IJPSR (2026), Volume 17, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 September 2025; received in revised form, 28 October 2025; accepted, 02 November 2025; published 01 March 2026

BIOEQUIVALENCE OF DAPAGLIFLOZIN, GLIMEPIRIDE, AND METFORMIN FDC IN HEALTHY INDIAN VOLUNTEERS: A PATH TO DIABETES TREATMENT SIMPLIFICATION

Kaushik Biswas [* 1], Maddukuri Hanumantha Rao [2], Bhagyashree Panda [3], Jay C. Mehta [4], Sonali Bhojane [5], Parminder Singh [6], Thamburaj Anthuvan [7], Amit Gupta [7] and Smriti Gadia [7]

Department of Endocrinology [1], Medica Superspeciality Hospital, Kolkata - 700099, West Bengal, India.
Department of Endocrinology [2], Aravinda Diabetes & Endocrine Clinic, Ongole - 523001, Andhra Pradesh, India.
Department of Medicine [3], Pandit Raghunathmurmu Medical College and Hospital, Baripada - 757107, Odisha, India.
Department of Medicine [4], Winlife Hospital, Ahmedabad - 382470, Gujarat, India.
Nectar Diabetes Care and Thyroid Centre [5], Pune - 411009, Maharashtra, India.
Department of Endocrinology & Diabetes [6], Deep Hospital, Ludhiana - 141002, Punjab, India.
USV Private Limited [7], Mumbai - 400088, Maharashtra, India.

Keywords:

Fixed-dose combination, Dapagliflozin, Glimepiride, Type 2 Diabetes, Bioequivalence, Pharmacokinetics

Correspondence to Author:
Dr. Kaushik Biswas

Senior Consultant,
Department of Endocrinology,
Medica Superspeciality Hospital,
Kolkata - 700099, West Bengal, India.

E-mail: biswask09@gmail.com

ABSTRACT: Objectives: A fixed-dose combination (FDC) of Dapagliflozin, Glimepiride, and Metformin Extended-Release (ER) offers a comprehensive strategy for Type 2 diabetes (T2D), focusing on glycemic control, reduction of cardiovascular (CV) risk, and improved adherence through decreased pill burden. This study aimed to assess the bioequivalence and safety of this FDC in healthy Indian adult volunteers under fed conditions. **Methods:** This was a randomized, open-label, two-treatment, two-period, two-sequence, single-dose, crossover bioequivalence study. Twenty-four healthy adult male subjects received either the test FDC tablet (Dapagliflozin 10 mg/Glimepiride 2 mg/Metformin ER 1000 mg) or the reference formulations Oxramet® XR (Dapagliflozin 10 mg/Metformin ER 1000 mg) plus Amaryl® 2 mg (Glimepiride) with a 7-day washout period. Plasma concentrations were measured up to 48 hours post-dose using LC-MS/MS, and pharmacokinetic parameters were calculated. Bioequivalence was concluded if the 90% confidence intervals (CIs) for Cmax, $AUC_{0–t}$, and $AUC_{0–\infty}$ were within the 80-125% range. **Results:** All subjects completed the study. The plasma concentration-time curves of the test and reference products were nearly superimposable. The 90% CIs for all three analytes fell within the bioequivalence range of 80-125%. No serious adverse events were reported, and both formulations were well tolerated. **Conclusion:** The Dapagliflozin/Glimepiride/Metformin ER FDC is bioequivalent to the reference products and well-tolerated under fed conditions. This FDC may serve as a simplified and effective therapeutic option for management in clinical practice.

INTRODUCTION: Diabetes mellitus is a major global health issue, with India at the centre of this epidemic [1]. Projections suggest that by 2025, around 69.9 million people in India will have diabetes, many of whom remain undiagnosed [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.17(3).892-00

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(3).892-00

Poor glycemic control is common, as more than half of Indian patients with diabetes have uncontrolled blood glucose levels, often alongside hypertension, dyslipidaemia, and vascular complications [3].

A key factor in this problem is poor medication adherence [4]. Polypharmacy, especially in chronic conditions like Type 2 diabetes (T2D), frequently leads to decreased compliance with therapy [5]. Evidence shows that patients on multiple medications or regimens requiring several daily

doses are considerably less likely to adhere to their treatment [6]. Fixed-dose combinations (FDCs), which combine two or more drugs in a single pill, present a promising solution [7]. When rationally designed, FDCs can simplify treatment, reduce pill burden, improve adherence, and help patients achieve glycemic targets more effectively, while also minimizing medication waste [8, 9]. However, glycemic control alone does not fully mitigate the risk of cardiovascular (CV) events or heart failure (HF) [9, 10]. The ICMR–INDIAB study revealed a high co-prevalence of CV risk factors among Indian patients with T2D, underscoring the urgent need for holistic, risk-reducing interventions [11]. This recognition has catalyzed a paradigm shift in diabetes management from a glucose-centric model to one that also targets associated metabolic, renal, and cardiac complications [12].

In line with this approach, an FDC of Dapagliflozin, Glimepiride, and Metformin Extended Release (ER) has been developed. Dapagliflozin, a selective SGLT2 inhibitor, reduces renal glucose reabsorption and facilitates urinary glucose excretion. It carries a low risk of hypoglycemia and exhibits no significant pharmacokinetic interactions with other antihyperglycemic agents, making it an ideal candidate for combination therapy [13, 14]. Beyond glycemic benefits, landmark trials such as DECLARE-TIMI 58, DAPA-HF, and DAPA-CKD have firmly established its cardioprotective and renoprotective properties [15].

Glimepiride and Metformin individually and in combination are among the most widely prescribed agents in India and continue to serve as the cornerstone of first-line therapy [16]. Glimepiride, a second-generation sulfonylurea, has demonstrated consistent efficacy and a relatively favourable safety profile compared to older drugs in its class. Recent evidence further supports its role in improving CV outcomes in patients with diabetes and chronic HF [17, 18]. Metformin remains the foundation of T2D management due to its durable glycemic control, weight neutrality, and long-term benefits in reducing macrovascular complications, as well as lowering cancer risk [19].

Taken together, the complementary mechanisms and extensive clinical evidence supporting Dapagliflozin, Glimepiride, and Metformin provide a strong rationale for their combination in a single FDC, offering a holistic and patient-centric strategy for treatment intensification. Establishing the pharmacokinetic equivalence of FDCs and their individual components is essential for regulatory approval, particularly when pivotal safety and efficacy data have been generated using separate tablets [20]. Such studies provide the scientific basis for substituting a combination product with its individual agents.

Accordingly, the present study was designed to evaluate the bioequivalence and safety of a new FDC containing Dapagliflozin 10 mg, Glimepiride 2 mg, and Metformin ER 1000 mg, compared with the corresponding individual reference formulations, under fed conditions in healthy adult Indian male subjects.

MATERIALS AND METHODS:

Study Design: This was an open-label, balanced, randomized, two-treatment, two-sequence, two-period, two-way crossover bioequivalence study. The test formulation Dapagliflozin 10 mg/ Glimepiride 2 mg/Metformin ER 1000 mg tablets (Mascot Health Series Pvt. Ltd., India) compared with the reference formulations: Oxramet® XR 10 mg/1000 mg (Dapagliflozin / Metformin ER; Sun Pharma Laboratories Ltd., India) and Amaryl® 2 mg (Glimepiride; Sanofi India Ltd.). The total study duration was 11 days, encompassing both periods. A washout interval of 7 days was maintained between the two periods to ensure the elimination of the drug and avoid carryover effects.

The study was conducted under fed conditions, in accordance with the US FDA and CDSCO guidelines for food-effect studies. These guidelines recommend fed-state evaluations when food may influence drug absorption. Moreover, this approach mirrors real-world usage, as these agents are typically administered with meals to enhance tolerability and minimize gastrointestinal side effects.

The Ethics Committee approved the protocol and informed consent for the clinical trial. The study strictly adhered to the clinical research guidelines established by the basic principles defined in the ICH-GCP guidelines, the ICMR Ethical Guidelines

for Biomedical Research on Human Subjects (2017), the Declaration of Helsinki (Fortaleza, Brazil, October 2013), G.S.R. 227(E) New Drugs and Clinical Trials Rules, 2019, and the Guidelines for Bioavailability and Bioequivalence Studies, CDSCO, March 2005.

Study Objective: The primary objective was to compare the bioequivalence of a single oral dose of the test formulation Dapagliflozin 10 mg, Glimepiride 2 mg, and Metformin ER 1000 mg FDC with the reference formulations in healthy adult human subjects under fed conditions. The secondary objective was to evaluate the safety and tolerability of the test formulation under the same conditions.

Study Population: The main inclusion criteria were healthy, non-smoking adult male volunteers aged 18–45 years (inclusive), with a body mass index (BMI) between 18.5 and 30 kg/m² and a body weight >50 kg. Eligibility was confirmed through a detailed medical history, a complete physical examination (including blood pressure and pulse rate), a 12-lead electrocardiogram (ECG), and clinical laboratory evaluations, with only participants showing no clinically relevant abnormalities being enrolled in the study.

The exclusion criteria included known hypersensitivity to Dapagliflozin, Metformin, Glimepiride, other sulfonylureas or sulfonamides, or any component of the study medication; inability to understand informed consent; history or presence of significant CV, pulmonary, hepatic, or renal disease (Estimated Ccr<70 mL/min or GFR <60 mL/min/1.73 m²); hematological abnormalities; or any other clinically significant medical disorder. Subjects with a history of hepatitis B, hepatitis C, syphilis, HIV infection, or diabetes mellitus were excluded, as were those with a history of major surgery or acute illness, blood donation within 90 days before screening, or significant allergic disease. Additional exclusions included alcohol or drug abuse, heavy smoking, and the use of any medication within 30 days prior to study initiation that could potentially interfere with study results.

Study Drug Administration: After fasting overnight for at least 10 hours, a high-fat, high-calorie breakfast was served 30 minutes before administering the investigational product (test or reference). All subjects were required to consume the entire meal within 30 minutes. Exactly 30 minutes after starting the meal, the investigational product was given orally. At the same time, while seated, each subject received 240 mL of a 20% aqueous glucose solution at room temperature according to the randomization schedule for that period, followed by a thorough mouth check to ensure the dose had been swallowed.

Blood Sample Collection and Processing: Pre-dose (0.00 hour) venous blood samples of 5 mL were collected, no more than one hour before dosing, in each period. Further samples of 5 ml were taken at 0.33, 0.67, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.33, 3.67, 4.00, 4.50, 5.00, 5.50, 6.00, 8.00, 10.00, 12.00, 16.00, 24.00, 36.00, and 48.00 hours post-dose. Subjects left the facility after the 24.00-hour sample. Blood samples at 36.00 and 48.00 hours post-dose were collected ambulatory. Blood was collected in pre-labelled sample collection tubes containing K2EDTA anticoagulant at each sampling point. Ambulatory samples were obtained by fresh venipuncture. After blood collection from all subjects, centrifugation was initiated under refrigeration within 1 hour of the last sample. The samples were centrifuged at 3800 rpm for 10 minutes at 10°C to separate the plasma. Plasma concentrations of Dapagliflozin, Glimepiride, and Metformin were determined by an LC-MS/MS method.

Pharmacokinetics Analysis: The primary pharmacokinetic parameters analysed were maximum plasma concentration (Cmax), area under the curve up to time t (AUC_{0}–t), and total area under the curve (AUC_{0}–∞). Secondary parameters included time to reach Cmax (Tmax), apparent first-order terminal elimination rate constant (Kel), terminal half-life (t½) calculated as 0.693/Kel, and the extrapolated AUC percentage (AUC_%Extrap_obs).

Safety Evaluation: The safety evaluation included clinical laboratory investigations, a chest X-ray (posteroanterior view), ECG, physical examination, and measurement of vital signs. Sitting blood pressure, radial pulse rate, and general well-being assessments were recorded at 1.00, 3.00-, and 5.00-hours post-dose in each period (within ±40 minutes

of the scheduled time). Blood glucose levels were monitored with a handheld glucometer at 1.00, 3.00, 5.00, and 7.00 hours (±30 minutes) post-dose. Subjects received 60 mL of 20% aqueous glucose solution every 15 minutes (±10 minutes) for 4 hours after dosing. Urine screens for drugs of abuse (amphetamines, barbiturates, benzodiazepines, marijuana, cocaine, and morphine), along with a breath alcohol test, were performed during check-in for each period. Post-study safety samples (hematology and biochemistry) were collected from all dosed subjects at the end of the study.

Statistical Analysis: Pharmacokinetic parameters were calculated for each formulation using SAS® software version 9.4. Analysis of variance (ANOVA) for the log-transformed (Ln) PK parameters (Cmax, AUC_{0}–t, and AUC_{0}–∞) of Dapagliflozin, Glimepiride, and Metformin was performed using the PROC GLM procedure. An F-test was applied to determine the statistical significance of model effects at a 5% significance level ($\alpha = 0.05$). Intra-subject variability for Cmax, AUC_{0}–t, and AUC_{0}–∞ was estimated from the root mean square error derived from the ANOVA model. For bioequivalence assessment, the least squares mean (LSM) ratios of the Ln-transformed Cmax, AUC_{0}–t, and AUC_{0}–∞ for Dapagliflozin, Glimepiride, and Metformin were calculated between the test and reference formulations. Bioequivalence was concluded if the 90% confidence intervals (CIs) for these ratios fell within the predefined acceptance range of 80%–125%.

RESULTS:

Subject Disposition and Demographics: General screening was conducted within 21 days prior to dosing, and 26 healthy adult male subjects were enrolled in accordance with the study protocol. All participants provided written informed consent and checked into the facility before the start of Period 01. Of these, 24 subjects received the assigned study treatments (test or reference) across both periods and completed the study as per protocol **Fig. 1.**

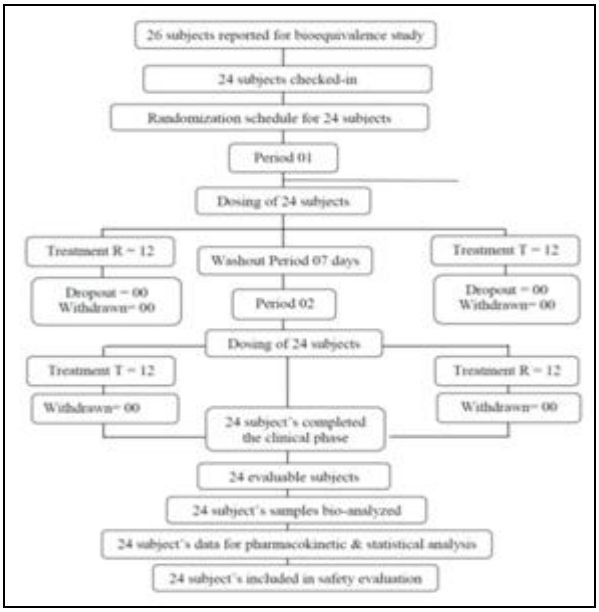

FIG. 1: SUBJECT DISPOSITION FLOWCHART. T: TEST PRODUCT; R: REFERENCE PRODUCT

All participants were healthy adult males of Asian origin, non-smokers, non-alcoholics, and non-vegetarians. The mean ± standard deviation (SD) values for age, height, weight, and body mass index (BMI) of the dosed subjects are summarized in **Table 1.**

TABLE 1: BASELINE DEMOGRAPHIC CHARACTERISTICS OF STUDY SUBJECTS (N = 24)

Parameter	Mean ± SD
Age (years)	30.8± 5.87
Height (cm)	166.8 ± 6.70
Weight (kg)	67.371 ±8.43
BMI (kg/m2)	24.221 ± 2.73

BMI: Body mass index; SD: Standard deviation.

Pharmacokinetic results of Dapagliflozin: Fig. 2 presents the mean plasma concentration time profiles of Dapagliflozin for the test and reference products. Both formulations demonstrated very similar values.

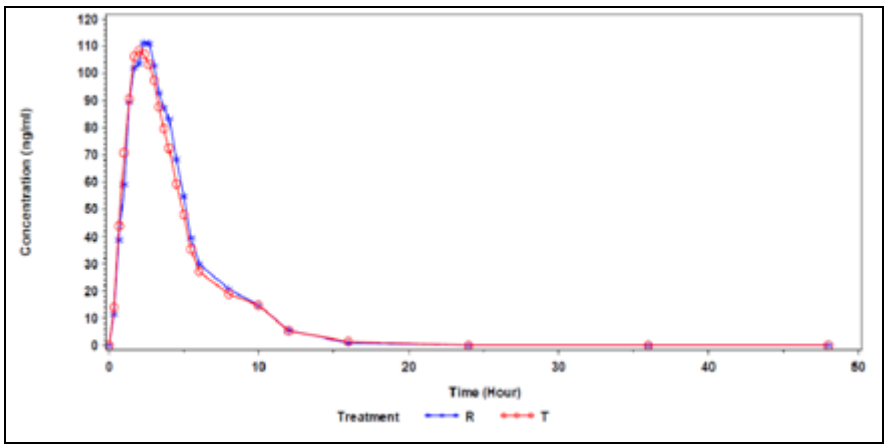

FIG. 2: LINEAR CONCENTRATION-TIME–TIME PROFILE OF DAPAGLIFLOZIN FOR THE TEST (T) AND REFERENCE (R) FORMULATIONS (N = 24)

Table 2 summarizes the geometric least squares means (LSMs) for the test and reference formulations. The 90% CIs for the ratios of Cmax, AUC_{0}–t, and AUC_{0}–∞ were all within the predefined bioequivalence acceptance range of 80%–125%. The median Tmax was 2.0 hours for the test product, compared to 2.3 hours for the reference, while the mean t½ was approximately 2.5 hours for both formulations.

TABLE 2: MEAN PHARMACOKINETIC PARAMETERS OF DAPAGLIFLOZIN FOR THE TEST (T) AND REFERENCE (R) FORMULATIONS (N = 24)

Pharmacokinetic Parameter	Test Product (T)	Reference Product (R)	Geometric Mean Ratio (90% CI)	ISCV (%)	Power (%)
Cmax (ng/mL)	133.56	139.17	95.97 (90.54–101.72)	11.78	99.99
AUC_{0}–t (ng·h/mL)	511.34	528.47	96.76 (91.55–102.26)	11.19	100
AUC_{0}–∞ (ng·h/mL)	532.28	550.07	96.77 (92.20–101.56)	9.77	100

AUC: Area under the curve; Cmax: Maximum plasma concentration; CI: Confidence interval; ISCV: Intra-subject coefficient of variation; LSM: Least squares mean.

Pharmacokinetic Results of Glimepiride: The mean plasma concentration-time profiles of Glimepiride obtained after a single oral administration of the test and the reference products under fed conditions are shown in **Fig. 3.**

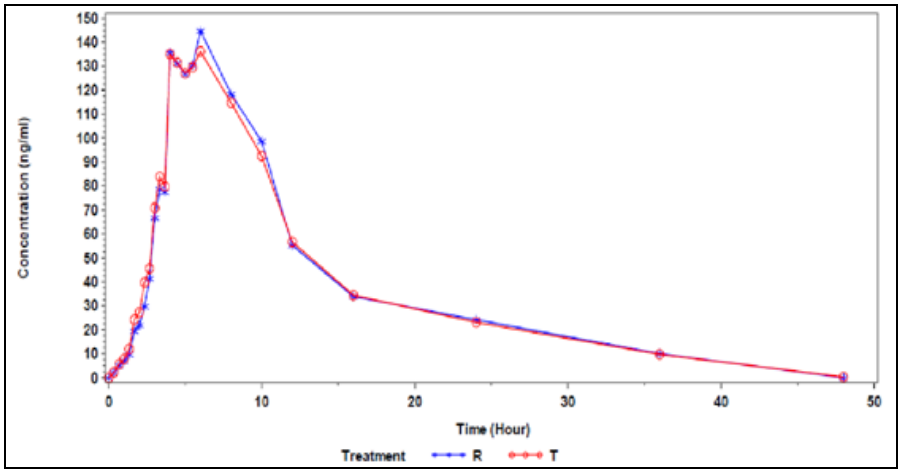

FIG. 3: LINEAR CONCENTRATION-TIME–TIME PROFILE OF GLIMEPIRIDE FOR THE TEST (T) AND REFERENCE (R) FORMULATIONS (N = 24)

The primary pharmacokinetic parameters of Glimepiride are summarized in **Table 3**. A statistical comparison of Cmax, AUC0–t, and AUC0–∞ between the test and reference formulations revealed 90% CIs within the predefined bioequivalence acceptance range of 80%–125%. The median Tmax was 4.5 hours for the test formulation compared with 6.0 hours for the reference product.

The mean t½ of Glimepiride was approximately 10 hours for both formulations.

TABLE 3: MEAN PHARMACOKINETIC PARAMETERS OF GLIMEPIRIDE IN TEST PRODUCT (T) VERSUS REFERENCE PRODUCT (R) (N = 24)

Pharmacokinetic Parameter	Test Product (T)	Reference Product (R)	Geometric Mean Ratio (90% CI)	ISCV (%)	Power (%)
Cmax (ng/mL)	145.52	143.80	101.20 (95.22–107.54)	12.32	99.98
AUC0–t (ng·h/mL)	1301.91	1326.49	98.15 (89.52–107.61)	18.73	97.58
AUC0–∞ (ng·h/mL)	1434.41	1468.89	97.65 (87.66–108.78)	22.03	92.3

AUC: Area under the curve; Cmax: Maximum plasma concentration; CI: Confidence interval; ISCV: Intra-subject coefficient of variation; LSM: Least squares mean.

Pharmacokinetic results of Metformin ER: Bioequivalence between the test and reference formulations of Metformin was demonstrated. The mean plasma concentration time profiles of both formulations, shown in **Fig. 4**, were nearly superimposable.

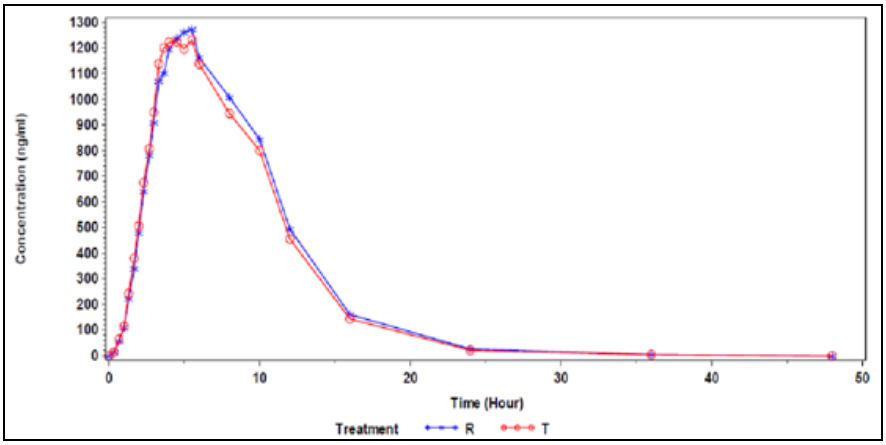

FIG. 4: LINEAR CONCENTRATION-TIME–TIME PROFILE OF METFORMIN FOR THE TEST (T) AND REFERENCE (R) FORMULATIONS (N = 24)

Consequently, the primary pharmacokinetic parameters (Cmax, AUC0–t, and AUC0–∞) were highly comparable between the two formulations **Table 4**. The 90% CIs of the geometric mean ratios for these parameters were within the predefined bioequivalence acceptance range of 80%–125%. No significant differences were observed in secondary pharmacokinetic parameters. The median Tmax was 4.7 hours for the test product, compared to 5.2 hours for the reference product. Meanwhile, the mean t½ was 3.2 hours for the test formulation, versus 3.0 hours for the reference.

TABLE 4: MEAN PHARMACOKINETIC PARAMETERS OF METFORMIN FOR THE TEST (T) AND REFERENCE (R) FORMULATIONS (N = 24)

Pharmacokinetic Parameter	Test Product (T)	Reference Product (R)	Geometric Mean Ratio (90% CI)	ISCV (%)	Power (%)
Cmax (ng/mL)	1330.43	1332.34	99.86 (91.31–109.20)	18.19	98.11
AUC0–t (ng·h/mL)	11216.03	11669.35	96.12 (89.88–102.78)	13.58	99.93
AUC0–∞ (ng·h/mL)	11456.43	11858.76	96.61 (90.97–102.59)	12.17	99.99

AUC: Area under the curve; Cmax: Maximum plasma concentration; CI: Confidence interval; ISCV: Intra-subject coefficient of variation; LSM: Least squares mean.

Safety Results: All subjects who received at least one dose of the investigational product (N = 24) were included in the safety analysis. The test and reference products were well tolerated in healthy

adult subjects under fed conditions. No abnormalities were observed in vital signs or physical examination findings. No serious adverse events or unsolicited adverse reactions were reported during the study.

DISCUSSION: This study demonstrated the bioequivalence of a FDC tablet containing Dapagliflozin 10 mg, Glimepiride 2 mg, and Metformin ER 1000 mg to the individual reference products—Oxramet® XR (Dapagliflozin 10 mg/Metformin ER 1000 mg) and Amaryl® 2 mg (Glimepiride)—in healthy adult Indian volunteers under fed conditions. The 90% CIs for Cmax, AUC_{0}–t, and AUC_{0}-∞ for all three analytes were within the regulatory acceptance range of 80–125%, confirming bioequivalence. The pharmacokinetic consistency of the Dapagliflozin/Glimepiride/Metformin ER FDC, combined with the lack of significant safety issues, supports its potential as a simplified and patient-friendly alternative to co-administering these medicines separately. This FDC offers a comprehensive approach to T2D, aiming to achieve optimal glycemic control while minimising the risk of complications.

Evidence from a Phase III trial in Indian patients with inadequate control on Metformin /Glimepiride FDC demonstrated a significantly greater reduction in HbA1c with the addition of Dapagliflozin, with mean changes of –1.37% versus –1.01% at week 12 ($p < 0.0001$) and –1.98% versus –1.64% at week 16 ($p = 0.0047$). All treatment regimens were well tolerated. [21]Similarly, a 24-week study evaluated Dapagliflozin as add-on therapy in patients with T2D inadequately controlled on Metformin and sulfonylurea. By week 24, a significantly higher proportion of patients receiving Dapagliflozin achieved the therapeutic glycemic target of HbA1c <7.0% compared with placebo (31.8% vs. 11.1%; $p < 0.0001$). Dapagliflozin was also associated with significant reductions in body weight (–2.1 kg; $p < 0.0001$) and systolic blood pressure (–3.8 mmHg; $p = 0.025$). [22]These findings are further supported by real-world evidence from India, where a multicentric randomized trial demonstrated superior glycemic control with triple FDCs in patients inadequately controlled on Metformin monotherapy [23].

In line with this evolving landscape of T2D management, several triple FDCs have been developed to simplify therapy and improve outcomes. For example, the Empagliflozin/ Linagliptin/Metformin FDC has been shown to provide improved glycemic control with the convenience of once-daily dosing and favorable tolerability.

The results of this bioequivalence study confirm the therapeutic equivalence of the Dapagliflozin/Glimepiride/Metformin FDC, emphasizing its clinical significance as a convenient alternative to administering the individual components separately. This FDC uniquely combines agents with complementary mechanisms - renal glucose excretion, stimulation of insulin secretion, and suppression of hepatic glucose production without the need for dose titration or complex sequencing. Such an approach is especially relevant in the Indian clinical setting, where sulfonylureas and Metformin remain widely prescribed and the adoption of SGLT2 inhibitors is growing among patients with CV or renal comorbidities.

Beyond clinical efficacy, FDCs such as this improve long-term adherence by simplifying treatment regimens, mitigate clinical inertia by enabling timely therapy intensification, and provide health system advantages by reducing medication errors and potentially lowering overall treatment costs. Collectively, these benefits support a more effective, patient-centric approach to type 2 diabetes management and highlight the promising role of this triple FDC in advancing diabetes care.

CONCLUSION: The FDC of Dapagliflozin 10 mg, Glimepiride 2 mg, and Metformin ER 1000 mg was bioequivalent to the corresponding reference formulations under fed conditions in healthy adult Indian subjects. All primary pharmacokinetic parameters met regulatory acceptance criteria, and no safety or tolerability concerns were identified. By combining established and novel antidiabetic agents, this FDC offers comprehensive glycemic control with additional cardiorenal benefits. Its simplified dosing and potential cost-effectiveness make it a practical and patient-friendly option, especially in the Indian clinical setting, where

treatment intensification beyond dual therapy is often necessary.

ACKNOWLEDGEMENTS: The authors gratefully acknowledge the contributions of Dr. Abdul Indikar (Principal Investigator), Dr. Amrut Jadhav (Clinical Investigator), Mr. Mansingh Rajput (Bioanalytical Investigator), and Mr. Swapnil Mahajan (Biostatistician) for their diligent efforts in conducting the study, analysing the data, and preparing the report. We also thank Synergen Bio Private Limited, Pune, India, for providing clinical, bioanalytical, pharmacokinetic, and biostatistical services. The study was sponsored by Mascot Health Series Pvt. Ltd., India. The medical writing support was provided by Medical Affairs Creative Solutions, funded by USV Private Limited, Mumbai, India.

CONFLICTS OF INTEREST: This study was sponsored by Mascot Health Series Pvt. Ltd., India. USV Pvt. Ltd., which markets the FDC product, provided manuscript development and submission support. Dr. Amit Gupta, Dr. Smriti Gadia, and Thamburaj Anthuvanare are full-time employees of USV Private Limited. The authors declare no other conflicts of interest related to this work.

REFERENCES:

1. Barman P, Das M and Verma M: Epidemiology of type 2 diabetes mellitus and treatment utilisation patterns among the elderly from the first wave of Longitudinal Aging Study in India (2017–18) using a Heckman selection model. BMC Public Health 2023; 23(1): 699.
2. Mathur P, Leburu S and Kulothungan V: Prevalence, awareness, treatment and control of diabetes in India from the countrywide National NCD Monitoring Survey. Front Public Health 2022; 10: 748157.
3. Das AK, Saboo B, Maheshwari A, Nair V M, Banerjee S, C J, V BP, Prasobh P S, Mohan AR, Potty VS and Kesavadev J: Health care delivery model in India with relevance to diabetes care. Heliyon 2022; 8(10): 10904.
4. Shaikh S, Vaidya V, Gupta A, Kulkarni R, Joshi A, Kulkarni M, Sharma V and Revankar S: A Review on Affordable Combinations in Type 2 Diabetes Care: Exploring the Cost-Effective Potential of Glipizide + Metformin and Glimepiride + Metformin + Pioglitazone. Cureus 2024; 16(5): 59850.
5. John M, Gopinath D and Kalra S: Triple fixed drug combinations in type 2 diabetes. Indian J Endocrinol Metab 2015; 19(3): 311–3.
6. Lingvay I, Beetz N, Sennewald R, Schuler-Metz A, Bertulis J, Loley C, Lang B, Lippert C, Lee J, Manning LS and Terada D: Triple fixed-dose combination empagliflozin, linagliptin, and metformin for patients with type 2 diabetes. Postgrad Med 2020; 132(4): 337-345.
7. Böhm AK, Schneider U, Aberle J and Stargardt T: Regimen simplification and medication adherence: Fixed-dose versus loose-dose combination therapy for type 2 diabetes. PLoS One 2021; 16(5): 0250993.
8. Chadha M, Das AK, Deb P, Gangopadhyay KK, Joshi S, Kesavadev J, Kovil R, Kumar S, Misra A and Mohan V: Expert Opinion: Optimum Clinical Approach to Combination-Use of SGLT2i + DPP4i in the Indian Diabetes Setting. Diabetes Ther 2022; 13(5): 1097-1114.
9. Vakkalagadda B, Vetter ML, Rana J, Smith CH, Huang J, Karkas J, Boulton DW and LaCreta F: Bioequivalence of saxagliptin/dapagliflozin fixed-dose combination tablets compared with coadministration of the individual tablets to healthy subjects. Pharmacol Res Perspect 2016; 3(6): 00201.
10. Giugliano D, Longo M, Scappaticcio L, Caruso P and Esposito K: Sodium-glucose transporter-2 inhibitors for prevention and treatment of cardiorenal complications of type 2 diabetes. Cardiovasc Diabetol 2021; 20(1): 17.
11. Chawla M, Panneerselvam D, Gundgurthy A, Sud S, Alamchandani R, Aneja P, Nair R and Korukonda KR: Retrospective Observational Study on Assessing Sitagliptin and Dapagliflozin as a Fixed-Dose Combination in the Indian Population With Type 2 Diabetes Mellitus: The SIDAXA Study. Cureus 2024; 16(5): 60815.
12. Galindo RJ, Trujillo JM, Low Wang CC and McCoy RG: Advances in the management of type 2 diabetes in adults. BMJ Med 2023; 2(1): 000372.
13. Zhao X, Ning R, Hui A, Boulton DW and Tang W: Pharmacokinetic Variables of Dapagliflozin/Metformin Extended-release Fixed-dose Combination in Healthy Chinese Volunteers and Regional Comparison. Clin Ther 2023; 45(8): 762-9.
14. Singh AK, Unnikrishnan AG, Zargar AH, Kumar A, Das AK, Saboo B, Sinha B, Gangopadhyay KK, Talwalkar PG, Ghosal S, Kalra S, Joshi S, Sharma SK, Sriram U and Mohan V: Evidence-Based Consensus on Positioning of SGLT2i in Type 2 Diabetes Mellitus in Indians. Diabetes Ther 2019; 10(2): 393-428.
15. Nicholson MK, Ghazal Asswad R and Wilding JP: Dapagliflozin for the treatment of type 2 diabetes mellitus an update. Expert Opin Pharmacother 2021; 22(17): 2303–10.
16. Sahay RK, Mittal V, Gopal GR, Kota S, Goyal G, Abhyankar M and Revenkar S: Glimepiride and Metformin Combinations in Diabetes Comorbidities and Complications: Real-World Evidence. Cureus 2020; 12(9): 10700.
17. Basit A, Riaz M and Fawwad A: Glimepiride: evidence-based facts, trends, and observations (GIFTS). Vasc Health Risk Manag 2012; 8: 463–72. Erratum in: Vasc Health Risk Manag 2013; 9: 1.
18. He W, Yuan G, Han Y, Yan Y, Li G, Zhao C, Shen J, Jiang X, Chen C, Ni L and Wang DW: Glimepiride Use is Associated with Reduced Cardiovascular Mortality in Patients with Type 2 Diabetes and Chronic Heart Failure: A Prospective Cohort Study. Eur J Prev Cardiol 2022; 312.
19. Tan J, Wang Y, Liu S, Shi Q, Zhou X, Zhou Y, Yang X, Chen P and Li S: Long-Acting Metformin Vs. Metformin Immediate Release in Patients With Type 2 Diabetes: A Systematic Review. Front Pharmacol 2021; 12: 669814.
20. Mitra A and Wu Y: Challenges and opportunities in achieving bioequivalence for fixed-dose combination products. AAPS J 2012; 14(3): 646-55.
21. Sahay R, Gangwani D, Singh M, Gupta S, Kale N, Srivastava M, Kurmi P, Ambaliya J, Lomte N, Gofne S, Agarwal S, Kashid P, Agarwal V, Rai P, Sharma S, Murthy LS, Rajurkar M, Saha S, Patel P, Patil D, Ghadge

P, Lakhwani L, Mehta S and Joglekar SJ: Fixed dose combination of dapagliflozin, glimepiride and extended-release metformin tablets in patients with type 2 diabetes poorly controlled by metformin and glimepiride: A phase III, open label, randomized clinical study in India. Diabetes Obes Metab 2025; 27(4): 2193-2205.

22. Parikh S: Study 05 Group. Dapagliflozin improves glycemic control and reduces body weight as add-on therapy to metformin plus sulfonylurea: a 24-week randomised, double-blind clinical trial. Diabetes Care 2015; 38(3): 365-72.
23. Singh AK, Das AK, Murthy LS, Ghosal S, Sahay R, Harikumar KVS, Keshava GH, Agarwal M, Vijayakumar G, Kalra P, Lodha P, Das S, Shaikh S, Goswami S, Ajish TP, Kumthekar P, Upadhyay M, Thamburaj A, Mahule A, Prasad A and Pednekar A: Efficacy of Dapagliflozin + Sitagliptin + Metformin Versus Sitagliptin + Metformin in T2DM Inadequately Controlled on Metformin Monotherapy: A Multicentric Randomized Trial. Adv Ther 2025; 42(2): 801-812.

How to cite this article:
Biswas K, Rao MH, Panda B, Mehta JC, Bhojane S, Singh P, Anthuvan T, Gupta A and Gadia S: Bioequivalence of dapagliflozin, glimepiride, and metformin FDC in healthy Indian volunteers: a path to diabetes treatment simplification. Int J Pharm Sci & Res 2026; 17(3): 892-00. doi: 10.13040/IJPSR.0975-8232.17(3).892-00.