

Original Article

Antidiabetic, antihyperlipidemic and immunomodulatory effects of *Trigonella foenum-graecum* extract in streptozotocin-induced diabetic rats

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ABSTRACT

Objectives: The objective of this study was to investigate the antidiabetic, lipid-lowering and immunomodulatory effects of ethanolic extract of *Trigonella foenum-graecum* (TFE) in streptozotocin (STZ)-induced diabetic rats fed a high-fat diet (HFD), with metformin serving as the reference standard.

Materials and Methods: Thirty-six male Wistar rats were randomly allocated into six groups ($n = 6$ each). Type 2 diabetes was induced by feeding a HFD followed by a single intraperitoneal dose of STZ (40 mg/kg). The diabetic animals were treated once daily for 21 days with either TFE extract (200, 500, or 1000 mg/kg, orally) or metformin (100 mg/kg, orally). Fasting blood glucose (FBS), serum lipid profile, body weight and resistin concentrations were assessed at baseline, week 5 and week 8. Statistical evaluation was carried out using one-way analysis of variance with appropriate *post hoc* analysis.

Results: Administration of TFE extract led to a dose-dependent decline in fasting glucose and serum resistin, with the 1000 mg/kg dose showing highly significant improvement ($P < 0.001$), comparable to metformin. Treated groups also exhibited favourable changes in lipid profile, with reductions in total cholesterol, triglycerides, low-density lipoprotein (LDL) and very LDL, alongside a significant rise in high-density lipoprotein. Furthermore, the weight loss observed in diabetic controls was attenuated in animals receiving TFE or metformin.

Conclusion: TFE extract markedly enhanced glycaemic regulation, corrected lipid disturbances and reduced systemic inflammation in diabetic rats. These actions are likely mediated by bioactive constituents such as trigonelline and 4-hydroxyisoleucine, supporting its promise as a safe, plant-based adjunct in the management of type 2 diabetes.

Keywords: Antihyperlipidaemic, immunomodulatory, resistin, *Trigonella foenum-graecum*, type 2 diabetes

INTRODUCTION

Diabetes mellitus (DM) is a long-standing metabolic condition marked by chronically raised blood glucose levels due to impaired insulin secretion, insulin resistance or both.^[1,2] Globally, the number of individuals living with diabetes was over 450 million in 2017, and projections suggest that this may rise beyond 690 million by 2045. Type 2 DM (T2DM), which represents over 90% of cases, is strongly associated with obesity, lack of physical activity and dietary changes.^[3] In addition to hyperglycaemia, T2DM is typically accompanied by lipid imbalance, oxidative stress

and inflammation, all of which contribute to cardiovascular and renal complications.^[4-6]

Chronic hyperglycaemia promotes oxidative damage through lipid peroxidation and protein glycation, mechanisms central to the development of both microvascular (e.g., nephropathy and retinopathy) and macrovascular complications such as coronary artery disease.^[7] In parallel, dyslipidaemia – characterised by elevated low-density lipoprotein (LDL) and reduced high-density lipoprotein (HDL) – further augments atherogenic risk.^[8] While several oral antidiabetic drugs are available, their long-term use is often limited by side effects, including hypoglycaemia and hepatotoxicity, as well as a gradual decline in therapeutic response. These limitations emphasise the need for safer interventions with broader metabolic benefits.

Herbal remedies have attracted renewed interest in recent years due to their multiple pharmacological properties, favourable safety margin and affordability.^[9] Among these, *Trigonella foenum-graecum* (TFE) (fenugreek), a Fabaceae family herb widely used in Indian and Mediterranean medicine, is noteworthy. Its seeds contain diverse phytochemicals – such as trigonelline, flavonoids, saponins, 4-hydroxyisoleucine and dietary fibres – that collectively contribute to reported insulinotropic, glucose-lowering, lipid-regulating and antioxidant effects.^[10,11]

While fenugreek's glucose-lowering and lipid-modifying properties are well recognised, its immunomodulatory potential under diabetic conditions has been less thoroughly studied. Given the established role of inflammation and immune imbalance in diabetes pathogenesis, it is important to explore interventions that provide dual metabolic and immune benefits. With this background, the present work was undertaken to investigate the antidiabetic, antihyperlipidaemic and immunomodulatory actions of ethanolic fenugreek extract in streptozotocin (STZ)-induced diabetic rats, with metformin as the comparator.

MATERIALS AND METHODS

Study design and ethical approval

The study was carried out in the Department of Pharmacology and Therapeutics, King George's Medical University, Lucknow, with the objective of assessing the antidiabetic, lipid-lowering and immunomodulatory effects of TFE extract. Ethical clearance was obtained from the Institutional Animal Ethics Committee (IAEC No. 183/IAEC/2023), and all experimental procedures complied with CCSEA regulations.

Experimental animals

Adult male Wistar rats (160–200 g) were used for the experiment. Thirty-six animals were procured from CDRI

(Old Campus), Lucknow, and housed in the Institutional Animal Facility under standard laboratory conditions: Ambient temperature 24–27°C, humidity 60–65% and a 12 h light/dark cycle. Food and water were provided ad libitum. Two diets were used – a normal pellet diet (NPD) and a high-fat diet (HFD). The HFD, sourced from Bharat Science Solution Company, Unnao (Uttar Pradesh), delivered 58% calories from fat, 25% from protein and 17% from carbohydrate. All rats were acclimatised for 1 week before starting the protocol.

Drugs and chemicals

STZ was obtained from SRL Diagnostics (India) and dissolved in freshly prepared cold 0.1 M citrate buffer (pH 4.5) immediately before intraperitoneal use. Metformin, purchased from Abhilasha Pharma Pvt. Ltd. (Ankleshwar, Gujarat), was dissolved in distilled water and administered orally. TFE extract in powdered form was procured from Tokyo Chemical Industry Co., Ltd. (TCI Chemicals), Tokyo, Japan, and suspended in distilled water for oral administration at doses of 200, 500 and 1000 mg/kg body weight (BW). All other chemicals used were of analytical grade.

Induction of T2DM

All groups except Group I (Normal Control) were placed on an HFD for 28 days to promote insulin resistance. On Day 29, following an overnight fast, these rats received a single intraperitoneal injection of STZ (40 mg/kg BW), prepared in freshly made cold citrate buffer (0.1 M, pH 4.5) and administered within 15–20 min.^[12] Group I animals were given citrate buffer alone. After 1 week, fasting blood glucose (FBG) was measured by tail vein sampling using a glucometer (Accu-Chek). Animals with glucose values above 250 mg/dL were confirmed diabetic and enrolled for further treatment.^[13]

Experimental design

A total of 36 rats were enrolled and, after 1 week of acclimatisation, randomly allocated into six groups of six animals each. Group I served as Normal Control (NPD-fed + citrate buffer injection). Group II represented the Diabetic Control (HFD-fed + STZ 40 mg/kg + distilled water). Groups III, IV and V consisted of diabetic rats receiving TFE at 200, 500 and 1000 mg/kg/day, respectively. Group VI was treated with metformin (100 mg/kg/day).^[14,15] STZ was administered on Day 29, and treatment with TFE or metformin was initiated thereafter for 21 days, following confirmation of hyperglycaemia (FBG >250 mg/dL) [Figure 1].

BW, FBG, lipid profile and serum resistin were evaluated at 3 time points: Baseline (Day 0), week 5 (post-STZ) and week 8 (after treatment). Blood was collected through tail

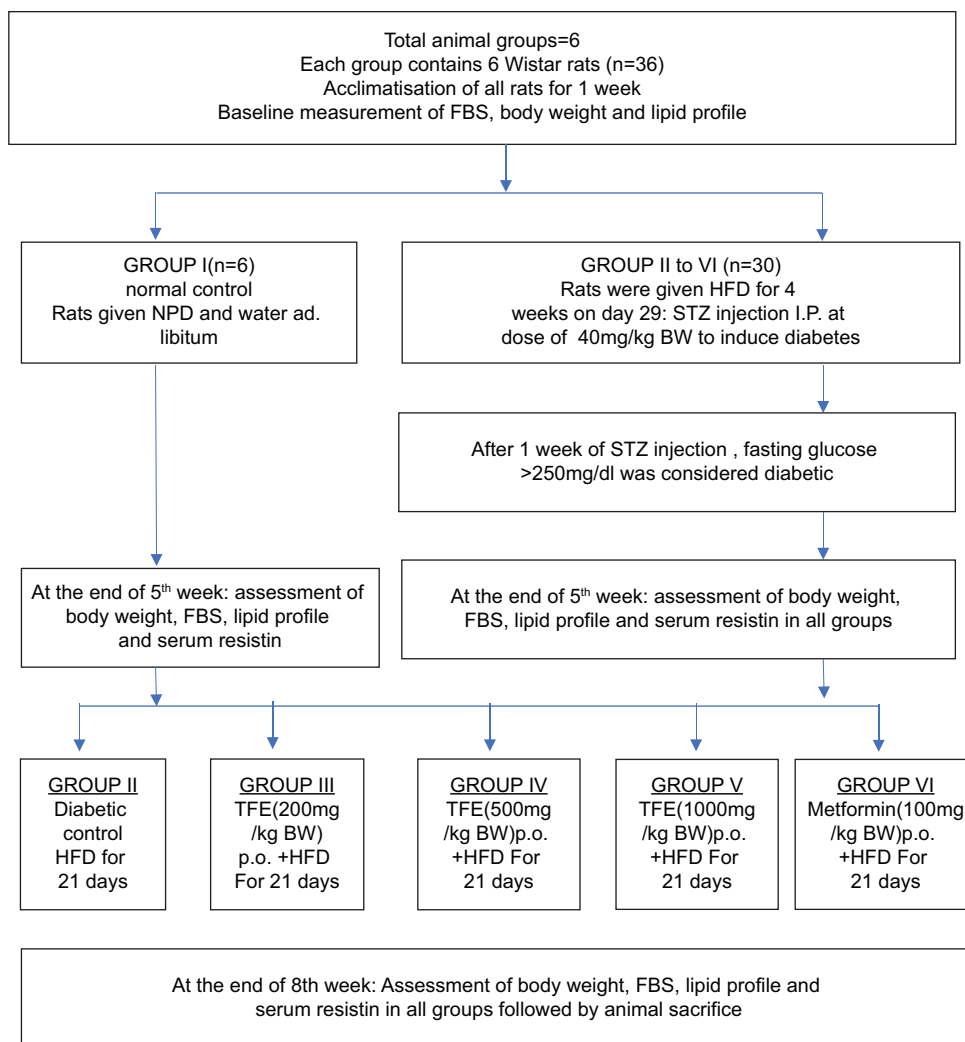


Figure 1: Flowchart showing experimental design, animal grouping, induction of diabetes using HFD and STZ and subsequent treatment with TFE or metformin. HFD: High-fat diet, NPD: Normal pellet diet, STZL: Streptozotocin, TFE: *Trigonella foenum-graecum* extract, BW: Body weight, FBS: Fasting blood sugar.

vein puncture and, at the terminal stage, through the retro-orbital plexus under anaesthesia.^[16,17] These assessments were aimed at determining the antidiabetic, lipid-regulating and immunomodulatory potential of TFE in STZ-induced diabetic rats on HFD.

Blood collection

Blood was obtained at baseline, week 5 and week 8 for analysis of fasting blood sugar (FBS), body weight, lipid profile and serum resistin. For tail vein collection, animals were gently restrained, and tails were briefly immersed in lukewarm water to dilate the veins. After cleaning with alcohol, blood was drawn from the lateral tail vein using a fine needle inserted nearly parallel to the vessel. Correct entry was confirmed by flashback, and samples were aspirated slowly.^[16] At study termination,

retro-orbital blood was collected under light anaesthesia using a capillary tube.^[17] Serum was separated and preserved for subsequent biochemical and immunological analyses.

Parameters measured

Estimation of blood glucose

FBG was assessed at all 3 time points (Day 0, week 5 and week 8) using an Accu-Chek glucometer with samples obtained from the tail vein.

Estimation of serum lipid profile

Lipid parameters, including serum total cholesterol (TC), triglycerides (TG) and HDL cholesterol, were measured

using a SELECTRA PRO XL autoanalyser. LDL and very LDL (VLDL) levels were calculated by applying the Friedewald formula: $LDL = TC - (HDL + TG/5)$ and $VLDL = TG/5$.

Estimation of serum resistin

Resistin was quantified using a rat resistin enzyme-linked immunosorbent assay kit (Elabsience Biotechnology, Cat. No. E-EL-R0614, Lot No. UFXO486H1975) following the manufacturer's instructions. Serum was obtained by centrifugation of blood samples and preserved at -20°C until testing.

Statistical analysis

Data entry and tabulation were performed using Microsoft Excel (Office 365), and statistical analysis was carried out with the Statistical Package for the Social Sciences version 24.0. Results were expressed as mean \pm standard deviation. Paired *t*-test was used for within-group comparisons across time points, while intergroup variations were assessed using one-way analysis of variance followed by Tukey's honest significant difference *post hoc* test. Significance was defined at $P < 0.05$, with $P < 0.01$ and $P < 0.001$ indicating stronger levels of significance.

RESULTS

Intergroup comparison of BW at different time intervals

At baseline (Day 0), mean BWs were similar across groups ($P = 0.853$), ranging from 164.00 ± 6.75 g in Group I to 168.32 ± 4.05 g in Group II. By the 5th week, all diabetic groups (II–VI) recorded significantly greater weights compared with Group I ($P < 0.001$), with the maximum increase observed in Group VI (263.01 ± 3.46 g). At the 8th week, Group II continued to show the highest weight (262.82 ± 5.84 g), while Groups III–V demonstrated reductions, most pronounced in Group IV (196.24 ± 8.61 g). The metformin-treated group (VI) showed partial weight control (170.48 ± 5.92 g). Intergroup variations remained strongly significant ($P < 0.001$), underscoring the therapeutic impact of both TFE and metformin [Figure 2].

Intergroup comparison of blood glucose (mg/dL) at different time intervals

At baseline, no significant differences in blood glucose were observed among groups ($P > 0.05$), with values ranging from 72.83 ± 8.7 mg/dL in Group I to 79.33 ± 8.7 mg/dL in Group IV. By the 5th week, glucose levels in Group I remained much lower (76.17 ± 5.38 mg/dL) compared with all diabetic groups ($P < 0.001$), confirming successful diabetes induction. At the 8th week, Group II continued to exhibit markedly high glucose (304 ± 10.43 mg/dL), whereas

Groups V (128 ± 7.85 mg/dL) and VI (95.17 ± 6.88 mg/dL) recorded the greatest reductions. Groups III and IV showed moderate declines. Overall, intergroup variation was strongly significant ($P < 0.001$), with Group VI providing the best glycaemic control [Figure 3].

Intergroup comparison of lipid levels at 5 weeks and 8 weeks

At both the 5th and 8th weeks, lipid parameters showed significant variation across groups ($P < 0.001$). By week 8, Group II displayed the most adverse profile, with the highest TC (151.9 ± 6.6 mg/dL), TG (122.4 ± 7.7 mg/dL), LDL (96.4 ± 6.2 mg/dL) and VLDL (24.5 ± 1.6 mg/dL), accompanied by the lowest HDL (33.2 ± 2.4 mg/dL). In contrast, Group I demonstrated the healthiest pattern, characterised by an HDL of 45.1 ± 3.3 mg/dL and LDL of 48.5 ± 4.3 mg/dL. Among the treatment arms, Group VI (metformin) achieved values closest to normal (TC: 112.5 ± 4.5 mg/dL; HDL: 46 ± 1.4 mg/dL), while Group V (TFE 1000 mg/kg) also showed marked improvement. These findings reinforce the lipid-lowering efficacy of both the test extract and the reference drug [Figure 4a and b].

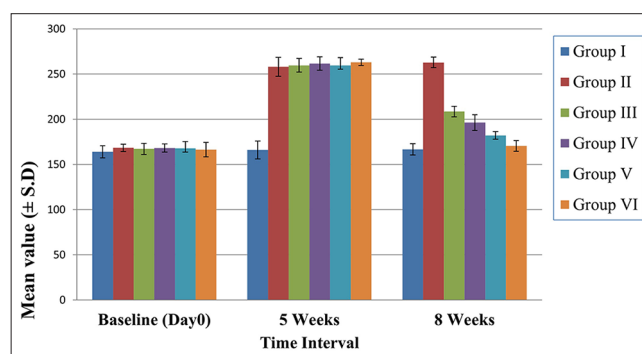


Figure 2: Bar graph showing intergroup comparison of body weight (g) at baseline (Day 0), 5th week and 8th week among control, diabetic and treatment groups. Values are expressed as mean \pm standard deviation ($n = 6$). SD: Standard deviation.

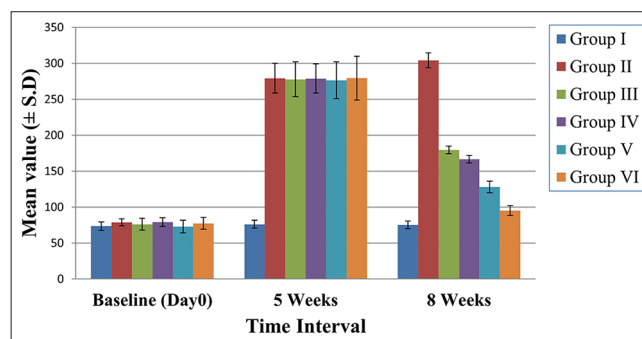


Figure 3: Bar graph showing intergroup comparison of fasting blood glucose (mg/dL) at baseline, 5th week and 8th week among control, diabetic and treatment groups. Values are expressed as mean \pm standard deviation ($n = 6$). SD: Standard deviation.

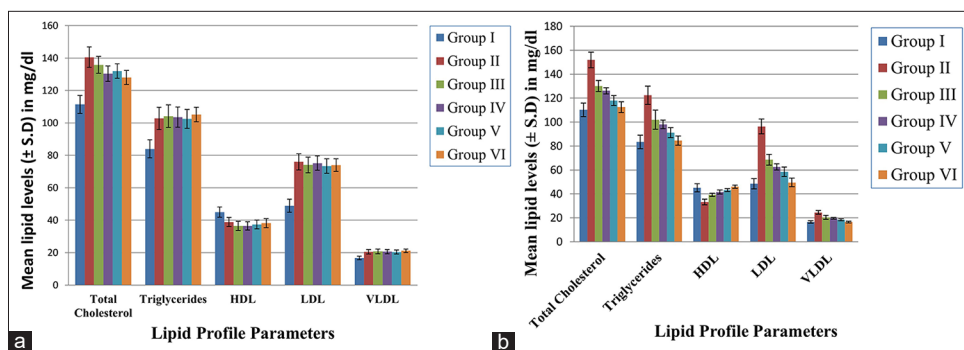


Figure 4: (a) Intergroup comparison of lipid levels at the end of the 5th week among control, diabetic and treatment groups. Parameters include TC, TG, LDL, VLDL and HDL. Values are expressed as mean \pm SD ($n = 6$). (b) Intergroup comparison of lipid levels at the end of the 8th week among control, diabetic and treatment groups. Parameters include TC, TG, LDL, VLDL and HDL. Values are expressed as mean \pm SD ($n = 6$). TC: Total cholesterol, TG: Triglycerides, VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein, SD: Standard deviation.

Intergroup comparison of serum resistin levels at 5 weeks and 8 weeks

At the 5th week, Group II recorded the highest serum resistin (18.17 ± 0.50), while Group I showed the lowest (10.14 ± 0.30). By the 8th week, marked intergroup differences persisted ($P < 0.001$). Group II continued to exhibit the highest concentration (19.64 ± 0.48), whereas the lowest value was noted in Group VI (10.65 ± 0.28), followed by Group V (11.83 ± 0.30) and Group I (10.32 ± 0.28). Groups III and IV displayed moderate declines. The overall ranking at 8 weeks was: VI < I < V < IV < III < II, underscoring the most pronounced immunomodulatory action of metformin and high-dose TFE [Figure 5].

DISCUSSION

Comparison of blood glucose levels among therapeutic groups and controls

At week 5, both the diabetic control (Group II) and treatment groups (III–VI) demonstrated a marked elevation in mean FBS relative to the normal control (Group I) ($P < 0.001$), confirming effective induction of diabetes. Group I maintained the lowest FBS (76.17 ± 5.38 mg/dL), while values in diabetic groups ranged from 276.33 ± 25.50 mg/dL to 279.33 ± 30.51 mg/dL. At this point, the treated groups did not differ significantly from the diabetic control.

By the 8th week, all treatment groups showed a significant fall in FBG compared with the diabetic control ($P < 0.001$). Group II maintained the highest glucose concentration (304.00 ± 10.43 mg/dL), while Group VI (metformin: 95.17 ± 6.88 mg/dL) recorded the lowest, followed by Group V (TFE 1000 mg/kg: 128.00 ± 7.85 mg/dL), indicating a dose-related antihyperglycaemic effect of TFE. Groups III and IV showed moderate improvements. These results reaffirm the glucose-

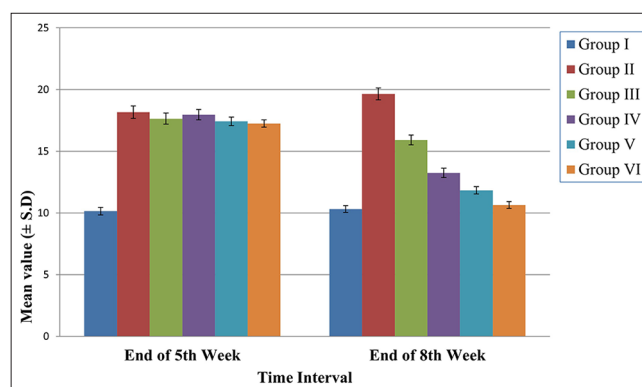


Figure 5: Bar graph showing intergroup comparison of serum resistin (pg/mL) at the 8th week among control, diabetic and treatment groups. Values are expressed as mean \pm standard deviation ($n = 6$). SD: Standard deviation.

lowering efficacy of both metformin and TFE, with greater benefit at higher TFE doses.

These observations are consistent with Alchalabi *et al.* (2019), who demonstrated that TFE significantly decreased fasting glucose and enhanced glucose tolerance in diabetic models, most effectively at 1000 mg/kg.^[18] Similarly, Tewari *et al.* (2024) noted that fenugreek promotes insulin release and hepatic glycogen storage, mechanisms that may underlie the glycaemic improvements seen in our study.^[10]

Comparison of BW among therapeutic groups and controls

At baseline, average BWs were similar across groups ($P = 0.853$), ranging from 164.00 ± 6.75 g in Group I to 168.32 ± 4.05 g in Group II, confirming uniform selection. By week 5, diabetic groups (II–VI) showed significantly greater weight than Group I ($P < 0.001$), with Group VI (metformin)

displaying the highest mean (263.01 ± 3.46 g), indicative of HFD-driven metabolic alterations.

At 8 weeks, Group II displayed a pronounced fall in BW (139.89 ± 5.84 g), reflecting a 16.89% decline from baseline, probably due to severe metabolic disturbances. Conversely, treatment groups showed significant recovery in a dose-related fashion. The highest restoration occurred in Group VI (metformin: 190.02 ± 5.92 g), followed by Group V (TFE 1000 mg/kg: 184.18 ± 4.15 g), Group IV (TFE 500 mg/kg: 178.24 ± 8.61 g) and Group III (TFE 200 mg/kg: 175.48 ± 5.83 g). These findings corroborate Tewari *et al.* (2024), who demonstrated that trigonelline, a major bioactive compound of TFE, improved weight gain and glycaemic control in diabetic rats in a dose-dependent pattern.^[10]

Weight reduction in diabetic rats primarily arises from insulin deficiency, increased protein breakdown and defective energy metabolism. The bioactive components of TFE appeared to correct feeding patterns and energy balance, leading to weight improvement. Metformin, known for its weight-regulating effects, also supported weight recovery, most likely through better glycaemic control and efficient energy use. These observations are consistent with earlier studies showing metformin's combined action on glucose regulation and BW improvement in diabetic models.^[19]

Comparison of lipid profile among therapeutic groups and controls

By the 8th week, the diabetic control group (Group II) exhibited pronounced dyslipidaemia, characterised by raised TC, TG, LDL and VLDL, together with decreased HDL. In contrast, treatment with TFE extract and metformin produced significant improvements in lipid parameters. The most pronounced reductions in TC (112.5 ± 4.5 mg/dL) and LDL (49.5 ± 3.6 mg/dL) were achieved in Group VI (metformin 100 mg/kg), followed sequentially by Groups V (TFE 1000 mg/kg), IV (TFE 500 mg/kg) and III (TFE 200 mg/kg). A comparable pattern was noted for TG and VLDL, with Group VI again showing the strongest effect, whereas Group III showed a non-significant declining trend.

HDL levels rose significantly in Groups IV, V and VI, with the greatest increase noted in Group VI (46.0 ± 1.4 mg/dL), reflecting restoration of anti-atherogenic potential. Group III showed only a slight, non-significant elevation. These results are consistent with Alchalabi *et al.* (2019), who demonstrated that fenugreek seed extract lowered TG, TC and LDL while raising HDL.^[18] Similar lipid-regulating actions were described by Geberemeskel *et al.* (2019) and Bafadam *et al.* (2021), reinforcing the cardioprotective and antihyperlipidaemic role of TFE.^[20,21]

The lipid-lowering effect of metformin in this study is consistent with previous findings by Solymar *et al.* (2018),

which attributed its benefits to the modulation of hepatic lipid metabolism and enhanced insulin sensitivity.^[22] The hypolipidaemic properties of TFE are most likely linked to trigonelline and associated alkaloids that suppress lipogenic enzymes such as peroxisome proliferator-activated receptor- γ , fatty acid synthase and acetyl-CoA carboxylase. In addition, trigonelline may stimulate bile acid production and improve hepatic lipid clearance, leading to better lipid regulation and a reduced cardiovascular risk in diabetes.

Comparison of serum resistin levels among therapeutic groups and controls

By the 8th week, serum resistin levels were markedly higher in the diabetic control group (Group II: 55.67 ± 3.5 pg/mL) compared with the normal control (Group I: 25.5 ± 3.02 pg/mL), reflecting increased inflammatory activity and insulin resistance. Administration of TFE produced a dose-related reduction, with Group V (1000 mg/kg: 37.17 ± 2.79 pg/mL) and Group IV (500 mg/kg: 47.17 ± 2.48 pg/mL) showing significant decreases relative to Group II. Group III (200 mg/kg: 51.00 ± 3.16 pg/mL) exhibited only a mild, non-significant decline. Among the treated groups, the lowest resistin was observed in Group VI (metformin 100 mg/kg: 30.00 ± 3.16 pg/mL), approaching values seen in normal controls.

Our findings are consistent with those of Visuvanathan *et al.*, who demonstrated that trigonelline – an active principle of fenugreek – improves insulin signalling by activating PPAR- γ and GLUT4, leading to reduced resistin expression.^[23] Similarly, Sfar *et al.* highlighted trigonelline's antioxidant and anti-inflammatory effects, noting its ability to influence cytokine profiles, including resistin, thereby mitigating metabolic inflammation in T2DM.^[24]

The immunomodulatory action of TFE is likely mediated through suppression of the nuclear factor-kappa B (NF- κ B) pathway, a central regulator of pro-inflammatory cytokine expression. Inhibiting NF- κ B decreases resistin and other inflammatory mediators, thereby enhancing insulin sensitivity. In addition, fenugreek bioactives may activate adenosine monophosphate-activated protein kinase (AMPK), further strengthening insulin signalling and attenuating resistin-associated inflammation. In support, Pandey *et al.* (2024) observed that metformin and sodium-glucose cotransporter 2 inhibitors lowered leptin while elevating adiponectin in diabetic rats, suggesting a shared mechanism of immunometabolic regulation in T2DM.^[25]

CONCLUSION

This study showed that TFE extract exerted notable antidiabetic, antihyperlipidaemic and immunomodulatory effects in STZ-induced diabetic rats. Administration of TFE

led to dose-dependent improvements in FBG, BW and lipid parameters, with maximum benefit observed at 1000 mg/kg. In addition, serum resistin – an indicator of inflammation and insulin resistance – was significantly lowered in TFE-treated groups, especially at higher doses.

The observed benefits are probably attributable to fenugreek's active constituents, such as trigonelline and 4-hydroxyisoleucine, which improve insulin responsiveness, influence inflammatory cascades and regulate lipid metabolism. At higher doses, TFE exhibited effects comparable to metformin, highlighting its promise as a natural alternative or adjunct therapy in type 2 diabetes and related metabolic disorders.

Overall, TFE appears to be a safe, plant-based therapeutic option with potential to address not only glycaemic regulation but also dyslipidaemia and inflammation in diabetes. Long-term studies, mechanistic exploration and clinical trials are warranted to confirm its efficacy and support its incorporation into standard diabetes care.

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Ethical approval: The research study was approved by the Institutional Animal Ethics Committee (IAEC), King George's Medical University, Lucknow, with approval no. 183/IAEC/2023, dated 10th October 2023, and all procedures were performed in accordance with CCSEA guidelines.

Declaration of patient consent: Patient's consent was not required as there are no patients in this study.

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Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2012;35(Suppl 1):S64-71.
- Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, *et al.* Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci* 2020;21:6275.
- Mohan V, Sudha V, Shobana S, Gayathri R, Krishnaswamy K. Are unhealthy diets contributing to the rapid rise of type 2 diabetes in India? *J Nutr* 2023;153:940-8.
- Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract* 2010;87:4-14.
- NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet* 2016;387:1513-30. Erratum in: *Lancet* 2017;389:e2.
- Cho NH, Shaw JE, Karuranga S, Huang Y, Da Rocha Fernandes JD, Ohlrogge AW, *et al.* IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract* 2018;138:271-81.
- Bello NA, Pfeffer MA, Skali H, McGill JB, Rossert J, Olson KA, *et al.* Retinopathy and clinical outcomes in patients with type 2 diabetes mellitus, chronic kidney disease, and anemia. *BMJ Open Diabetes Res Care* 2014;2:e000011.
- Fowler MJ. Microvascular and macrovascular complications of diabetes. *Clin Diabetes* 2008;26:77-82.
- El-Tantawy WH, Temraz A. Management of diabetes using herbal extracts: Review. *Arch Physiol Biochem* 2018;124:383-9.
- Tewari A, Singh R, Brar JK. Pharmacological and therapeutic properties of fenugreek (*Trigonella foenum-graecum*) seed: A review. *J Phytopharmacol* 2024;13:97-104.
- Ruwali P, Pandey N, Jindal K, Singh RV. Fenugreek (*Trigonella foenum-graecum*): Nutraceutical values, phytochemical, ethnomedicinal and pharmacological overview. *S Afr J Bot* 2022;151:423-31.
- Akbarzadeh A, Norouzi D, Mehrabi MR, Jamshidi SH, Farhangi A, Verdi AA, *et al.* Induction of diabetes by Streptozotocin in rats. *Indian J Clin Biochem* 2007;22:60-4.
- Srinivasan K, Viswanad B, Asrat L, Kaul CL, Ramarao P. Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: A model for type 2 diabetes and pharmacological screening. *Pharmacol Res* 2005;52:313-20.
- Xue WL, Li XS, Zhang J, Liu YH, Wang ZL, Zhang RJ. Effect of *Trigonella foenum-graecum* (fenugreek) extract on blood glucose, blood lipid and hemorheological properties in streptozotocin-induced diabetic rats. *Asia Pac J Clin Nutr* 2007;16 Suppl 1:422-6.
- Zhou X, Zhou J, Ban Q, Zhang M, Ban B. Effects of metformin on the glucose regulation, lipid levels and gut microbiota in high-fat diet with streptozotocin induced type 2 diabetes mellitus rats. *Endocrine* 2024;86:163-72.
- Brown C. Blood collection from the tail of a rat. *Lab Anim (NY)* 2006;35:24-5.
- Medhi B, Prakash A. Practical manual of experimental and clinical pharmacology. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2016. p. 38-9.
- Alchalabi SM, Abdul-Lattif RF, Mahdawi FA, Abud HN. Effect of fenugreek (*Trigonella foenum graecum*) seed aqueous extract on blood glucose, lipid profile and some hormonal assay in streptozotocin-induced diabetic male albino rats. *Int J Drug Deliv Technol* 2019;39:444-8.
- Golay A. Metformin and body weight. *Int J Obes (Lond)* 2008;32:61-72.
- Geberemeskel GA, Debebe YG, Nguse NA. Antidiabetic effect of fenugreek seed powder solution (*Trigonella foenum-graecum* L.) on hyperlipidemia in diabetic patients. *J Diabetes Res* 2019;2019:8507453.
- Bafadam S, Mahmoudabady M, Niazmand S, Rezaee SA, Soukhtanloo M. Cardioprotective effects of Fenugreek (*Trigonella foenum-graecum*) seed extract in streptozotocin induced diabetic rats. *J Cardiovasc Thorac Res* 2021;13:28-36.
- Solymár M, Ivic I, Pótó L, Hegyi P, Garami A, Hartmann P, *et al.* Metformin induces significant reduction of body weight, total cholesterol and LDL levels in the elderly - A meta-analysis. *PLoS One* 2018;13:e0207947.

23. Visuvanathan T, Than LT, Stanslas J, Chew SY, Vellasamy S. Revisiting *Trigonella foenum-graecum* L.: Pharmacology and therapeutic potentialities. *Plants (Basel)* 2022;11:1450.
24. Sfar M, Jaouani A, Ben-Mahrez K, Skhiri HA, Ben Rayana C, Chemli R, *et al.* The effect of fenugreek on blood glucose, lipid parameters, insulin and resistin in obese women with type 2 diabetes. *Hum J* 2018;11:108-23.
25. Pandey R, Dwivedi S, Hussain MS, Dixit AK, Sachan AK, Singh SK, *et al.* An experimental study to evaluate the effect of antihyperglycemic drugs on serum leptin and adiponectin levels in streptozotocin-induced diabetes in Wistar rats. *Int J Pharm Sci Rev Res* 2024;84:136-44.

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