ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 12| Issue: 1| January2026|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2025: 8.691 || ISI Value: 1.188

SCIENTIFIC VALIDATION OF VIDANGADI GUGGULU IN DIABETES MELLITUS USING STREPTOZOTOCIN-INDUCED WISTAR RAT MODEL

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Article DOI: https://doi.org/10.36713/epra25883
DOI No: 10.36713/epra25883

ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia and associated complications. In Ayurveda, diabetes is correlated with Prameha, and Vidangadi Guggulu is traditionally indicated for Meha as per classical texts (Chakradatta, 44/69-70).[10] Despite its traditional use, experimental validation is limited.

*The present study evaluated the **antihyperglycaemic activity** of Vidangadi Guggulu in streptozotocin (STZ)-induced diabetic Wistar rats. Twenty-four healthy adult Wistar albino male rats were divided into four groups (n = 6): normal control, diabetic control, standard drug treated (Metformin 100 mg/kg, p.o.), and test drug treated (Vidangadi Guggulu 50 mg/kg, p.o.). Diabetes was induced by a single intraperitoneal injection of STZ (40 mg/kg). Fasting blood glucose (FBG) was measured at baseline, after STZ induction, and after 14 days of treatment.*

STZ administration caused significant hyperglycaemia in all diabetic groups. Treatment with Vidangadi Guggulu significantly reduced FBG levels (63.98%), comparable to Metformin (69.41%) ($p < 0.001$).

*These results suggest that Vidangadi Guggulu, as described in Chakradatta (44/69-70), possesses significant **antihyperglycaemic activity**, supporting its traditional use in the management of Prameha. **Further studies are needed to confirm its therapeutic potential in humans.***

KEYWORDS: *Vidangadi Guggulu, Meha, Prameha, Diabetes mellitus, Streptozotocin, Antihyperglycaemic activity, Antidiabetic activity*

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia due to impaired insulin secretion, insulin action, or both. [3] Clinically, it manifests as polyuria, polydipsia, polyphagia, fatigue, and weight loss. Prolonged hyperglycaemia can lead to complications such as neuropathy, nephropathy, retinopathy, and cardiovascular disorders.

Globally, more than 500 million individuals are affected by diabetes, with India accounting for approximately 77 million cases. [3] The prevalence is rising among both adults and children due to lifestyle changes, urbanization, and dietary habits.

In Ayurveda, diabetes is correlated with *Prameha*, a metabolic disorder primarily involving vitiation of *Kapha* and *Meda*, progressing to *Madhumeha* due to aggravated *Vata*. [8,9] Pathogenesis involves impaired *Agni*, accumulation of *Kleda*, and obstruction of *Srotas*, which parallels insulin resistance and metabolic dysregulation in modern medicine.

Vidangadi Guggulu, a classical formulation described in *Chakradatta* (44/69-70) [10] , is indicated for **Meha, Kustha, Shwasa, Kasa, Jwara, Dusht Vrana, and Nadi-Vrana**. The formulation possesses *Kapha-Medohara*, *Deepana*, *Pachana*, and *Lekhana* properties, which are expected to support glycaemic control and metabolic balance. Despite its classical use, experimental validation of its **antidiabetic activity** is limited.

Therefore, this study was designed to evaluate the efficacy of *Vidangadi Guggulu* in STZ-induced diabetic Wistar rats and compare its effects with the standard drug Metformin.

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MATERIALS & METHODS

Ethical Approval

The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of Siksha 'O' Anusandhan, Bhubaneswar, India, in accordance with CPCSEA guidelines.

Experimental Animals

A total of 24 healthy adult male Wistar albino rats (180–250 g), were procured from the Animal House Facility, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan, Bhubaneswar. Prior to experimentation, all rats were examined and confirmed to be healthy, active, and free from clinical abnormalities.

Housing and Feeding

Wistar albino rats were housed individually in polypropylene cages under controlled environmental conditions: 22 ± 2°C temperature, 45–55% relative humidity (not exceeding 70%) and 12-hour light/dark cycle. Standard laboratory pellet diet and filtered drinking water were provided **ad libitum,** and bedding was replaced regularly to ensure hygienic conditions. All animals were acclimatized to laboratory conditions for 7 days prior to experimentation and were observed daily for general health and normal behaviour.

Drugs and Chemicals

1. **Streptozotocin (STZ) (40 mg/kg)** – for induction of diabetes, freshly prepared in 0.1 M citrate buffer (pH 4.5) before administration.
2. **Standard Drug – Metformin (100 mg/kg)** – used as the reference anti-diabetic drug. [4-6]
3. **Test Drug – Vidangadi Guggulu (50 mg/kg)** – prepared as per classical Ayurvedic guidelines and administered orally.
4. **Normal Saline** – used as the vehicle control.

All chemicals were of analytical grade.

Dose selection

The dose of Vidangadi Guggulu (50 mg/kg, p.o.) was selected based on classical Ayurvedic references and previous preclinical studies. The Metformin dose (100 mg/kg, p.o.) was chosen as the standard reference based on widely accepted experimental protocols. The dose selection ensures safety and relevance for evaluating anti-diabetic efficacy in the STZ-induced Wistar rat model.

Preparation and Administration of Doses

The required dose of Vidangadi Guggulu (50 mg/kg) was accurately weighed and freshly suspended in warm distilled water. Metformin (100 mg/kg) was freshly dissolved in distilled water. Streptozotocin was freshly prepared in 0.1 M citrate buffer immediately before use and protected from light until administration.

All drugs were administered orally once daily for 14 consecutive days using a soft, flexible, ball-tipped gavage needle attached to a calibrated syringe, minimizing the risk of esophageal irritation. Both normal and diabetic control groups received normal saline orally throughout the study. The standard drug group received Metformin (100 mg/kg), while the test drug group received Vidangadi Guggulu (50 mg/kg). All administrations were carried out at approximately the same time each day, and animals were observed for immediate adverse effects after dosing.

Induction of Diabetes

Diabetes was induced in Wistar rats by a single intraperitoneal injection of STZ (40 mg/kg body weight) [1,2], which is widely used for experimental induction of diabetes mellitus. On Day 1, rats were fasted overnight prior to STZ administration. STZ was freshly prepared in citrate buffer and administered intraperitoneally using a 1-mL syringe with a 23-G needle. The normal control group received an equivalent volume of normal saline via the same route. After STZ administration, animals were allowed free access to food and water.

Confirmation of Diabetes and Randomization

Fasting blood glucose levels were measured on the 7th day following STZ administration using blood samples obtained from the tail vein. Wistar albino Rats with FBG levels ≥ 250 mg/dL were considered diabetic. Out of 24 rats, 18 met the diabetes criteria and were randomly assigned to experimental groups for evaluation.

Experimental Design

The rats were divided into four groups (n = 6 per group):

- **Group I (G1) – Normal Control:** Non-diabetic rats receiving normal saline orally.
- **Group II (G2) – Diabetic Control:** STZ-induced diabetic rats receiving normal saline orally.
- **Group III (G3)– Standard Drug Treated:** STZ-induced diabetic rats receiving Metformin (100 mg/kg, p.o.) once daily for 14 days.
- **Group IV (G4) – Test Drug Treated:** STZ-induced diabetic rats receiving Vidangadi Guggulu (50 mg/kg, p.o.) once daily for 14 days.

Assessment of Fasting Blood Glucose

Fasting blood glucose levels were measured at three stages:

1. **Baseline (Day 0):** Before STZ administration.
2. **Post-STZ induction (Day 7):** To confirm diabetes.
3. **After treatment (Day 21):** One hour after the last dose to evaluate the anti-diabetic effect.

Treatment Protocol (Day-wise)

- **Day 1:** Baseline FBG measured in all groups; STZ administered to Groups II, III, IV; Group I received normal saline.
- **Day 7:** FBG measured to confirm induction of diabetes in Groups II, III, IV.
- **Day 7–21:** Daily oral administration of respective treatments:
  - G1 – normal saline
  - G2 – normal saline
  - G3 – Metformin 100 mg/kg
  - G4 – Vidangadi Guggulu 50 mg/kg
- **Day 21:** FBG measured one hour after last dose in all groups.

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Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Comparisons between groups were performed using **one-way analysis of variance (ANOVA)** followed by **Tukey's post-hoc test**. Differences were considered statistically significant at $p < 0.05$. Percentage reduction in fasting blood glucose (FBG) levels was calculated as:

$$\%\text{Reduction} = \frac{\text{FBG after STZ} - \text{FBG after treatment}}{\text{FBG after STZ}} \times 100$$

RESULTS

Baseline fasting blood glucose levels recorded before streptozotocin (STZ) administration showed no statistically significant difference among all experimental groups ($p > 0.05$), indicating uniformity and homogeneity of the experimental animals.

Administration of streptozotocin produced a marked elevation in fasting blood glucose levels in all STZ-treated groups (G2, G3, and G4) when compared with the normal control group (G1). The increase in FBG levels was highly significant ($p < 0.001$), confirming successful induction of diabetes in the experimental animals. No significant difference was observed among the diabetic groups before initiation of treatment ($p > 0.05$), indicating equal severity of diabetes across groups.

After 14 days of treatment, the diabetic control group (G2) showed persistently elevated fasting blood glucose levels (296.16 ± 17.61 mg/dL) indicating sustained hyperglycaemia in the absence of treatment. In contrast, the standard drug treated group (G3) receiving Metformin (100 mg/kg) resulted in a significant reduction in fasting blood glucose levels (126.0 ± 2.52 mg/dL) compared to the diabetic control group ($p < 0.01$), corresponding to a percentage reduction of 69.41%. The test drug treated group (G4) administered Vidangadi Guggulu (50 mg/kg) also demonstrated a significant reduction in fasting blood glucose levels (141.5 ± 2.07 mg/dL) when compared to the diabetic control group ($p < 0.01$), with a percentage reduction of 63.98%. (**Figure 1**).

The reduction observed with Vidangadi Guggulu was comparable to Metformin, with a small but statistically significant difference between standard and test drug groups (**$p < 0.05$**). (**Figure 2**).

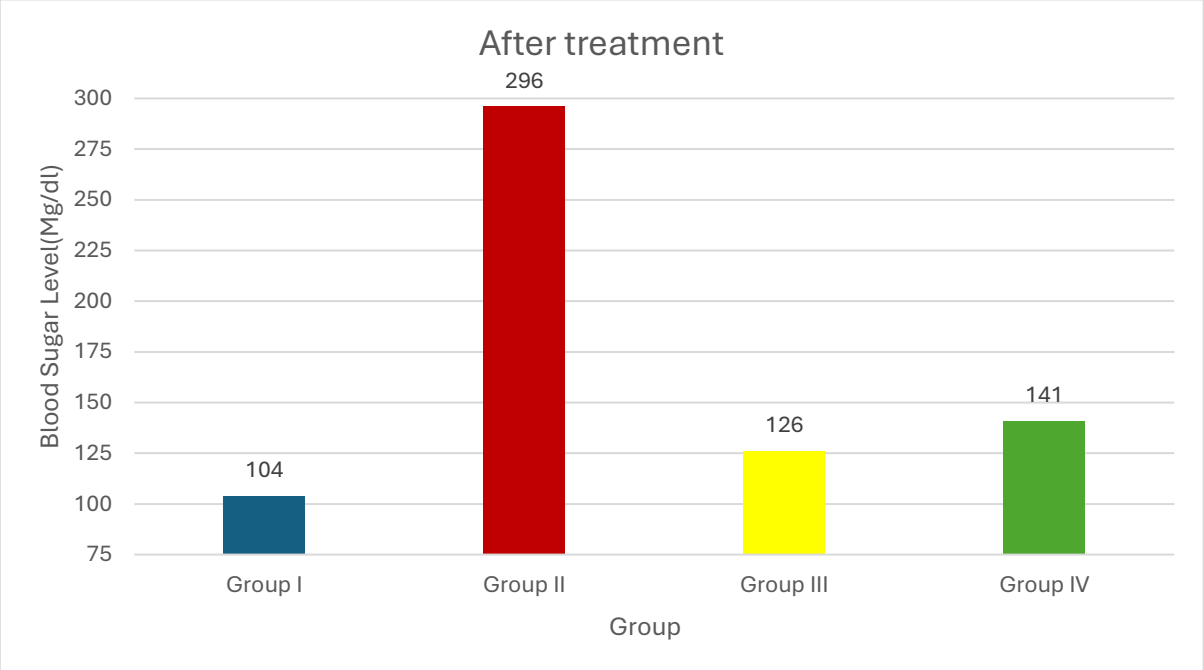

Figure 1: Comparison of fasting blood glucose levels after 14 days of treatment in STZ-induced diabetic rats (Mean ± SD, n = 6).

Description: After 14 days, diabetic control (G2) maintained elevated FBG, whereas Metformin (G3) and Vidangadi Guggulu (G4) significantly reduced FBG (**$p < 0.01$**). The percentage reduction was 69.41% for Metformin and 63.98% for Vidangadi Guggulu, indicating comparable antihyperglycaemic efficacy.

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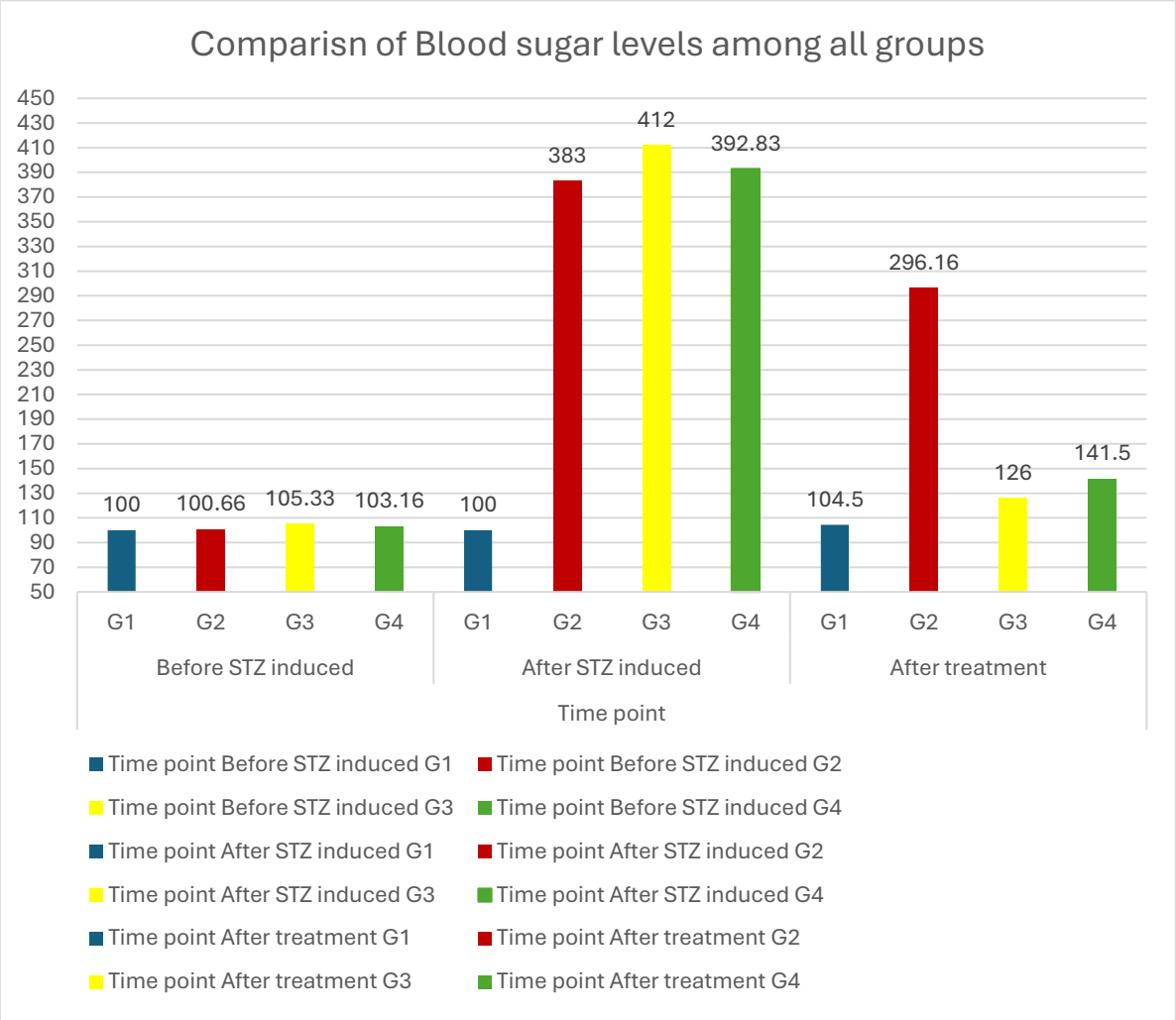

Figure 2: Overall comparison of fasting blood glucose levels in STZ-induced diabetic rats across all experimental groups (Mean ± SD, n = 6).

Description: Baseline FBG was comparable among all groups ($p > 0.05$). STZ administration caused a significant increase in FBG in diabetic groups (G2–G4) compared to normal control (G1) ($p < 0.001$). After 14 days of treatment, Metformin (G3) and Vidangadi Guggulu (G4) significantly reduced FBG compared to diabetic control (G2) ($p < 0.01$), with 69.41% and 63.98% reduction, respectively, indicating comparable antihyperglycaemic efficacy of Vidangadi Guggulu.

Percentage Reduction in Fasting Blood Glucose

The percentage reduction in fasting blood glucose levels was calculated to assess the antihyperglycaemic effect of the treatments. Metformin produced a 69.41% reduction in fasting blood glucose levels, while Vidangadi Guggulu produced a 63.98% reduction. This finding indicates substantial antihyperglycaemic activity of Vidangadi Guggulu, comparable to the standard drug.

Table 1: Effect of Vidangadi Guggulu on fasting blood glucose levels in STZ-induced diabetic Wistar rats

Group	No. of Animals	Drug & Dose (P.O.)	Fasting Blood Glucose (FBG)			% Reduction
			Before STZ	After STZ	After treatment	
G1– Normal Control	6	Vehicle (Normal Saline)	100 ± 2.82	100 ± 2.82	104.5 ± 2.07	---
G2 – Diabetic Control	6	Vehicle (Normal Saline)	100.66 ± 6.5	383.00 ± 130.28	296.16 ± 17.61	---
G3 – Standard Drug Treated	6	Metformin 100 mg/kg	105.33 ± 11.29	412.00 ± 87.12	126 ± 2.52	69.41%
G4 – Test Drug Treated	6	Vidangadi Guggulu 50 mg/kg	103.16 ± 8.72	392.83 ± 117.41	141.5± 2.07	63.98%

Data were expressed as Mean ± SD (n = 6).

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Summary of Findings

- Baseline fasting blood glucose levels were comparable across all groups, indicating homogeneity of experimental animals.
- STZ administration resulted in significant hyperglycaemia in all diabetic groups.
- Treatment with Metformin and Vidangadi Guggulu significantly reduced fasting blood glucose levels.
- The antihyperglycaemic effect of Vidangadi Guggulu was comparable to the standard drug Metformin.

DISCUSSION

Baseline fasting blood glucose (FBG) levels were comparable among all experimental groups, confirming uniformity prior to STZ administration. STZ injection caused a significant elevation in FBG in diabetic groups (G2–G4), validating successful induction of diabetes through pancreatic β-cell damage, consistent with previous studies. [1,2]

Treatment with Metformin (G3) significantly reduced FBG levels, confirming its well-known antihyperglycaemic mechanism via enhancement of peripheral glucose uptake and inhibition of hepatic gluconeogenesis. [4-6] The test drug, Vidangadi Guggulu (G4), also significantly reduced FBG, with a percentage reduction of 63.98%, comparable to Metformin. This demonstrates the potential of Vidangadi Guggulu as an effective antidiabetic formulation.

The glucose-lowering effect of Vidangadi Guggulu may result from the combined action of its constituent herbs, which are reported to enhance insulin sensitivity, improve glucose utilization, and provide antioxidant protection to pancreatic β-cells. Minor differences between Metformin and Vidangadi Guggulu were statistically significant but not biologically substantial, indicating that Vidangadi Guggulu could serve as a complementary or alternative therapy for diabetes management.

These results are in agreement with prior studies on herbal formulations containing Guggulu, which have reported significant reductions in blood glucose in experimental models of diabetes. [7,11]

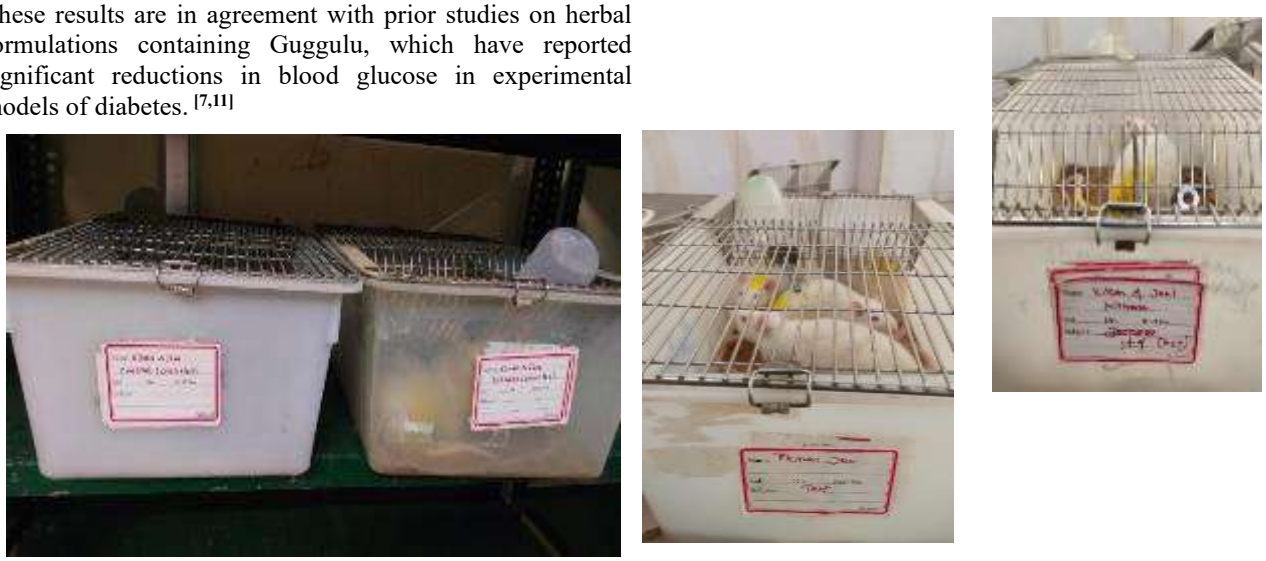

Figure 3: Experimental Group Off Animals

CONCLUSION

Vidangadi Guggulu demonstrated significant antihyperglycaemic activity in STZ-induced diabetic rats, comparable to the standard drug Metformin. These findings suggest that Vidangadi Guggulu has potential therapeutic value in the management of type 2 diabetes. Further studies examining dose optimization, long-term efficacy, and mechanism of action at the molecular level are recommended to substantiate its clinical applicability

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Figure 4,5: STZ-induction and blood glucose sample check from tail vain



Figure 6,7,8: test drug solution, standard drug solution and Oral gavage syringe for precise dosing


Figure 9,10: Dose Administration