver is the metabolic hub and injury to it results in elevated levels of aminotransferases namely, Alanine aminotransferase (ALT) and Aspartate aminitransferases (AST) (Kamimoto Y *et al.*, 1985). Diabetic rats showed significant recovery and the concentration of ALT (1.41 times) and AST (1.5 times) reached towards normal in the 30 days of *Tinospora cordifolia* treatment which were significant ($p<0.05$) (Table II). Mild increase in ALT (3.2 times) indicates damage to the hepatic cell of the liver while AST (3.2 times) in Diabetic subjects indicates ischemic condition in zone 3 and hepatic cells. Restoration of ALT and AST with aid of *Tinospora cordifolia* extract clearly indicates the pharmacological potential of the plants in remodeling of hepatic acinus and other tissues. The above results co-relates with the finding of (Green *et al.*, 2001)

Effect of Tinospora cordifolia (TCE) 250 mg/kg.b.wt on Superoxide, Glutathione, and Catalase

Superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) are the first line defense enzymes generated specially through the mitochondrial energy production pathway (MEPP) (Ighrodaro *et al.*, 2018). Diabetic rats showed lowered superoxide dismutase (SOD) (2.23 times) ($p<0.001$), glutathione peroxidase (3.1 times) ($p<0.001$) and catalase (3.83 times) ($p<0.001$) shows high peroxide stress which upon treatment with the ethanolic extract of the desired plant normalization in the concentration was noticed SOD to 1.19 times ($p<0.01$), Glutathione peroxidase (1.24 times) ($p<0.001$) and catalase (1.24 times) ($p<0.01$) (Table III) as compared to the normal controlled rats which were in accordance with the findings (Shivkumar *et al.*, 2010).

Effect of Tinospora cordifolia (TCE) 500mg/kg.b.wt on Glutathione peroxidase, Glutathione s transferase, and Total thiol

GSTs are a superfamily of Phase 2 detoxification enzymes that detoxify both RS and toxic xenobiotics, primarily by catalysing GSH-dependent conjugation and redox reactions (Xiancham Li, 2011). Total thiol contents give an idea of oxidative stress and status of the other enzymatic parameters because most of the enzymes have sulphadryl group in their active site (Prakash *et al.*, 2009). In the present investigation in diabetic rats demonstrated decreased Glutathione (2.25 times) ($p<0.001$), Glutathione s transferase (2.4 times) ($p<0.001$), and total thiol (3.93 times) ($p<0.001$). The decrease level below normal depicts more oxidative stress than the available enzymes. The extract administration led to restoration of the desired enzyme to nearly normal level GSH (1.10 times) ($p<0.001$), GST (1.15 times) ($p<0.001$), and Thiol (1.11 times) ($p<0.001$) (Table IV) to the normal control. The results are more convincing for the treatment of diabetes by anti-oxidative approach.

Effect of Tinospora cordifolia (TCE) on the status of serum electrolyte in treated and non treated groups

In diabetic cases, altered electrolyte level is often associated which affects serum as well urine osmolality. There is an evidence of hyponatrimea as found in the present case although it is marginal towards lower reference limit. The effect on electrolyte imbalance was found that low sodium and higher potassium was seen in the diabetic rats with insignificant difference. Similar results were obtained by (Javaid *et al.*, 2007) which pronounce alterations in electrolytes homeostasis may lead to physiologic disorders. Insulin has been shown to activate Na^+ /K -ATPase enzyme. Therefore, low serum insulin level reduces Na^+ /K^- -ATPase activity and hence hyponatrimia and increased potassium (Oziako *et al.*, 2015). Treatment with

the extract restored the electrolyte concentration. The results were statistically significant ($p<0.001$) (Table V), however, the margin in altered parameters were very less to conclude any pathological situations.

Effect of Tinospora cordifolia (TCE) 250 mg/kg.b.wt on the status of RBC, Hb, and WBC in treated and non treated groups.

RBC in diabetic rats was lying in the normal range but towards the lower extreme (1.35 times) ($p<0.001$) the normal control. The reason behind decrease in the RBC count may be its membrane modification and reduced Na+K+ATPase activity and high lipid peroxidation of the RBC membrane (Buys *et al.,* 2013). Diabetic rats treated with *Tinospora cordifolia* treated rat showed recovery ($p<0.05$). This recovery was due to availability of ATP to the membrane and thus increased Na+K+ATPase activity to the cell which led to increased cell viability along with reduced peroxide stress and this finding can be correlated with results of (Chakraborty *et al.,* 2011). Reduced hemoglobin (1.20 times) ($p<0.001$) (Table VI) concentrations are the common findings in diabetic condition. Study on the Alloxan induced diabetic rats were represented with lower hemoglobin, in the present study which correlated with (Thomas *et al.,* 2003). Challenged oxidative enzyme (Catalase) pertaining oxidative stress also mediates low hemoglobin in diabetic state (Goth *et al.,* 2005). Peripheral total WBC counts in the diabetic rats were increased showing diabetic mediated inflammation and strongly support the association of diabetes with elevated WBC count. The findings were in association with MELANY cohort study (Twig *et al.,* 2013 and Gkrania-Klotas *et al.,* 2010). Treatment with the ethanolic extract (TCE) led to significant restoration in RBC ($p<0.05$), WBC ($p<0.05$), and Hemoglobin concentration ($p<0.01$), and the finding co-relates with (Sharma *et al.,* 2010).

Effect of Tinospora cordifolia (TCE) 250 mg/kg.b.wt on the status of differential leukocyte count in treated and non treated groups.

There is an evidence of leucocytosis with increased oxidative stress and and related nephritic syndrome (Chung *et al.,* 2005). Diabetic group showed increased lymphocyte to 1.25 times ($p<0.001$) (Table VI), decreased Neutrophil to 1.21 times ($p<0.001$), increased eosinophil to 1.8 times ($p<0.001$), Basophil remained unchanged and increased Monocyte level. In the present study treatment with the *Tinospora cordifolia* herbal extract showed insignificant result in lymphocyte count ($p>0.05$), Eosinophils ($p>0.05$) were found with irregular pattern, in other differential count like Neutrophil ($p>0.05$), Basophil ($p>0.05$), and Monocyte ($p>0.05$) (Table VII), same trend in results were noticed after 30 days of extract administration. However, the involvement of other hematological parameters needs to be probed in depth as the previous results has shown some connection after treatment.

CONCLUSION

T. cordifolia is a medicinal plant having various types of compounds. Present research spotlights the antihyperglycemic and anti-oxidative properties of *Tinospora cordifolia*. *It* has been used successfully in Ayurvedic medicine from the ancient era. Present study reveals the much needed beneficial effect of this plant which should be used for better economic and therapeutic utilization against diabetes and its complication. In this regard, further studies need to be carried out to explore more about *Tinospora cordifolia* for its potential in preventing and treating diabetes. The outcome of the present research could be used for further research investigations as well as clinical purpose in the development of novel drugs.

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CONFLICT OF INTEREST

Authors declare no conflict of interest regarding publication or any other activity related to this article.

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