Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v29i04.3933

THERAPEUTIC EVALUATION OF *GENTIANA OLIVIERI GRISEB* AND *FICUS RACEMOSA LINN* FOR DIABETES TREATMENT: AN ALLOXAN-INDUCED DIABETIC ANIMAL MODEL STUDY

Sirivella Pravallika[1*], Dr. Md sultan Ali Basha[2], Boya Minigi Jyothi[3], Mangali Jaya Prakash[4], D. Riyazunnisa[5], Shaik Mahaboob Bee[6]

[1, 3, 4] Research scholar, Department of Pharmacology, Safa College of Pharmacy, Kurnool
[2]Professor, Department of Pharmacology, Safa College of Pharmacy, Kurnool
[5]Associate Professor, Safa College of Pharmacy, Kurnool
[6]Assistant Professor, Safa College of Pharmacy, Kurnool

***Corresponding Author: -** Sirivella Pravallika
*Department of Pharmacology, Safa College of Pharmacy, Kurnool,
Email: sirivellapravallika123@gmail.com

Abstract
Diabetes mellitus is a prevalent metabolic disorder characterized by elevated blood glucose levels and impaired insulin function. The search for effective natural treatments has led to the investigation of botanical extracts, including *Gentiana olivieri Griseb and Ficus racemosa Linn*, for their therapeutic potential in diabetes management. In this study, we evaluated the antidiabetic effects of these extracts using an alloxan-induced diabetic animal model. Animals were divided into five treatment groups: normal control, diabetic control, standard drug (glibenclamide), *Gentiana olivieri Griseb* extract (M.G.O), and *Ficus racemosa Linn* extract (M.F.R). Daily administration of the respective interventions was carried out for a predetermined duration. Phytochemical screening was conducted to identify the bioactive compounds present in the extracts. Fasting blood glucose (FBG) and postprandial blood glucose (PPG) levels were measured as indicators of glycemic control. Histopathological analysis was performed to assess tissue morphology and inflammation. Phytochemical screening revealed the presence of bioactive compounds in the methanolic extracts of *Gentiana olivieri Griseb* and *Ficus racemosa Linn.* Treatment with these extracts resulted in significant reductions in FBG levels compared to the diabetic control group. Furthermore, the extracts exhibited promising effects in lowering PPG levels. Histopathological examination demonstrated improvements in tissue morphology and reduced inflammation in the treated groups. The findings of this study suggest that *Gentiana olivieri Griseb* and *Ficus racemosa Linn* extracts possess therapeutic potential for the management of diabetes. These botanical extracts showed significant hypoglycemic effects and ameliorated tissue inflammation. The presence of bioactive compounds in the extracts may contribute to their antidiabetic properties.

Keywords: *Gentiana olivieri Griseb, Ficus racemosa Linn*, alloxan-induced diabetic animal model, hypoglycemic activity.

Introduction

Diabetes mellitus is a complex metabolic disorder characterized by elevated blood glucose levels resulting from inadequate insulin production or impaired insulin action. It is a major global health

concern, with rising prevalence and significant implications for morbidity and mortality rates. Conventional pharmacological interventions for diabetes, while effective in many cases, are associated with limitations such as side effects and reduced long-term efficacy. Therefore, there is a growing interest in exploring alternative therapeutic approaches, including the use of plant-based remedies, to address the unmet needs in diabetes management [1]. *Gentiana olivieri Griseb* and *Ficus racemosa Linn* are among the plant species that have been traditionally employed in folk medicine for their purported anti-diabetic effects. These plants have attracted scientific attention due to their rich content of bioactive compounds, which have demonstrated potential for modulating key pathways involved in glucose regulation and diabetes management.

Gentiana olivieri Griseb, commonly known as Olivieri's gentian, is a plant species that holds significance in traditional medicine systems. It is a perennial herb belonging to the Gentianaceae family. *Gentiana olivieri Griseb* is native to certain regions of Europe and Asia, where it is traditionally utilized for its potential therapeutic properties. The plant is characterized by its vibrant blue flowers and lance-shaped leaves. Various parts of *Gentiana olivieri Griseb*, including the plant, stem, leaf, and flower, have been extensively studied for their bioactive constituents and pharmacological activities. The plant is known to contain compounds such as secoiridoid glycosides, flavonoids, and phenolic compounds, which contribute to its purported medicinal effects. The pharmacological activities of *Gentiana olivieri Griseb* include antidepressant, immunomodulatory, antiepileptic, hepatoprotective, and hypoglycemic properties. These diverse therapeutic potentials highlight the plant's significance as a potential source of natural compounds for the development of novel therapeutic agents. However, further research is required to fully understand the mechanisms of action and to explore the clinical applications of *Gentiana olivieri Griseb* in various health conditions [2- 9].

Ficus racemosa Linn, commonly known as the cluster fig tree or the Indian fig tree, is a plant species that has been extensively studied for its diverse pharmacological activities. The literature review provides insights into various aspects of *Ficus racemosa Linn*, including its antidiabetic, immunomodulatory, hypolipidemic, antioxidant, cardioprotective, hepatoprotective, and antitussive effects. Studies have demonstrated the antidiabetic potential of *Ficus racemosa Linn* through the modulation of carbohydrate hydrolyzing enzymes, glucose-lowering efficacy, and amelioration of diabetic complications. The plant's immunomodulatory activity has been investigated, suggesting its potential role in regulating the immune system and enhancing immune responses. *Ficus racemosa Linn* has also exhibited hypolipidemic effects, contributing to the improvement of lipid profiles in animal models. Furthermore, the plant has demonstrated antioxidant and cardioprotective properties, protecting against oxidative stress and mitigating doxorubicin-induced toxicity. Hepatoprotective effects have also been observed, characterized by the prevention of carbon tetrachloride-induced hepatic damage. *Ficus racemosa Linn* has shown antitussive activity, reducing cough reflexes, and has been evaluated for its anticoccidial efficacy against avian parasite infections. Phytochemical studies have identified bioactive compounds in *Ficus racemosa Linn*, such as oleanolic acid, which contribute to its pharmacological activities. Additionally, studies have explored its potential as an antifilarial agent, an antipyretic, and an antidiuretic agent. The complex interactions between *Ficus racemosa Linn* and its mutualistic fig wasp, as investigated in ecological studies, have also shed light on the trade-offs and resource dynamics within this unique plant-insect relationship [9-29].

This accumulating body of evidence highlights the potential of plant-based remedies as viable alternative or adjunctive treatments for diabetes. However, further scientific investigations are necessary to comprehensively understand and validate their efficacy, elucidate the underlying molecular mechanisms, and explore their long-term safety and therapeutic benefits. To contribute to this field of research, the present study aims to evaluate the anti-diabetic activity of selected plant extracts, including *Gentiana olivieri Griseb* and *Ficus racemosa Linn*, by employing an alloxan-induced diabetic animal model. Alloxan is a chemical compound that selectively destroys insulin-producing cells in the pancreas, resulting in a diabetic state in animal models. The study involved experiments including phytochemical screening, assessment of fasting and postprandial blood glucose

levels, evaluation of liver and renal profiles, analysis of lipid profile, measurement of glucose oxidase activity, and histopathological studies. The use of the alloxan-induced diabetic animal model provides a well-established and controlled experimental platform to evaluate the anti-diabetic potential of these plant extracts. By conducting this study aims to contribute to the growing body of scientific knowledge surrounding plant-based therapeutics for diabetes. This knowledge could play a crucial role in the development of innovative pharmacological interventions and lay the groundwork for future research endeavors targeting diabetes.

Materials and Methods

Plant Material and Extraction

Plants were collected from a designated location and identified by a botanist. The plants were thoroughly washed, air-dried, and ground to a fine powder. The powdered material was subjected to methanol extraction using a Soxhlet apparatus. The crude extract was concentrated using a rotary evaporator under reduced pressure, followed by drying in an oven at a specified temperature.

Phytochemical Screening

The methanolic plant extract was subjected to phytochemical screening to identify the presence of various secondary metabolites. Qualitative tests were performed for the detection of tannins, saponins, flavonoids, alkaloids, steroids, phenols, anthraquinones, phlobatannins, glycosides, and terpenoids. Quantitative analysis was also carried out to determine the percentage of selected phytochemicals present in the extract [30].

Experimental Animals

Male rodents (species and strain) weighing a specific range were sourced from a reputable supplier. The animals were housed under standard laboratory conditions with controlled temperature, humidity, and lighting. They were acclimatized for a suitable period and provided with standard rodent feed and water ad libitum.

Induction of Diabetes

Diabetes was induced in the rodents using alloxan administration. Alloxan was dissolved in an appropriate vehicle and administered intravenously or through a suitable route at a specific dose per kilogram of body weight [31].

Grouping and Treatment

Group 1: Normal control - Received CMC 0.5% w/v orally (p.o)
Group 2: Negative control - Received Alloxan-150 mg/kg intraperitoneally (I.P)
Group 3: Standard glibenclamide - Received 10 mg/kg orally (p.o)
Group 4:
- Trail 1 - Received 150 mg of alloxan + 30 mg of methanolic extract of *Gentiana olivieri Griseb* (MGO) intramuscularly (I.M) + 0.5% CMC orally
Group 5:
- Trail 2 - Received 150 mg of alloxan + 60 mg of methanolic extract of Ficus racemosa Linn (MFR) intramuscularly (I.M) + 0.5% CMC orally.

Fasting Blood Glucose (FBG) Measurement

Fasting blood glucose levels were measured using a suitable method before diabetes induction, after induction, and at regular intervals during the treatment period. Blood samples were collected from the animals after an overnight fast, and glucose levels were determined using a glucose oxidase method [32].

Postprandial Glucose (PPG) Assessment

The effect of the treatments on postprandial blood glucose levels was assessed at specific time points after a standardized meal. Blood samples were collected, and glucose levels were measured using an appropriate method [33].

Biochemical Parameters Evaluation

At the end of the treatment period, blood samples were collected to assess liver and renal profiles. Alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), serum creatinine, and blood urea levels were determined using standard biochemical methods [33].

Lipid Profile Analysis

The levels of serum cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) were measured using appropriate enzymatic assays [33].

Histopathological Studies

*T*issue samples from relevant organs (such as liver, pancreas, and sciatic nerve) were collected at the end of the treatment period. The tissues were fixed in 10% formalin, processed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (H&E). The stained sections were examined under a light microscope for histopathological changes [34].

Statistical Analysis

All data were expressed as mean ± standard deviation (SD) or standard error of mean (SEM). Statistical analysis was performed using suitable statistical tests to determine the significance of the results obtained.

Results

Phytochemical Composition

The research findings revealed important insights into the composition of MGO and MFR. The moisture content was determined to be 83.98% and 84.36% for MGO and MFR, respectively. Loss on drying was found to be 4.98% for MGO and 6.43% for MFR, indicating the amount of weight lost during drying. Ash value assessments provided further information about mineral content. MGO had a total ash value of 4.78%, acid-insoluble ash value of 0.46%, water-soluble ash value of 3.99%, and sulphated ash value of 1.42%. Similarly, MFR had a total ash value of 6.29%, acid-insoluble ash value of 0.65%, water-soluble ash value of 4.02%, and sulphated ash value of 1.86%. Evaluation of crude fiber contents revealed 7.59% in MGO and 8.23% in MFR.

Parameters	**MGO Values**	**MFR Values**
Moisture content	83.98	84.36
Loss on drying	4.98	6.43
Ash value		
Total ash	4.78	6.29
Acid-insoluble ash	0.46	0.65
Water-soluble ash	3.99	4.02
Sulphated ash	1.42	1.86
Crude fibre contents	7.59	8.23

Table 1: Phytochemical Screening Test (Values in % w/w)

Moving on to the phytochemical analysis, both MGO and MFR were found to contain tannins, saponins, flavonoids, alkaloids, and steroids. Quantitatively, MGO contained 4.92% tannins, 6.26% saponins, 2.96% flavonoids, 1.73% alkaloids, and 0.72% steroids. In MFR, the quantities were 2.4%

for tannins, 1.5% for saponins, 2.4% for flavonoids, 2.1% for alkaloids, and 1.2% for steroids. Other phytochemicals present in varying amounts included phenol, anthraquinone, phlobatannin, glycosides, and terpenoids.

MGO Phytochemicals	**Qualitative**	**Quantitative *%at***	**MFO Phytochemicals**	**Qualitative**	**Quantitative *%at***
Tannins	++	4.92	***Tannins***	++	2.4
Saponin	++	6.26	***Saponin***	+	1.5
Flavonoid	++	2.96	***Flavonoid***	++	2.4
Alkaloids	+	1.73	***Alkaloids***	++	2.1
Steroids	+	0.72	***Steroids***	+	1.2
Phenol	+	0.89	***Phenol***	+	1.5
Anthraquinone	+	2.83	***Anthraquinone***	-	0.3
Phlobatannin	+	0.48	***Phlobatannin***	_	1.4
Glycosides	+	0.38	***Glycosides***	+	1.1
Terpenoides	+	0.72	***Terpenoides***	++	2.3

Table 2: displays the qualitative and quantitative composition of various phytochemicals in *Gentiana olivieri Griseb* and *Ficus racemosa Linn.*

*(+ for present, - for absent)

Evaluation of the Antidiabetic Potential

Effect on Fasting Blood Glucose (FBG) Level

The FBG levels of the five groups of rodents were within the normal range before induction. After the induction of diabetes using alloxan, there was a significant increase in FBG levels in all groups. Treatment with the extract for one week led to a decrease in FBG levels, which became more pronounced with prolonged treatment. Treatment with the standard drug glipizide also showed a similar trend in lowering blood glucose levels. Combination treatments with the extract and glipizide showed significant effects after just one week of treatment and became more pronounced with longer treatment durations. Among the groups, Group 4, which received an extract dosage of 30 mg/kg/day, showed the most pronounced effect on lowering FBG levels.

Baseline		63.59	73.59	69.78	65.46	67.84
5 days after ALLOXAN		208.38	203.82	207.32	209.26	212.26
After week	**1-**	220.56	192.56	194.99	194.57	184.18
After week	**2-**	213.78	174.28	174.29	168.24	138.59
After week	**3-**	208.59	164.29	167.56	156.23	128.36
After week	**4-**	198.42	150.39	148.23	148.29	114.59

Table 3: Effect on Fasting Blood Glucose (FBG) Level

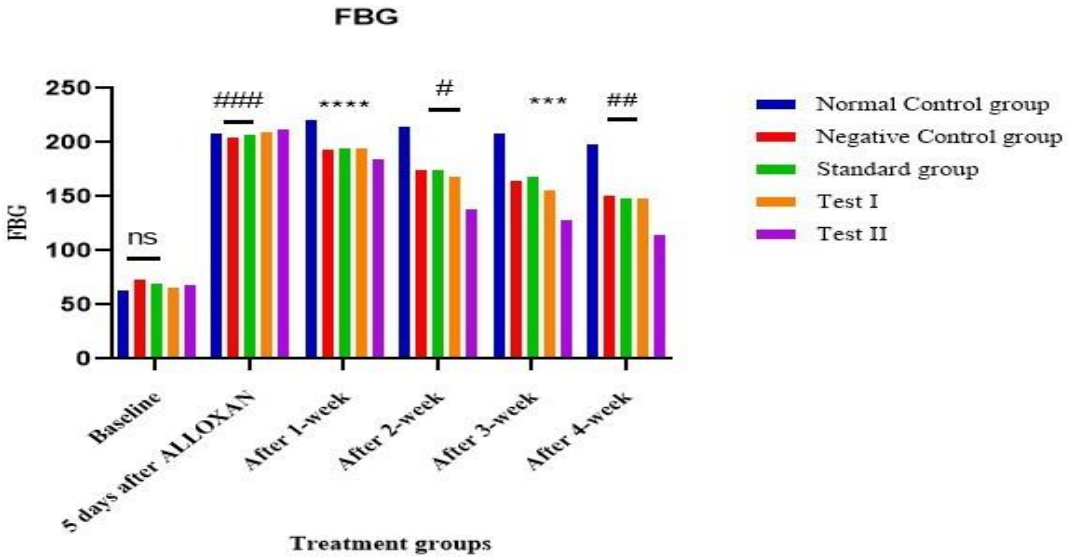

Fig 1: Effect on Fasting Blood Glucose (FBG) Level

Effect on Postprandial Blood Glucose (PPG) Level

After one week of treatment, both glipizide and extract treatments reduced PPG levels in Group 1 and Group 2. The magnitude of improvement was relative to the duration of treatment in all groups. After one week of treatment, Group 4 (extract, 30 mg/kg) showed a significant synergistic effect in reducing PPG levels. Prolonged treatment allowed for further improvement in PPG levels.

Groups	**Dosage (m)**	**Glucose levels (mg/dl) post treatment with the extracts**			
		Before induction	***After induction***	***After treatment***	***% Sugar Reduced***
Group 1	(1%w/v CMC), orally	103.26	506.38	247.39	48.85%
Group 2	(1%w/v), orally	100.59	107.56	96.48	11.14%
Group 3	(30mg/kg orally	101.62	428.93	209.27	48.78%
Group 4	(30mg/kg orally) MGO	97.98	418.27	174.63	41.75%
Group 5	(60mg/kg orally) MFR	94.28	409.72	166.25	40.57%
SD		**00.45436**	**1.5460**	**1.54959**	**00.2077**
SEM		**00.20319**	**00.69140**	**00.2457**	**00.92908**

Table 4: Effects of Different Groups on Sugar Level of ALLOXAN-Induced Diabetic Rats

Effect of Methanolic Plant Extract on Liver Profile in Alloxan-Induced Diabetic Rats

The levels of alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine transaminase (ALT) were measured. The results showed that in Group 2, which received the 1%w/v CMC solution orally, there were elevated levels of ALP, AST, and ALT, indicating potential liver damage. However, in Groups 3, 4, and 5, which received the methanolic plant extracts orally, the levels of these liver enzymes were reduced compared to Group 2.

Groups	Treatment/Dose	Alkaline Phosphatase (ALP) (IU/L)	Aspartate Aminotransferase (AST) (IU/L)	alanine transaminase (ALT) (IU/L)
Group 1	(1%w/v CMC), orally	87.12	82.36	24.65
Group 2	(1%w/v), orally	167.87	159. 07	127.92
Group 3	(30mg/kg orally	123.12	86.10	43.36
Group 4	(30mg/kg orally) MGO	103.87	76.87	35.73
Group 5	(60mg/kg orally) MFR	87.76	89.75	28.68

Table 5: Effect of Methanolic Plant Extract on Liver Profile in Alloxan-Induced Diabetic Rats

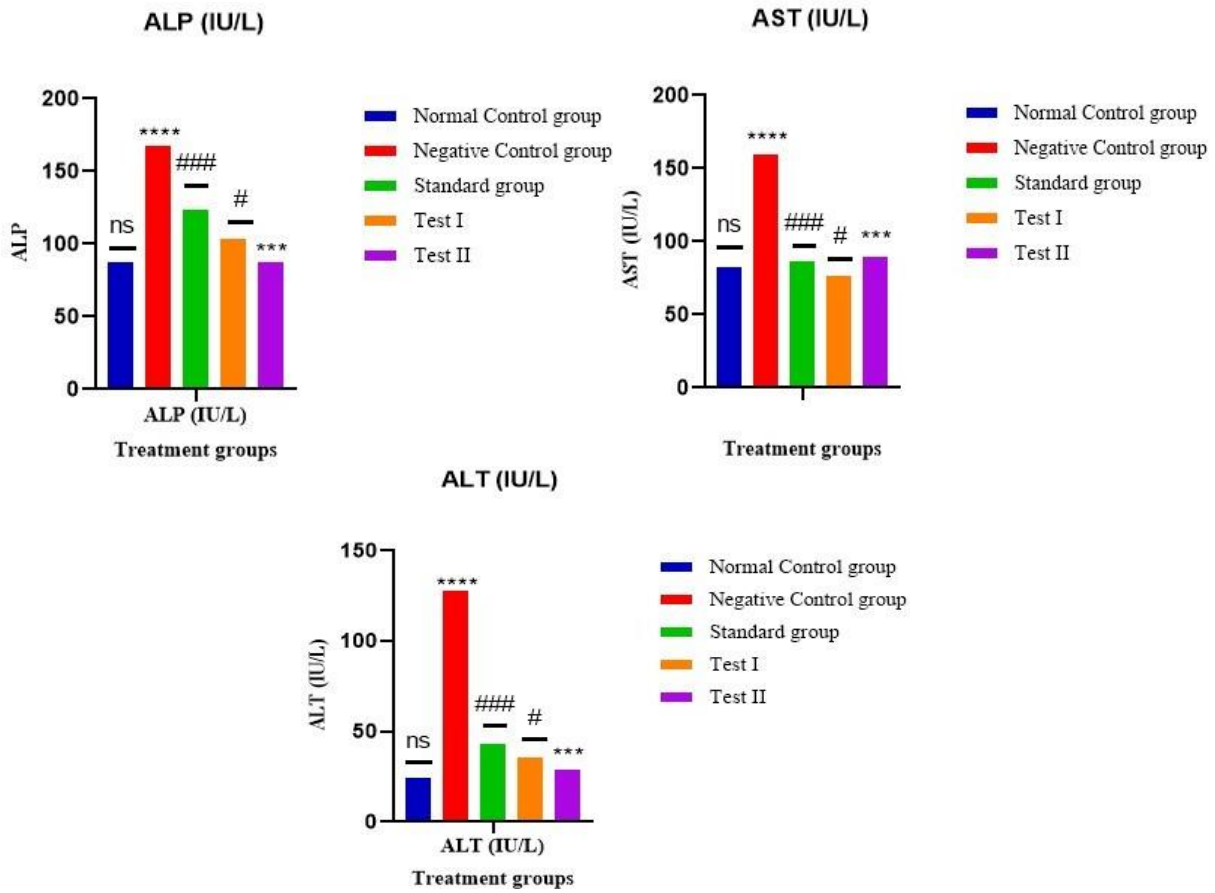

Fig 2: Effect of methanolic plant extract of *Extracts* on liver profile on Alloxan induced diabetic rats.

Effect of Methanolic Plant Extract on Renal Profile in Alloxan-Induced Diabetic Rats

The measurement parameters included serum creatinine and blood urea. Results revealed that in Group 2, which received the 1%w/v CMC solution orally, elevated levels of serum creatinine and blood urea were observed, suggesting renal dysfunction. However, in Groups 3, 4, and 5, which received the methanolic plant extracts orally, the levels of serum creatinine and blood urea were reduced compared to Group 2.

Groups	Treatment/Dose	Serum Creatinine (mg/dl)	Blood Urea (mg/dl)
Group 1	(1%w/v CMC), orally	1.35	25.26
Group 2	(1%w/v), orally	2.16	41.61
Group 3	(30mg/kg orally	1.31	30.89
Group 4	(30mg/kg orally) MGO MGO	1.27	27.74
Group 5	(60mg/kg orally) MFR MFR	1.68	23.83

Table 6: Effect of Methanolic Plant Extract on Renal Profile in Alloxan-Induced Diabetic Rats

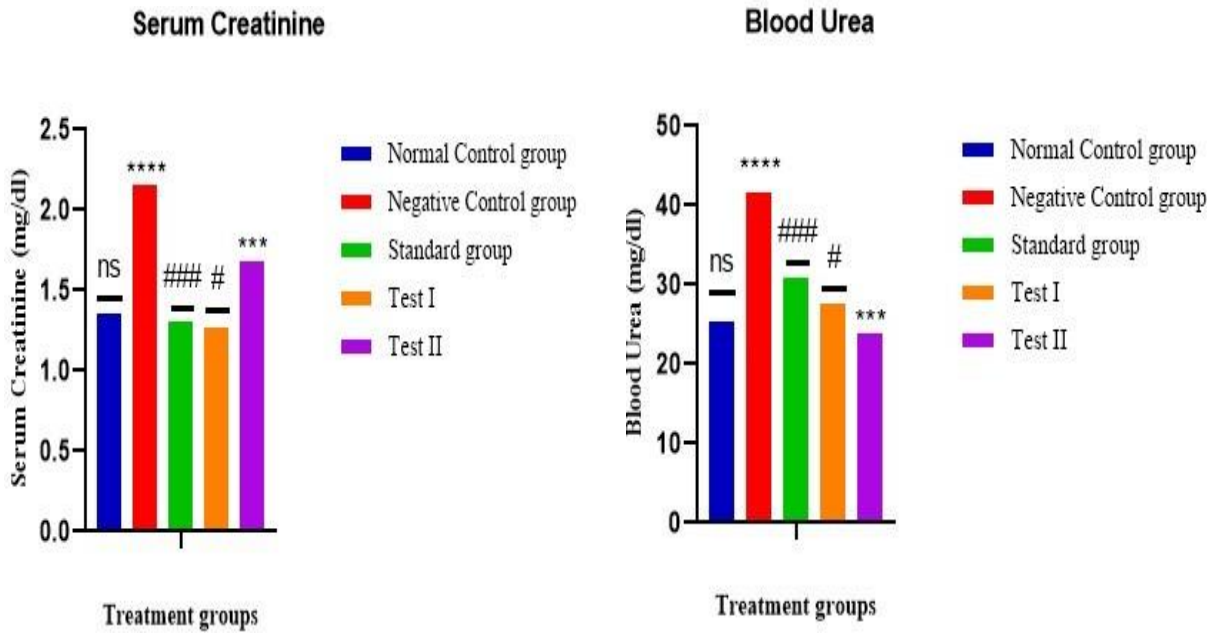

Fig 3: Effect of methanolic plant extract of *Extracts* on renal profile in Alloxan in diabetes

Lipid Profile

The results showed that in the alloxan-induced diabetic group (Group 2), elevated levels of cholesterol, TG, and LDL were observed compared to the control group (Group 1). However, treatment with either Glibenclamide or the methanolic plant extracts in Groups 3, 4, and 5 resulted in reduced levels of cholesterol, TG, and LDL, indicating a potential lipid-lowering effect. Additionally, treatment with the methanolic plant extracts led to an increase in serum HDL levels, indicating a beneficial impact on HDL cholesterol, commonly known as "good" cholesterol.

Lipid Profile	**Group 1 Vehicle only (CMC 0.5% w/v, p.o)**	**Group 2 Alloxan-150 mg/kg (I.P)**	**Group 3 -Glibenclamide 10 mg/kg (P.O)**	**Group 4 Alloxan-150 mg/kg (I.M) + Methanolic extract of *Gentiana olivieri Griseb* (30 mg/kg, I.M) + CMC 0.5% w/v (p.o)**	**Group 5 Alloxan-150 mg/kg (I.M) + *Ficus racemosa Linn* (60 mg/kg, I.M) + CMC 0.5% w/v (p.o)**
Serum Cholestrol	67.64	113.96	66.54	73.64	64.63
Serum TG	65.38	94.87	58.84	54.73	49.26
Serum HDL	38.29	26.28	42.84	36.98	33.13
Serum LDL	24.23	79.43	27.66	29.58	18.73
Serum VLDL	15.92	22.67	19.45	19.83	14.26
SD	0.2177	0.4157	0.2103	0.2154	0.2062
SEM	0.09739	0.01859	0.0940	0.0963	0.0922

Table 8: Lipid Profile (Values in mg/dl)

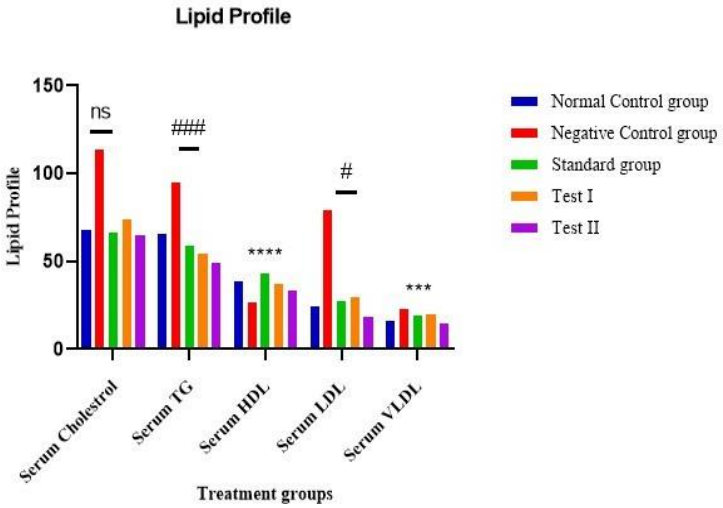

Fig 4: Lipid profile

Glucose Oxidase Method (GOD)

The Glucose Oxidase Method (GOD) was employed to assess the glucose levels in the different groups. The results demonstrated a decrease in glucose levels in Groups 3, 4, and 5, which received treatment with Glibenclamide, MGO, and MFR, respectively. Group 2, consisting of alloxan-induced diabetic rats, exhibited the highest glucose level compared to the other groups. These findings indicate a potential glucose-lowering effect of the methanolic plant extracts and Glibenclamide, supporting their potential use in managing diabetes.

Groups	**GOD**
Group 1	0.67
Group 2	0.38
Group 3	0.29
Group 4	0.26
Group 5	0.24
SD	**0.1263**
SEM	**0.0326**

Table 7: Glucose Oxidase Method (GOD)

Histopathological Studies

In Group 1 and Group 2, scattered mononuclear cells and epithelial granulomas were detected throughout the tissue, indicating signs of inflammation. Inflammatory cell counts around ports and waterways suggested the dissemination of pathogens, accompanied by significant thrombosis in the sciatic nerve. In Group 3, the pancreas exhibited numerous lymphocytes, macrophages, and histiocytes. Clear degeneration or enlargement of pancreatic cells in the central regions was observed, accompanied by the migration of mononuclear inflammatory cells towards the periphery. In Group 4, hepatocytes appeared active and healthy, with occasional clusters of mononuclear inflammatory cells deep within the tissue. Scattered inflammatory cells, including lymphocytes and histiocytes, gathered in the portal and perivascular sites, while bile duct proliferation was also observed. In Group 5, hepatocytes displayed enlarged and congested sinusoids. Although only a small number of parenchymas contained epithelioid structures, these structures were considered significant. The periportal and perivasive spaces were colonized by scattered mononuclear inflammatory cells, and signs of inflammation and necrosis extended to the sciatic nerve.

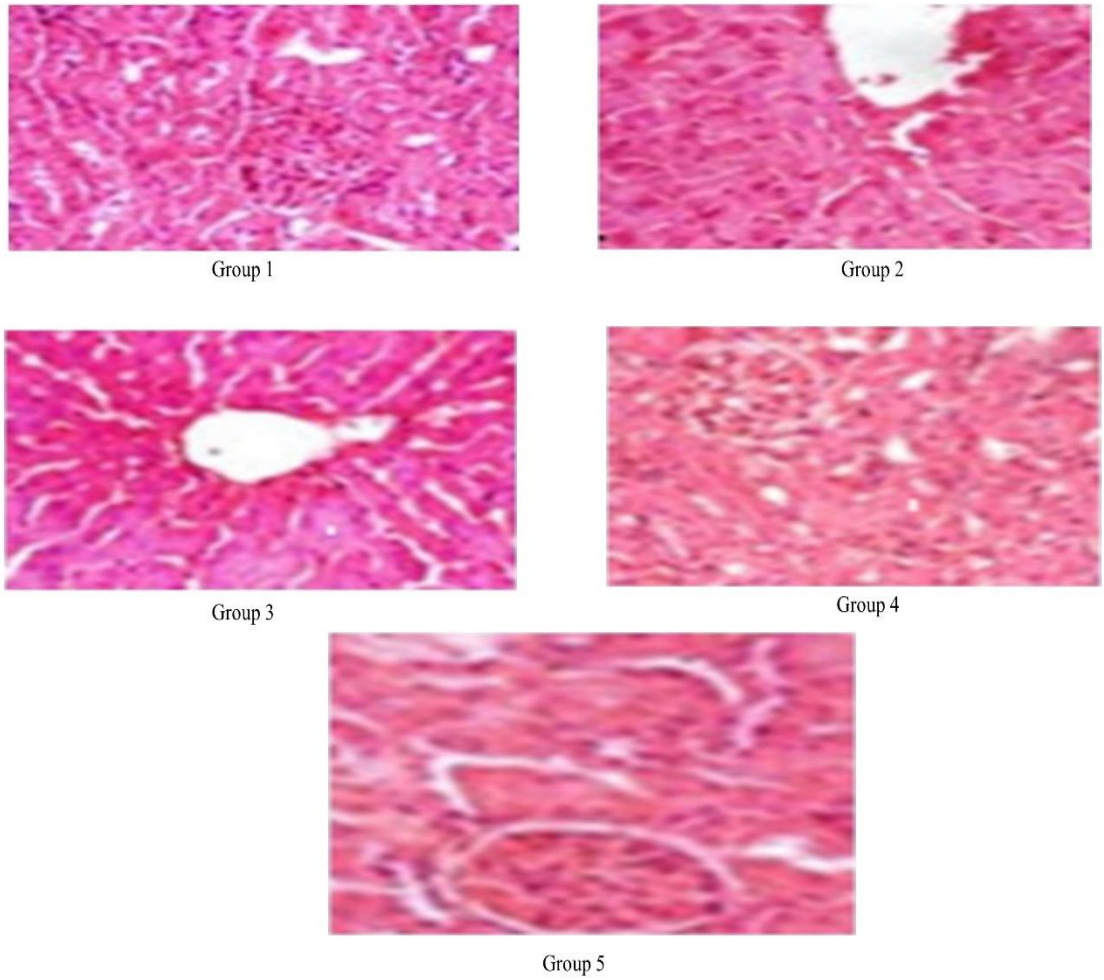

Fig 5: Histopathological studies

Overall, the results demonstrate the significant antidiabetic potential of the methanolic plant extract. Treatment with the extract led to remarkable reductions in fasting and postprandial blood glucose levels. The extract also showed positive effects on the liver profile by reducing the levels of alkaline phosphatase, aspartate aminotransferase, and alanine transaminase. Moreover, the extract exhibited beneficial effects on the renal profile by decreasing serum creatinine and blood urea levels. Regarding the lipid profile, the extract demonstrated improvements by reducing serum cholesterol and triglyceride levels, increasing serum HDL levels, and lowering serum LDL levels. The histopathological analysis further supported the anti-inflammatory effects of the extract by reducing mononuclear inflammatory cell infiltration in various tissues. These findings indicate the potential of the methanolic plant extract as a promising treatment for diabetes-related complications.

Discussion

Diabetes mellitus is a complex metabolic disorder characterized by persistent hyperglycemia due to impaired insulin secretion or insulin resistance. Effective management of diabetes necessitates interventions that can normalize blood glucose levels and mitigate associated complications. In this study, we aimed to evaluate the therapeutic potential of the methanolic plant extracts of MGO and MFR in an alloxan-induced diabetic animal model. Phytochemical screening of the methanolic plant extracts provided valuable insights into their chemical compositions. The presence of various bioactive compounds, including tannins, saponins, flavonoids, alkaloids, steroids, phenols, anthraquinones, phlobatannins, glycosides, and terpenoids, indicates the potential health benefits

associated with these extracts (Table 2). The experimental design comprised different treatment groups, allowing for a comprehensive evaluation of the antidiabetic effects of the plant extracts. Group 1 served as the normal control, receiving only the vehicle (CMC 0.5% w/v, p.o), which helped establish the baseline parameters. Group 2 represented the diabetic control group, induced by alloxan administration (150 mg/kg, I.P), and served as a reference for the diabetic state. Treatment Group 3 received the standard drug glibenclamide (10 mg/kg, P.O), which acted as a positive control. Glibenclamide is a well-established antidiabetic agent that stimulates insulin secretion and enhances the utilization of glucose in peripheral tissues. The inclusion of this group allowed for comparisons between the effects of the plant extracts and a recognized pharmaceutical intervention (Table 4, Fig 1). Group 4 received a combination treatment including alloxan induction (150 mg/kg, I.M), 30 mg/kg of the methanolic extract of MGO, and CMC 0.5% w/v (p.o). Group 5 also underwent alloxan induction (150 mg/kg, I.M) and received 60 mg/kg of MFR extract, along with CMC 0.5% w/v (p.o). The objective was to assess the antidiabetic potential of these plant extracts and their ability to reduce fasting blood glucose (FBG) and postprandial blood glucose (PPG) levels (Table 3). The results showed that pretreatment FBG levels in the control and treatment groups were within the normal range. However, following alloxan induction, all groups exhibited a significant increase in FBG levels, indicating the successful establishment of the diabetic condition. Subsequent treatment with the plant extracts and the standard drug led to reductions in FBG levels. Notably, Group 4, which received the methanolic extract of MGO at a dose of 30 mg/kg, demonstrated the most pronounced effect on lowering FBG levels (Table 3). In parallel with FBG evaluation, postprandial blood glucose levels were assessed to understand the impact of the treatments on glucose metabolism following a meal. Both the plant extracts and the standard drug exhibited notable reductions in PPG levels compared to the diabetic control group. Among the treatment groups, Group 4, which received the combination treatment with MGO, displayed a significant synergistic effect in reducing PPG levels after one week of treatment (Table 4). Histopathological analysis provided further insights into the effects of the plant extracts and their potential mechanisms of action. Group 1, the normal control, exhibited normal tissue morphology with minimal inflammatory cell infiltration. In contrast, Group 2, the diabetic control, showed significant inflammation and granuloma formation, indicating the presence of the diabetic condition. Group 3, treated with the standard drug glibenclamide, displayed improved tissue morphology and reduced inflammation in comparison to the diabetic control group. Similarly, Groups 4 and 5, treated with the methanolic extracts of MGO and MFR, respectively, exhibited improved tissue structure and reduced inflammatory cell infiltration (Fig 5). A notable finding of this study was the beneficial impact of the plant extracts on liver and renal profiles. Evaluation of liver function markers, including alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine transaminase (ALT), revealed significant reductions in the plant extract-treated groups compared to the diabetic control group. This indicates a hepato-protective effect of the extracts and improved liver function. Moreover, the plant extracts demonstrated renoprotective effects, as evidenced by reduced levels of serum creatinine and blood urea, indicating improved renal function (Table 5, Table 6). Assessment of lipid profiles provided additional insights into the potential cardioprotective effects of the plant extracts. Treatment with the plant extracts resulted in desirable alterations in serum lipid parameters. Reduced serum total cholesterol and triglyceride levels, along with increased levels of high-density lipoprotein (HDL) cholesterol, suggest improved lipid metabolism. These changes are associated with a decreased risk of lipid-related complications often observed in diabetes (Table 8). In summary, the results of this study demonstrate the potential of MGO and MFR extracts in the management of diabetes. The plant extracts showed significant antidiabetic effects, as evidenced by reductions in FBG and PPG levels. Moreover, the extracts exhibited hepato-protective and renoprotective effects, as well as favorable changes in lipid profiles. The observed histopathological improvements further support the potential mechanism underlying the antidiabetic effects of these extracts. Nonetheless, the results from this study contribute to our understanding of the potential therapeutic applications of *Gentiana olivieri Griseb* and *Ficus racemosa* Linn extracts in the management of diabetes.

Conclusion

In conclusion, the findings of this study highlight the potential therapeutic benefits of the methanolic plant extracts of *Gentiana olivieri Griseb* and *Ficus racemosa* Linn in the management of diabetes. The extracts demonstrated significant hypoglycemic effects, as evidenced by their ability to reduce fasting blood glucose and postprandial blood glucose levels. Additionally, they exhibited hepatoprotective and renoprotective effects, along with favorable modifications in lipid profiles.

Conflict of interest

All Authors declare no conflict of interest.

References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2009 Jan;32 Suppl 1(Suppl 1):S62-7. doi: 10.2337/dc09-S062.
2. Berk A, Yılmaz İ, Abacıoğlu N, Kaymaz MB, Karaaslan MG, Savan EK. Antidepressant effect of Gentiana olivieri Griseb. in male rats exposed to chronic mild stress. Libyan J Med. 2020;15(1):1760188.
3. Singh S, Yadav CP, Noolvi MN. Immunomodulatory activity of butanol fraction of Gentiana olivieri Griseb. on Balb/C mice. Asian Pac J Trop Biomed. 2012 Jun;2(6):433-7.
4. Aslan M, Orhan DD, Orhan N. Effect of Gentiana olivieri on experimental epilepsy models. Pharmacogn Mag. 2011 Oct;7(28):344-9.
5. Singh S, Yadav CP, Noolvi MN. Quantification of oleanolic acid in the flower of Gentiana olivieri Griseb. by HPLC. J Basic Clin Pharm. 2012 Mar;3(2):241-5.
6. Tüzün CY, Toker MC, Toker G. Anatomical investigations on root, stem, and leaf of Gentiana olivieri Griseb. Pharmacogn Mag. 2011 Jan;7(25):9-15.
7. Kırmızıbekmez H, Tatar D, Erdoğan M, Kúsz N, Hohmann J. A new depside and a new secoiridoid from the aerial parts of Gentiana olivieri from flora of Turkey. Nat Prod Res. 2022 May 3;36(9):2208-14.
8. Sezik E, Aslan M, Yesilada E, Ito S. Hypoglycaemic activity of Gentiana olivieri and isolation of the active constituent through bioassay-directed fractionation techniques. Life Sci. 2005 Jan 28;76(11):1223-38.
9. Orhan DD, Aslan M, Aktay G, Ergun E, Yesilada E, Ergun F. Evaluation of hepatoprotective effect of Gentiana olivieri herbs on subacute administration and isolation of active principle. Life Sci. 2003 Apr 4;72(20):2273-83.
10. Veerapur VP, Prabhakar KR, Thippeswamy BS, Bansal P, Srinivasan KK, Unnikrishnan MK. Antidiabetic effect of Ficus racemosa Linn. stem bark in high-fat diet and low-dose streptozotocin-induced type 2 diabetic rats: a mechanistic study. Food Chem. 2012 May 1;132(1):186-93. doi: 10.1016/j.foodchem.2011.10.052.
11. Ahmed F, Urooj A. Traditional uses, medicinal properties, and phytopharmacology of Ficus racemosa: a review. Pharm Biol. 2010 Jun;48(6):672-81. doi: 10.3109/13880200903241861.
12. Sophia D, Manoharan S. Hypolipidemic activities of Ficus racemosa Linn. bark in alloxan-induced diabetic rats. Afr J Tradit Complement Altern Med. 2007 Feb 16;4(3):279-88. doi: 10.4314/ajtcam.v4i3.31220.
13. Jahan IA, Nahar N, Mosihuzzaman M, Rokeya B, Ali L, Azad Khan AK, Makhmur T, Iqbal Choudhary M. Hypoglycaemic and antioxidant activities of Ficus racemose Linn. fruits. Nat Prod Res. 2009;23(4):399-408. doi: 10.1080/14786410802230757.
14. Mandal SC, Maity TK, Das J, Saba BP, Pal M. Anti-inflammatory evaluation of Ficus racemosa Linn. leaf extract. J Ethnopharmacol. 2000 Sep;72(1-2):87-92. doi: 10.1016/s0378-8741(00)00210-5.
15. Solanki ND, Bhavsar SK. An evaluation of the protective role of Ficus racemosa Linn. in streptozotocin-induced diabetic neuropathy with neurodegeneration. Indian J Pharmacol. 2015 Nov-Dec;47(6):610-5. doi: 10.4103/0253-7613.169579.

16. Mandal SC, Saha BP, Pal M. Studies on antibacterial activity of Ficus racemosa Linn. leaf extract. Phytother Res. 2000 Jun;14(4):278-80. doi: 10.1002/1099-1573(200006)14:4<278::aid-ptr592>3.0.co;2-7.
17. Ahmed F, Urooj A, Karim AA. Protective effects of Ficus racemosa stem bark against doxorubicin-induced renal and testicular toxicity. Pharmacogn Mag. 2013 Apr;9(34):130-4. doi: 10.4103/0973-1296.111265.
18. Ahmed F, Chandra JN, Manjunath S. Acetylcholine and memory-enhancing activity of Ficus racemosa bark. Pharmacognosy Res. 2011 Oct;3(4):246-9. doi: 10.4103/0974-8490.89744.
19. Rahuman AA, Venkatesan P, Geetha K, Gopalakrishnan G, Bagavan A, Kamaraj C. Mosquito larvicidal activity of gluanol acetate, a tetracyclic triterpene derived from Ficus racemosa Linn. Parasitol Res. 2008 Jul;103(2):333-9. doi: 10.1007/s00436-008-0976-6.
20. Bhaskara Rao R, Murugesan T, Pal M, Saha BP, Mandal SC. Antitussive potential of methanol extract of stem bark of Ficus racemosa Linn. Phytother Res. 2003 Nov;17(9):1117-8. doi: 10.1002/ptr.1325.
21. Ahmed F, Urooj A. Cardioprotective activity of standardized extract of Ficus racemosa stem bark against doxorubicin-induced toxicity. Pharmacogn Mag. 2012 Apr;8(30):97-101. doi: 10.4103/0973-1296.96505.
22. Ahmed F, Urooj A. Effect of Ficus racemosa stem bark on the activities of carbohydrate hydrolyzing enzymes: an in vitro study. Pharmacogn Mag. 2010 May;6(22):125-9. doi: 10.4103/0973-1296.62893.
23. Ahmed F, Urooj A. Hepatoprotective effects of Ficus racemosa stem bark against carbon tetrachloride-induced hepatic damage in albino rats. Pharmacogn Mag. 2010 Feb;6(21):37-42. doi: 10.4103/0973-1296.59968.
24. Rao RB, Anupama K, Swaroop KR, Murugesan T, Pal M, Mandal SC. Evaluation of anti-pyretic potential of Ficus racemosa bark. Phytomedicine. 2002 Dec;9(8):731-3. doi: 10.1078/094471102321621340.
25. Mishra V, Khan NU, Singhal KC. Potential antifilarial activity of fruit extracts of Ficus racemosa Linn. against Setaria cervi in vitro. Indian J Exp Biol. 2005 Apr;43(4):346-50.
26. Bakir Çilesizoğlu N, Yalçin E, Çavuşoğlu K, et al. Qualitative and quantitative phytochemical screening of Nerium oleander L. extracts associated with toxicity profile. Sci Rep. 2022 Jan 13;12(1):21421. doi: 10.1038/s41598-022-26087-0.
27. Ighodaro OM, Adeosun AM, Akinloye OA. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plant extracts in experimental studies. Medicina (Kaunas). 2017 Jul 31;53(4):365-374.
28. Tafesse TB, Hymete A, Mekonnen Y, Tadesse M. Antidiabetic activity and phytochemical screening of extracts of the leaves of Ajuga remota Benth on alloxan-induced diabetic mice. BMC Complement Altern Med. 2017 May 2;17(1):243. doi: 10.1186/s12906-017-1757-5.
29. Jarald EE, Joshi SB, Jain DC, Edwin S. Biochemical evaluation of the hypoglycemic effects of extract and fraction of Cassia fistula Linn. in alloxan-induced diabetic rats. Indian J Pharm Sci. 2013 Jul;75(4):427-434. doi: 10.4103/0250-474X.119823.
30. Shaik HS. Effect of Nigella Sativa Seed Extract on Glucose, Lipid Profile, Liver Function Tests, Oxidative Stress and Histological Changes In Pancreas, Kidney, Liver and Tibial Nerve In Normal and Streptozotocin Induced Diabetic Rats [dissertation]. Karnataka University, 2018.
31. Macdonald Ighodaro O, Mohammed Adeosun A, Adeboye Akinloye O. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. Medicina (Kaunas). 2017 Dec;53(6):365-74.
32. Tafesse TB, Hymete A, Mekonnen Y, Tadesse M. Antidiabetic activity and phytochemical screening of extracts of the leaves of Ajuga remota Benth on alloxan-induced diabetic mice. BMC Complement Altern Med. 2017 May 2;17(1):243.

33. Jarald EE, Joshi SB, Jain DC, Edwin S. Biochemical evaluation of the hypoglycemic effects of extract and fraction of Cassia fistula Linn. in alloxan-induced diabetic rats. Indian J Pharm Sci. 2013 Jul;75(4):427-34.
34. Shaik HS. Effect of Nigella Sativa Seed Extract on Glucose, Lipid Profile, Liver Function Tests, Oxidative Stress and Histological Changes In Pancreas, Kidney, Liver and Tibial Nerve In Normal and Streptozotocin Induced Diabetic Rats (Doctoral dissertation, BLDE (Deemed to be University)).