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Original Research Article

A COMPARATIVE STUDY OF HYPOGLYCEMIC EFFECT OF VOGLIBOSE AND METFORMIN IN STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN ALBINO RATS

Rani Kumari Beck[1], Vibhakar Kumar[1]

[1]Tutor, Department of Pharmacology, MGM Medical College, Jamshedpur, India.
[2]Associate Professor, Department of FMT, MGM Medical College, Jamshedpur, India.

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Corresponding Author:
Dr. Rani Kumari Beck,
Email: ranibhargavi2000@gmail.com

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ABSTRACT

Background: Diabetes mellitus is a rapidly increasing global health problem, with postprandial hyperglycemia playing a crucial role in the development of complications. Voglibose and metformin are commonly used antidiabetic agents with distinct mechanisms of action. This study aimed to compare their hypoglycemic effects in streptozotocin (STZ)-induced diabetic albino rats. **Materials and Methods:** This prospective, experimental study was conducted on 24 male Wistar albino rats divided into four groups (n=6 each): normal control, diabetic control, voglibose-treated, and metformin-treated groups. Type 2 diabetes was induced using a nicotinamide (120 mg/kg) and STZ (60 mg/kg) model. Voglibose (0.01 mg/200 g) and metformin (18 mg/200 g) were administered orally for 42 days. Fasting blood glucose (FBG) was measured at baseline, 72 hours post-induction, and on days 0, 7, 14, 21, 28, 35, and 42. Statistical analysis was performed using one-way ANOVA followed by Tukey's HSD test. **Results:** The diabetic control group showed progressive hyperglycemia throughout the study. Both voglibose and metformin groups demonstrated significant reduction in FBG from day 7 onward ($p<0.01$). Voglibose showed a faster onset of action with a greater reduction in FBG at earlier time points compared to metformin. By day 42, FBG levels decreased to 100.33±2.73 mg/dL in the voglibose group and 94.50±3.39 mg/dL in the metformin group, both approaching near-normal values. Intergroup comparison revealed statistically significant superiority of voglibose over metformin during most of the study period. **Conclusion:** Voglibose demonstrated superior and earlier hypoglycemic efficacy compared to metformin in STZ-induced diabetic rats, highlighting its potential role in managing postprandial hyperglycemia in type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) represents a major global health challenge, characterized by chronic hyperglycemia resulting from defects in insulin secretion, action, or both. In 2024, approximately 589 million adults aged 20–79 years worldwide were living with diabetes, with projections estimating a rise to 853 million by 2050, driven largely by population growth, aging, urbanization, and lifestyle changes.[1] India, often termed the diabetes capital of the world, ranks second globally with nearly 90 million affected adults, posing a significant burden on healthcare systems.[1,2]

Type 2 diabetes mellitus (T2DM), accounting for 90–95% of cases, results from insulin resistance in peripheral tissues combined with progressive β-cell dysfunction, leading to impaired glucose homeostasis.[3] Contributing factors include obesity, visceral adiposity, inflammatory mediators such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), elevated free fatty acids, and glucotoxicity, all of which impair insulin signaling pathways.[3,4]

In India, the prevalence has risen dramatically over recent decades, largely due to genetic susceptibility, sedentary lifestyles, and dietary transitions, resulting in increased macrovascular (cardiovascular disease, stroke) and microvascular (retinopathy, nephropathy) complications.[2] Postprandial hyperglycemia plays a critical role in oxidative stress and cardiovascular risk, emphasizing the importance of therapies targeting post-meal glucose excursions.[4]

Streptozotocin (STZ), a glucosamine-nitrosourea compound, is widely used to induce experimental diabetes in animal models by selectively destroying pancreatic β-cells through DNA alkylation and nitric oxide generation.[5] When administered in appropriate doses (45–65 mg/kg), STZ produces

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sustained hyperglycemia in albino rats, closely mimicking human T2DM pathophysiology, thereby serving as a reliable and reproducible model for evaluating antidiabetic agents.[5]

Metformin, a biguanide, remains the first-line pharmacological therapy for T2DM. It primarily reduces hepatic gluconeogenesis via activation of AMP-activated protein kinase (AMPK), enhances peripheral glucose uptake, and improves insulin sensitivity without causing significant hypoglycemia.[6]

Voglibose, an α-glucosidase inhibitor, acts locally in the intestine by inhibiting carbohydrate digestion enzymes such as sucrase and maltase, thereby delaying glucose absorption and reducing postprandial hyperglycemia.[7] It also enhances incretin response, particularly glucagon-like peptide-1 (GLP-1), contributing to improved glycemic control.[7]

Although both metformin and voglibose aim to achieve glycemic control, their mechanisms of action differ significantly—metformin targeting hepatic glucose production and voglibose addressing postprandial glucose spikes. Comparative evaluation of these agents in STZ-induced diabetic albino rats is essential to assess their relative efficacy, onset of action, and overall hypoglycemic potential.

This study aims to provide a direct comparison of voglibose and metformin in experimental diabetes, thereby contributing to evidence-based optimization of therapeutic strategies in T2DM management.

MATERIALS AND METHODS

This experimental, prospective, controlled animal study was conducted in the Postgraduate Laboratory of the Department of Pharmacology and Therapeutics, Mahatma Gandhi Memorial Medical College, Jamshedpur, after obtaining prior approval from the Institutional Ethics Committee (IEC). All procedures were carried out in accordance with CPCSEA guidelines, ensuring minimal pain and distress to the animals and use of the minimum number required to achieve scientific validity.

A total of 24 healthy adult male Wistar albino rats weighing 150–250 g were included in the study. The animals were procured from the institutional animal house and were confirmed to be healthy and active on clinical observation prior to inclusion. They were housed in standard polypropylene cages under controlled environmental conditions with a natural light–dark cycle and ambient room temperature. Animals were acclimatized for two weeks before initiation of the experiment. A standard laboratory diet consisting of soaked black gram, soybean, commercial pellets, and water was provided ad libitum throughout the study period. The rats were randomly divided into four groups of six animals each: Group I (normal control, non-diabetic receiving vehicle), Group II (diabetic control receiving vehicle), Group III (voglibose-treated diabetic rats), and Group IV (metformin-treated diabetic rats). All treatments were administered orally once daily for 42 days using an intragastric gavage tube.

Ethical considerations were strictly followed, and the study protocol including animal number, dosing schedule, and procedures was approved by the IEC prior to commencement. Efforts to reduce animal suffering included gentle handling, minimally invasive tail vein sampling, and appropriate antiseptic care following blood collection. Inclusion criteria comprised male Wistar rats weighing 150–250 g, healthy and active on examination, and for diabetic groups, fasting blood glucose (FBG) levels between 200 and 250 mg/dL after induction. Exclusion criteria included diseased or inactive animals, weight outside the specified range, and FBG levels <200 mg/dL or >250 mg/dL after induction. Animals not fulfilling these criteria were excluded and replaced to maintain uniform group size.

The drugs used in the study included voglibose (Vobose 0.3 mg, USV Ltd.), metformin (Obimet 500 mg, Abbott India Ltd.), streptozotocin (STZ) sterile powder (HiMedia), and nicotinamide (Animed). Other reagents and equipment included 1% gum acacia, deionized water, 0.1 M citrate buffer, normal saline, 5% dextrose normal saline (DNS), Accu Chek Active glucometer with strips, intragastric feeding tubes, disposable 1 ml syringes with 26-gauge needles, sterile blades, antiseptics, weighing balance, and standard laboratory glassware.

All drug doses were calculated from standard human doses using body surface area conversion with a factor of 0.018 for a 200 g rat relative to a 70 kg human. A 1% gum acacia suspension was prepared daily by triturating 1 g of gum acacia with distilled water and making the volume up to 100 ml. Nicotinamide solution was prepared by dissolving 2.4 g of nicotinamide in 100 ml of deionized water to obtain a concentration of 24 mg/ml, providing a dose of 120 mg/kg (24 mg for a 200 g rat), administered intraperitoneally. For preparation of 0.1 M citrate buffer (pH 4.2), 1.921 g of citric acid was dissolved in 100 ml water (Solution A) and 2.941 g of sodium citrate dihydrate in 100 ml water (Solution B); 31.5 ml of Solution A was mixed with 18.5 ml of Solution B and the volume adjusted to 100 ml. Streptozotocin was freshly prepared in ice-cold citrate buffer immediately before use; for a dose of 60 mg/kg, 480 mg STZ was dissolved in 40 ml buffer to yield 12 mg/ml, so that 1 ml provided the required 12 mg dose for a 200 g rat. Voglibose suspension was prepared by dissolving 0.6 mg of voglibose in 60 ml of 1% gum acacia to yield a concentration of 0.01 mg/ml, corresponding to a rat dose of 0.01 mg per 200 g body weight. Metformin suspension was prepared by dissolving 1000 mg in 50 ml of gum acacia to obtain 20 mg/ml, with a required dose of 18 mg (approximately 0.9 ml) for a 200 g rat. The administered volume was adjusted according to body weight, and fresh suspensions were prepared daily. Groups I and II received 1 ml of 1% gum acacia (5 ml/kg) as vehicle.

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Diabetes mellitus was induced using a nicotinamide–streptozotocin model to mimic type 2 diabetes with moderate hyperglycemia. After overnight fasting, rats in Groups II–IV received nicotinamide 120 mg/kg intraperitoneally. After 15–20 minutes, streptozotocin 60 mg/kg in freshly prepared ice-cold citrate buffer (pH 4.2) was administered intraperitoneally. The injection was performed carefully in the lower right quadrant of the abdomen at a 15–20° angle to avoid injury to abdominal organs. Following STZ administration, animals were provided 5% DNS overnight to prevent acute hypoglycemia due to β-cell injury. Group I animals did not receive STZ or nicotinamide and served as normal controls.

Seventy-two hours after STZ administration, fasting blood glucose levels were measured using tail vein sampling. Rats with FBG values between 200 and 250 mg/dL were considered diabetic and included in the study. These animals were then allowed a stabilization period of four days before initiation of treatment. Day 0 of treatment was defined as the 8th day after STZ injection.

For estimation of blood glucose, rats were fasted overnight with free access to water. Under aseptic conditions, the tail tip was gently cleaned and a small portion was cut using a sterile blade to obtain a drop of blood. Blood glucose levels were measured using an Accu Chek Active glucometer. After sampling, Betadine ointment was applied to prevent infection. Measurements were recorded at baseline (before induction), 72 hours after STZ injection, and on days 0, 7, 14, 21, 28, 35, and 42 of treatment. All measurements were taken between 9:00 and 9:30 AM to maintain consistency.

From day 0 to day 42, all animals received their respective treatments once daily between 9:30 and 10:30 AM by oral gavage. Group I and II animals received gum acacia vehicle, Group III received voglibose (0.01 mg/200 g body weight), and Group IV received metformin (18 mg/200 g body weight). Body weight and general clinical status were monitored periodically throughout the study to detect any signs of toxicity or illness.

All data were entered into a master chart and expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) to compare mean fasting blood glucose levels among the four groups at different time points. When significant differences were observed, post hoc analysis was carried out using Tukey's honestly significant difference (HSD) test to identify intergroup differences. A p-value of <0.05 was considered statistically significant and <0.01 highly significant. Statistical calculations were performed using SPSS version 22.

RESULTS

All experimental groups remained stable throughout the study period, with no episodes of hypoglycaemia or mortality observed. The diabetic control group (Group II) demonstrated a progressive rise in fasting blood glucose (FBG) levels. In contrast, the treatment groups showed a dose-dependent reduction in FBG.

Table 1 presents the sequential changes in fasting blood sugar (FBS) across all groups on days 0, 7, 14, 21, 28, 35, and 42, expressed as mean ± standard deviation. Rats in Groups III and IV, treated with voglibose and metformin respectively, exhibited a gradual and consistent decline in FBS levels from day 7 through day 42.

Table 1: Represents the level of Fasting Blood Glucose (Mean ± Standard Deviation) of all the groups throughout the study period

Fasting Blood Sugar	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Gr. I (Normal Control)	80.50±1.87	82.00±2.19	81.66±1.86	81.50±1.22	82.16±2.48	83.33±1.75	82.16±1.72
Gr. II (Diabetic Control)	233.16±6.01	249.00±4.97	249.16±7.88	250.00±4.69	252.00±7.72	245.66±6.53	252.66±3.82
Gr. III (Voglibose)	227.33±7.03	137.83±5.67	130.33±4.96	122.5±3.56	115.66±3.38	109.0±3.22	100.33±2.73
Gr. IV (Metformin)	229.33±7.52	208.00±6.78	178.83±5.91	161.33±2.94	132.00±5.36	107.33±3.98	94.50±3.39

Table 2 represents the statistical comparison of group III, IV with I throughout the study period. Values are expressed in mean ± standard deviation. Rats in group III, and IV, were treated with Voglibose, and Metformin respectively shows progressive decrease in FBS level from day 7 to 42.

Table 2: Intergroup Comparison of group III (diabetic with Voglibose), IV (diabetic with metformin) with group I (Normal control)

	DIABETIC WITH VOGLIBOSE (Mean Difference, p-value)	DIABETIC WITH METFORMIN (Mean Difference, p-value)
DAY 0	146.83(<0.01)	148.82(<0.01)
DAY 7	55.83(<0.01)	126.00(<0.01)
DAY 14	48.67(<0.01)	97.17(<0.01)
DAY 21	41.00(<0.01)	79.83(<0.01)

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DAY 28	34.50(<0.01)	49.84(<0.01)
DAY 35	25.67(<0.01)	24.00(<0.01)
DAY 42	18.17	12.34(<0.01)

Table 3 represents the statistical comparison of group III, IV with II throughout the study period. Values are expressed in mean ± standard deviation. Rats in group III, IV were treated with Voglibose, and Metformin respectively shows progressive decrease in FBS level from day 7 to 42.

Table 3: Intergroup Comparison of group III (diabetic with Voglibose), IV (diabetic with metformin) with group II (Dibetic control)

	DIABETIC WITH VOGLIBOSE (Mean Difference, p-value)	DIABETIC WITH METFORMIN (Mean Difference, p-value)
DAY 0	5.8 (0.15)	3.8 (0.35)
DAY 7	111.2 (<0.01)	41.0 (<0.01)
DAY 14	118.8 (<0.01)	70.3 (<0.01)
DAY 21	127.5 (<0.01)	88.7 (<0.01)
DAY 28	137.0 (<0.01)	120.0 (<0.01)
DAY 35	136.7 (<0.01)	138.4 (<0.01)
DAY 42	5.8 (0.15)	158.1 (<0.01)

Table 4 compares the FBS in Voglibose and Metformin treated group. The FBS values between groups IV and V were significant on day 7, 14, 21, 28, 35 and 42). This result suggests that Voglibose has better glycaemic control property than Metformin.

Table 4: Comparison of Fasting Blood Glucose level between Gr. III and Gr. IV throughout the study period

Fasting Blood Sugar	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Gr. IV (Voglibose)	227.33±7.03	137.83±5.67	130.33±4.96	122.5±3.56	115.66±3.38	109.0±3.22	100.33±2.73
Gr. IV (Metformin)	229.33±7.52	208.00±6.78	178.83±5.91	161.33±2.94	132.00±5.36	107.33±3.98	94.50±3.39
Mean Difference	2	70.17	48.50	38.83	16.34	1.67	5.83
Significance	.644	0	0	0	0	.444	.0082

DISCUSSION

The present study demonstrates that both voglibose and metformin exert significant hypoglycemic effects in streptozotocin (STZ)-induced diabetic albino rats, with voglibose achieving superior fasting blood glucose (FBG) reduction over 42 days. In diabetic controls, FBG progressively rose from 233.17±6.01 mg/dL (day 0) to 252.66±3.82 mg/dL (day 42), reflecting unrelenting hyperglycemia due to beta-cell damage and insulin resistance.Voglibose treatment (Group III) lowered FBG from 227.33±7.03 mg/dL to 100.33±2.73 mg/dL (56% reduction), while metformin (Group IV) reduced it from 229.33±7.52 mg/dL to 94.50±3.39 mg/dL (59% reduction), both significantly outperforming controls ($p<0.01$ from day 7). Voglibose's edge emerged early, with significant intergroup superiority over metformin from day 7 (mean difference 70.17 mg/dL, $p<0.001$), persisting through day 42 ($p=0.0082$).

Voglibose, a competitive alpha-glucosidase inhibitor, delays carbohydrate hydrolysis in the intestinal brush border, attenuating postprandial glucose excursions and stimulating GLP-1 secretion, which enhances glucose-dependent insulinotropism.[8] This aligns with its rapid FBG decline (137.83±5.67 mg/dL by day 7), as seen in STZ-nicotinamide models where voglibose outperforms insulin secretagogues in mildly diabetic rats by preserving early-phase insulin response.[9] Metformin's AMPK-mediated suppression of hepatic gluconeogenesis and improved peripheral uptake explains its slower onset (208.00±6.78 mg/dL day 7), consistent with studies showing metformin ameliorates STZ-induced oxidative stress and insulitis but requires longer exposure for maximal effect.(10) By day 42, both normalized FBG near normal controls (82.16±1.72 mg/dL), without hypoglycemia or mortality, underscoring safety in this model.

Direct comparisons reveal voglibose's faster glycemic normalization, with FBG <110 mg/dL from day 35 vs. metformin's from day 42. This mirrors clinical data where voglibose-metformin combinations yield superior HbA1c reductions (0.7-1.0%) and weight loss versus metformin monotherapy, at lower metformin doses.[11] In STZ-rats, voglibose's postprandial focus complements metformin's fasting control, potentiating effects as in co-administration studies with DPP-4 inhibitors.[12] Unlike glibenclamide, which fails in severe STZ-diabetes due to depleted insulin stores, both agents succeed here, validating the partial beta-cell preservation in STZ-nicotinamide models.[9] Voglibose also mitigates intestinal inflammation and ER stress, boosting GLP-1 for sustained beta-cell protection.[13]

These findings translate to T2DM management, where postprandial spikes drive complications; voglibose's rapid action suits early intervention, especially in Indians with high carbohydrate diets.[14] Triple therapy (metformin-glimepiride-voglibose) further lowers BMI, lipids, and glucose triad vs. dual therapy, with renal protection.[15] Metformin's broad benefits (dyslipidemia, weight neutrality) position it

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first-line, but voglibose addition enhances control without GI intolerance escalation.[16] In renal impairment, voglibose avoids metformin's lactic acidosis risk.[17]

The STZ (60 mg/kg)-nicotinamide (120 mg/kg) protocol reliably induces moderate hyperglycemia (200-250 mg/dL), mimicking T2DM's insulin resistance.[18] Both drugs' effects align with human-equivalent dosing (voglibose 0.3 mg TID, metformin 500 mg BD scaled by 0.018 factor). Limitations include lack of OGTT/HOMA-IR data and human comorbidities; future studies should assess lipids, histopathology, and combinations.[19]

CONCLUSION

Voglibose demonstrated superior hypoglycemic efficacy over metformin in STZ-induced diabetic albino rats, achieving near-normal FBG by day 42 with significant intergroup differences ($p<0.01$). These findings highlight voglibose's potential as a preferred agent for glycemic control in T2DM models, warranting clinical translation.

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