

Herb–Drug Interaction at the Dissolution Level: Effect of *Fenugreek Galactomannan* on Glibenclamide Release Profiles

*¹Garba M.A, ¹Bashir, A., ¹Ishak B.K, ²Idris A, A, ³Yunusa, A.A and ⁴Nasiru, H.

¹Department of Pharmaceutical and medicinal Chemistry, Faculty of Pharmaceutical Sciences, Kaduna State University, Kaduna State, Nigeria.

²Department of Physiology, Faculty of Basic Medical Sciences, College of Medicine, Kaduna State University, Kaduna State, Nigeria.

³Department of Environmental Health, Shehu Idris College of Health Sciences and Technology, Kaduna State, Nigeria.

⁴Department of Pure and Applied Chemistry, Faculty of Physical Sciences, Kaduna State University, Kaduna State, Nigeria.

*Corresponding authors' email: musagarbaabdullahi26@kasu.edu.ng Phone: +2348034509999

ORCID ID: <https://orcid.org/0000-0002-6261-5348>

ABSTRACT

This study looked into the in vitro dissolution profile of Glibenclamide tablets in the presence of *Trigonella foenum-graecum* (fenugreek) seed extract. Glibenclamide, a second-generation sulfonylurea with poor aqueous solubility, is associated with variable dissolution and absorption characteristics. At the same time, fenugreek is widely used in traditional diabetes management because of its hypoglycemic phytoconstituents. Fenugreek seeds were extracted by cold maceration using methanol and screened for phytochemical constituents, revealing the presence of alkaloids, flavonoids, saponins, terpenoids, tannins, and polysaccharides. Four commercial brands of Glibenclamide tablets were evaluated for physicochemical quality parameters and subjected to dissolution studies using a USP type II dissolution apparatus in 0.1 N HCl kept at 37 ± 0.5 °C, both in the absence and presence of fenugreek extract. Dissolution samples were analyzed spectrophotometrically at 275 nm. Each experiment was conducted in triplicate (n = 3), and the results were reported as mean ± standard deviation. One-way ANOVA p < 0.05 was considered statistically significant for the statistical analysis. The outcomes revealed that the presence of fenugreek extract altered the dissolution profile of Glibenclamide across the tested brands, with a significant reduction in percentage drug release observed at 30 min compared with the control formulations (p < 0.05). Some brands failed to achieve the British Pharmacopoeia dissolution requirement of not less than 80% drug release within 30 min in the presence of the extract. These findings suggest a potential in-vitro herb–drug interaction between fenugreek and Glibenclamide, which may influence the drug dissolution characteristics and warrants further in-vivo investigation.

Received: 06 Aug. 2026

Accepted: 08 Aug. 2026

Published: 21 Aug. 2026

Keywords:

Dissolution profile; Diabetes mellitus; Fenugreek; Glibenclamide; Hypoglycemia; Herb–drug interaction

INTRODUCTION

The use of medicinal plants as complementary therapies in the management of chronic diseases, including diabetes mellitus, has increased considerably worldwide, particularly in developing countries where herbal remedies are often more accessible and affordable than conventional medicines (Mutombo *et al.*, 2023), reflecting a long-standing global history of herbal use that continues to shape current phytotherapeutic practice (Giannenas *et al.*, 2020). Many medicinal plants contain bioactive phytochemicals such as flavonoids, alkaloids, saponins, and terpenoids that may contribute to therapeutic effects and serve as potential sources of novel drug candidates (Pan *et al.*, 2013; Tran *et al.*, 2020). However, the concurrent use of herbal products with prescribed medications raises concerns regarding possible herb–drug interactions that may alter drug performance and therapeutic outcomes, arising through a range of pharmacokinetic and pharmaceutical mechanisms (Fasinu *et al.*, 2015).

However, the concurrent use of herbal products with prescribed medications raises concerns regarding possible herb–drug interactions that may alter drug performance and therapeutic outcomes, arising through a range of

pharmacokinetic and pharmaceutical mechanisms (Fasinu *et al.*, 2015).

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both (Jadon *et al.*, 2024). Glibenclamide, a second-generation sulfonylurea, remains widely used in the management of type 2 diabetes mellitus because of its ability to stimulate pancreatic insulin secretion (Tomlinson *et al.*, 2022). It is also categorized as a Biopharmaceutics Classification System (BCS) class II medicine despite its clinical efficacy because of its limited water solubility, hence the rate-limiting stage of absorption involves dissolution and bioavailability (Ahmed *et al.*, 2023), a challenge commonly addressed in formulation science through the use of functional excipients designed to overcome poor drug dissolution (Van der Merwe *et al.*, 2020), and one that reflects the broader clinical importance of dissolution as a determinant of oral drug bioavailability (Stielow *et al.*, 2023). Consequently, factors that influence the dissolution behaviour of Glibenclamide may significantly affect its therapeutic performance.

Trigonella foenum-graecum (fenugreek) is a medicinal herb traditionally used in diabetes management because of its

hypoglycemic and lipid-lowering properties (Al-Asadi, 2014). Its pharmacological activity has been linked to the presence of soluble fibre, alkaloids, flavonoids, and saponins, which may improve glycemic control by enhancing insulin sensitivity and delaying carbohydrate absorption (Akhtar *et al.*, 2025), consistent with the broader pattern of combining conventional pharmaceutical agents with natural therapeutic products in type 2 diabetes management (Blahova *et al.*, 2021).

Previous studies have reported pharmacodynamic interactions between fenugreek and antidiabetic agents, including sulfonylureas (Lal *et al.*, 2011; Rahman *et al.*, 2014). However, these investigations mainly focused on glycemic outcomes and in vivo antidiabetic effects, with limited attention given to possible pharmaceutical interactions affecting drug dissolution behaviour, despite similar dissolution-level herb–drug interactions having

previously been demonstrated for other antidiabetic agents such as metformin in combination with plant extracts (Garba *et al.*, 2026).

Currently, not much is known about how fenugreek extract affects the dissolution kinetics of commercially available Glibenclamide tablet formulations under simulated gastric conditions. Considering that dissolution is a critical determinant of the bioavailability of BCS class II drugs, understanding such interactions is important in predicting possible alterations in drug release and therapeutic response during concomitant use.

Therefore, the present research aims to address the gaps by evaluating the in vitro dissolution profile of glibenclamide in the presence of fenugreek extract, providing essential insights for optimising diabetes treatment.

The hypothesis (H₁) stated that *fenugreek* extract significantly alters the dissolution kinetics of Glibenclamide tablets



Figure 1: *Fenugreek (Trigonella foenum-graecum)*

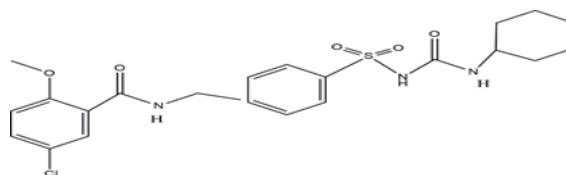


Figure 2: Molecular structure of Glibenclamide

MATERIALS AND METHODS

Sampling of Glibenclamide Tablets

Four commercial brands of Glibenclamide tablets (5 mg) were randomly purchased from registered pharmacies within

Kaduna North and Zaria, Kaduna State, Nigeria. The products were selected based on availability and valid regulatory registration.

Table 1: Description of Glibenclamide Tablet Brands

Brand	Batch Number	NAFDAC Number	Manufacturing Date	Expiry Date
A	DTB2301	04-1234	02/01/2024	02/01/2027
B	HVD2402	04-5678	03/04/2024	02/02/2027
C	CLZ2503	04-9101	03/2/2025	03/05/2028
D	NRN042450	04-1121	02/03/2025	05/05/2028

Collection and Authentication of Plant Material

Fenugreek (Trigonella foenum-graecum) seeds were purchased from Zaria market on October 23, 2024. The plant sample was recognized and verified by Gallah, U.S (Taxonomist) in the Department of Pharmacognosy and Drug Development, Faculty of Pharmaceutical Sciences, Kaduna State University. In the departmental herbarium, a voucher number (KADSU/FPS/879) was eventually assigned.

Extraction of Fenugreek Seeds

The fenugreek seeds were cleaned, allowed to air dry for eighteen days at room temperature, and then ground into a coarse powder. One hundred and fifty grams (150 g) of powdered material was extracted with 1 L of methanol by cold maceration for 24 hrs. With intermittent shaking. The extract was filtered and concentrated to dryness under reduced pressure. The dried extract yielded 11.6 g (7.73% w/w). The extract was stored in an airtight container until use (Bukata, 2015).

Identification of Glibenclamide Tablets by FTIR

Identification of the active pharmaceutical ingredient in the tablet formulations was performed using the FTIR method described in the British Pharmacopoeia (BP, 2009). Powdered tablet samples were extracted with ethanol, filtered, evaporated to dryness, and analyzed using FTIR spectroscopy. The spectra obtained were compared with the BP reference spectrum for Glibenclamide.

Evaluation of Physicochemical Parameters

Every tablet brand was assessed for thickness, diameter, hardness, friability, weight consistency, and disintegration time according to USP/NF procedures.

Weight Uniformity

Twenty tablets from each brand were individually weighed using an analytical balance, and the mean weight and percentage deviation were the computed using the following formula:-

$$\% \text{ STD} = \frac{(\text{Individual tablet weight} - \text{Average tablet weight})}{\text{Average weight}} \times 100$$

Table 2: Weight variation of various brands of Glibenclamide Tablets (A, B, C, D).

Tablet Number	A	B	C	D
1	+0.58	+0.30	-0.45	+0.34
2	+0.15	-0.36	-0.17	+1.45
3	-0.09	-0.64	-1.04	-0.04
4	-0.23	+0.57	-1.12	+1.47
5	-1.15	+0.97	+0.77	-2.46
6	-0.56	+0.87	+1.28	+0.77
7	-0.36	-0.79	-0.07	+0.08
8	+0.83	-0.29	+0.94	-0.28
9	+0.27	+0.31	+0.34	+0.09
10	-1.37	+0.92	-0.61	-1.87

All values fall within the $\pm 5\%$ weight variation limit specified by the pharmacopoeia (for tablets in this weight class), indicating that all four brands comply with the official weight uniformity requirement.

Hardness Test

Ten tablets from each brand were tested using a Monsanto hardness tester, and the crushing strength was recorded in kilogram-force (kgf) (Table 3).

Table 3: Hardness Test Results For Glibenclamide Tablets in Kg/F for Brands A, B, C, and D (N=9)

Tablet Number	A	B	C	D
1	6.0	5.0	7.5	7.5
2	5.5	5.5	7.0	7.1
3	6.5	5.0	7.5	7.8
4	6.0	6.0	6.5	6.9
5	5.5	5.1	7.0	7.3
6	6.0	5.3	7.5	7.7
7	5.5	5.2	7.0	6.8
8	6.5	5.1	7.5	7.2
9	6.0	5.0	6.5	7.6
Mean $\pm$ SD	6.19 $\pm$ 0.43	7.29 $\pm$ 0.33	6.70 $\pm$ 0.33	5.85 $\pm$ 0.29

Friability Test

A total of ten tablets were weighed (W_1), rotated for four minutes at 25 rpm in a friabilator, dusted, and then weighed again (W_2). We computed the percentage friability using:

$$\% \text{ Friability} = \frac{W_1 - W_2}{W_1} \times 100$$

Where W_2 is the weight following the test and W_1 is the initial weight.

Table 4: The Results of Friability of Various Brands of Glibenclamide Tablet Brands A, B, C, and D (N=10)

S/N	Brand A (%)	Brand B (%)	Brand C (%)	Brand D (%)
1	0.00	0.72	0.00	0.33
2	0.00	0.17	0.00	0.12
3	0.55	2.11	0.31	0.36
4	0.19	0.35	0.00	0.20
5	0.19	0.36	0.63	0.17
6	0.00	0.18	0.48	0.62
7	0.37	0.17	0.48	0.50
8	0.19	0.00	0.00	0.70
9	0.00	0.89	1.75	0.19
10	0.00	0.175	0.00	0.61
Mean $\pm$ SD	0.15 $\pm$ 0.06	0.51 $\pm$ 0.20	0.37 $\pm$ 0.12	0.39 $\pm$ 0.07

All four brands exhibit acceptable mechanical strength and abrasion resistance, falling well under the USP/BP friability criterion of $\leq 1\%$.

Test for Disintegration

Using a USP disintegration device, six pills from each brand were evaluated in distilled water kept at $37 \pm 0.5^\circ\text{C}$. The amount of time needed for total breakdown was noted.

Dissolution Studies**Dissolution Testing of Glibenclamide Tablets**

Dissolution testing was carried out according to BP (2009) using a USP type II (paddle) dissolution apparatus. To eliminate confounding variables, identical dissolution conditions were maintained for both the control and herb-

interaction studies. The dissolution medium consisted of 900 ml of 0.1 N HCl maintained at $37 \pm 0.5^\circ\text{C}$ with a paddle rotation speed of 100 rpm.

Six tablets ($n = 6$) from each brand were tested. To maintain sink conditions, samples (10 mL) were taken out at 5, 10, 20, 30, 40, and 50 minutes, and they were promptly replaced with equal amounts of new dissolving medium kept at the same temperature. The samples were filtered and assessed using a validated UV spectrophotometric method at 275 nm.

Dissolution Study in the Presence of Fenugreek Extract

The herb–drug interaction study was performed under the same dissolution conditions used for the control experiment. Fenugreek extract equivalent to 1 g/L was dispersed uniformly in the dissolution medium prior to tablet introduction. The selected concentration was based on preliminary solubility and viscosity studies designed to simulate physiologically relevant exposure following concurrent oral intake of fenugreek preparations. One tablet from each brand was introduced into the vessel containing the extract-enriched dissolution medium. Sampling intervals and analytical procedures were identical to those used in the control dissolution study. All experiments were conducted in triplicate.

Validation of UV Spectrophotometric Method

The analytical method used for quantification of Glibenclamide was validated according to ICH Q2 (R1) guidelines for specificity, linearity, accuracy, precision, limit of detection (LOD), and limit of quantification (LOQ).

Specificity and Interference Study

An interference study was conducted to evaluate possible spectral overlap between fenugreek extract constituents and Glibenclamide at 275 nm. Blank fenugreek extract solutions, Glibenclamide standard solutions, and combined mixtures were scanned within the UV range to confirm specificity of the analytical wavelength.

Linearity

Glibenclamide standard solutions were used to create calibration curves across a suitable concentration range, and regression analysis was used to evaluate linearity.

Accuracy and Precision

Accuracy was evaluated by recovery studies, while intra-day and inter-day precision were determined using replicate analyses and represented as a percentage of the relative standard deviation (%RSD).

LOD and LOQ

The calibration curve's slope and response standard deviation were used to determine the limits of detection and quantification.

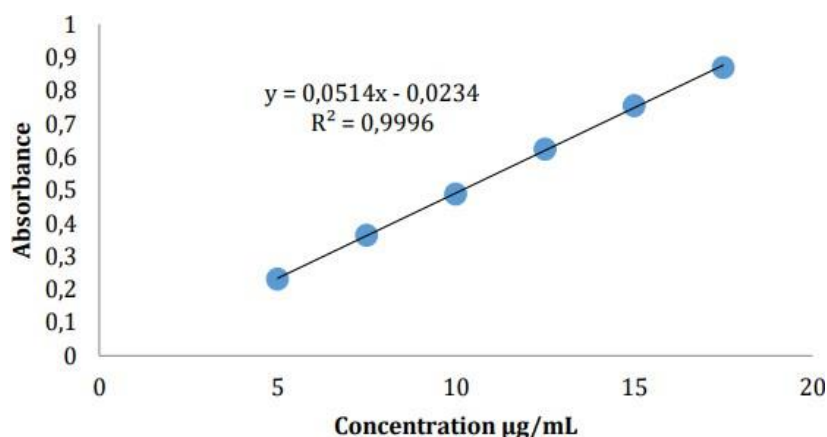


Figure 3: Calibration curve of UV spectra of standard Glibenclamide (adopted from Nindya et al., 2023)

Assay of Glibenclamide

Twenty (20) tablets of Glibenclamide were weighed and ground into a powder. A 0.1g of Glibenclamide was agitated with 70 ml of distilled water for 15 minutes and diluted to 100 ml. After filtration (discarding the first 20 ml), serial dilutions were made, and absorbance was measured at 300 nm. Using a specific absorbance value (1%, 1 cm) of 494.0, (Khalaf & Hassen, 2012; Sabbaghi et al., 2024), the Glibenclamide content ($C_{23}H_{28}ClN_3O_5S$) was determined using the following equation:

$$\% \text{ Content} = \left(\frac{A_u}{A_{(1\%, 1\text{cm})} \times C} \right) \times 100$$

Where A_u is the test solution's absorbance measured at 300 nm, $A_{(1\%, 1\text{cm})}$ is Glibenclamide's specific absorbance (494.0), which represents the absorbance value of a 1% w/v solution in a 1 cm cell. C is the test solution's concentration expressed as % w/v (g per 100 mL), accounting for the dilution factor used during sample preparation.

Statistical Analysis

The data were presented using the mean $\pm$ SD. The statistical analysis was performed using GraphPad Prism 9.0. The dissolution profiles of the fenugreek-treated groups and the control were compared using Tukey's post hoc test and two-way analysis of variance (ANOVA). When $p < 0.05$, a

statistically significant difference was present. According to pharmacopeial requirements for comparative dissolution testing, a sample size of six was chosen for the dissolution tests. There was a statistically significant difference.

RESULTS AND DISCUSSION

FTIR Identification of Glibenclamide Tablets

The FTIR spectra of all evaluated Glibenclamide brands demonstrated characteristic absorption peaks corresponding to the functional groups of the reference Glibenclamide standard, confirming the identity and chemical integrity of the active pharmaceutical ingredient. Prominent peaks observed included N–H stretching vibrations at 3313–3522 cm^{-1} , carbonyl (C=O) stretching at approximately 1712–1715 cm^{-1} , and sulfonyl (S=O) stretching bands at 1339–1341 cm^{-1} . These findings are consistent with the characteristic spectral profile of Glibenclamide reported in the British Pharmacopoeia. The brands did not exhibit any notable peak shifts or the loss of distinctive functional groups, suggesting that there was no significant drug–excipient incompatibility or degradation during manufacturing.

Physicochemical Evaluation of Glibenclamide Tablets Weight Uniformity

All evaluated tablet brands complied with British Pharmacopoeia specifications for weight uniformity, as no individual tablet deviated by more than $\pm 5\%$ from the mean tablet weight. The low percentage deviations observed indicate acceptable dosage uniformity and consistency of the manufacturing process. Uniform tablet weight is particularly important for low-dose drugs such as Glibenclamide, where variations in tablet mass may significantly affect drug content and therapeutic performance, since blend segregation during manufacturing is a well-recognised contributor to poor content uniformity in solid dosage forms (Jakubowska and Ciepluch, 2021).

Friability and Hardness

The hardness values of the evaluated brands ranged from 5.85 ± 0.29 to 7.29 ± 0.33 kgf, which falls within the acceptable range for conventional uncoated tablets. Adequate crushing strength is necessary to ensure mechanical stability during packaging, transportation, and handling without compromising tablet disintegration and dissolution properties.

Similarly, the friability values for all brands were below the pharmacopeial limit of 1%, indicating sufficient resistance to abrasion and mechanical stress, an important measure of tablet mechanical durability during handling and transport (Zhao et al., 2022). Although Brand B showed relatively higher friability values compared with the other formulations, the tablets remained within acceptable limits, suggesting satisfactory formulation integrity.

Disintegration Time

The disintegration times of all Glibenclamide brands ranged from 2.86 to 4.44 min, which complied with the BP requirement for uncoated tablets (≤ 15 min). Rapid tablet disintegration is advantageous for immediate-release formulations because it increases the exposure of drug particles to the dissolution medium, thereby facilitating dissolution and subsequent absorption, consistent with current mechanistic understanding of the disintegration process and its relationship to downstream dissolution performance (Berardi et al., 2021).

In-vitro Dissolution Studies

Dissolution Profile of Glibenclamide Tablets

All Glibenclamide brands exhibited progressive drug release with increasing dissolution time. Most formulations achieved the BP dissolution requirement of not less than 80% drug release within 30 min under controlled conditions, indicating satisfactory in vitro release performance. Two-way ANOVA statistical analysis revealed significant differences ($p < 0.05$), between dissolution profiles obtained in the absence and presence of fenugreek extract. However, the magnitude of these differences varied among brands, indicating formulation-dependent interaction behavior.

Effect of Fenugreek Extract on Dissolution Behavior

The addition of fenugreek extract altered the dissolution characteristics of Glibenclamide tablets. Some formulations demonstrated slightly enhanced drug release in the initial phases of dissolution, whereas others exhibited delayed release at later sampling times. Although certain differences were statistically significant, not all alterations were pharmaceutically significant because several formulations still satisfied the BP dissolution criterion.

The observed interaction may be explained using dissolution and diffusion principles described by the Noyes–Whitney equation:

$$(DcA(C_s - C)) / h = dC/dt$$

dC/dt = rate of dissolution; D = diffusion coefficient of the drug; A = surface area of the solid drug particle; C_s = saturation solubility of the drug in the diffusion layer; C = concentration of drug in the bulk dissolution medium at time t ; h = thickness of the diffusion boundary layer

Fenugreek contains galactomannan-rich mucilage capable of modifying the physicochemical properties of the dissolution medium, a polysaccharide fraction increasingly recognized for its diverse functional and pharmaceutical applications (Nalbantova et al., 2024). The hydrophilic nature of galactomannan may initially improve wettability and dispersion of hydrophobic Glibenclamide particles, thereby enhancing early-stage dissolution in some formulations. However, the mucilaginous properties of the extract may also increase medium viscosity, resulting in a thicker diffusion boundary layer and reduced diffusion coefficient, which could subsequently retard drug release at later stages.

Viscosity measurements of the extract-containing dissolution medium demonstrated a measurable increase compared with the control medium, supporting the hypothesis that viscosity-mediated diffusion effects contributed to the altered dissolution behavior observed in this study. Nevertheless, direct evaluation of wettability and particle surface interactions, such as contact-angle analysis, was not performed and therefore the proposed mechanism remains inferential.

Dissolution Kinetic Modeling

The dissolution data were fitted using Higuchi, Korsmeyer–Peppas, zero-order, and first-order kinetic models. The dissolution profiles showed the highest correlation coefficients (R^2) with the Higuchi and Korsmeyer–Peppas models, suggesting that diffusion-controlled release mechanisms predominated in both control and fenugreek-containing media. The reduction in dissolution rate observed in some formulations following addition of fenugreek extract may therefore be associated with altered diffusion dynamics within the dissolution boundary layer.

$$M_t/M_\infty = KKP t^n$$

where M_t/M_∞ is the fraction of drug released at time t , KKP is the release rate constant incorporating structural and geometric characteristics of the dosage form, and n is the release exponent used to characterize the drug release mechanism ($n \leq 0.45$: Fickian diffusion; $0.45 < n < 0.89$: anomalous/non-Fickian transport; $n \geq 0.89$: Case-II/zero-order transport).

Similarity Factor (f_2) Analysis

Similarity factor analysis revealed formulation-dependent variation in dissolution profile similarity between control and fenugreek-treated formulations. Brands with f_2 values below 50 demonstrated dissimilar dissolution behavior in the presence of fenugreek extract, indicating that the herbal extract significantly modified drug release characteristics. Conversely, brands with f_2 values above 50 maintained comparable dissolution profiles despite the presence of the extract.

$$f_2 = 50 \log \left\{ \left[1 + \frac{1}{n} \sum_{t=1}^n (R_t - T_t)^2 \right]^{-0.5} \times 100 \right\}$$

Where f_2 is the similarity factor, n is the number of dissolving time points, R_t is the mean % of drug dissolved for the reference (control) formulation at time t , and T_t is the mean

% of drug dissolved for the test (fenugreek-treated) formulation at time t.

Clinical and Pharmaceutical Relevance

The present findings demonstrate that *fenugreek extract* can significantly influence the dissolution kinetics of Glibenclamide under simulated gastric conditions. However, in vitro dissolution changes should not be interpreted directly as evidence of altered in vivo bioavailability or therapeutic failure, because drug absorption is also influenced by permeability, gastrointestinal transit, metabolism, and physiological variables not evaluated in this study. Although some formulations exhibited reduced dissolution in the presence of fenugreek extract, several brands still met pharmacopeial dissolution requirements, suggesting that the observed interaction may not translate into a clinically meaningful reduction in drug exposure. Therefore, the distinction between statistical significance and clinical significance is important when interpreting these findings. Further investigations involving permeability studies, in vivo pharmacokinetic evaluation, and rheological characterization of the dissolution medium are required to establish the clinical relevance of the observed herb–drug interaction.

CONCLUSION

All evaluated Glibenclamide tablet brands met the British Pharmacopoeia requirement specifications for disintegration, dissolution, friability, hardness, and weight uniformity under standard test conditions. FTIR analysis confirmed the identity and structural integrity of the active pharmaceutical ingredient in all formulations. Fenugreek extract significantly modified the dissolution behavior of Glibenclamide tablets under simulated gastric conditions, although the extent of interaction varied among formulations. The observed effects may be related to changes in wettability and viscosity-mediated diffusion processes associated with fenugreek galactomannan. Despite these alterations, several formulations continued to meet pharmacopeial dissolution requirements, indicating that the interaction was not uniformly pharmaceutically significant. The present findings demonstrated a potential in vitro herb–drug interaction at the dissolution level; however, conclusions regarding altered bioavailability or therapeutic outcome cannot be made without additional in vivo pharmacokinetic and permeability studies.

REFERENCES

Ahmed, N., Abo-Zeid, Y., Sakran, W. (2023). Strategies adopted to improve bioavailability of glibenclamide: Insights on novel delivery systems. *J. Adv. Pharm. Res.*, 7 (1): 35–49.

Akhtar, H., Ali, Y. A., Wei, C. R., Albassam, R. S., Ahmed, F., Yasmin, A., Rasheed, M., Naseer, M. S., Islam, F., and Zahra, S. M. (2025). Bioactive potential and health benefits of *Trigonella foenum-graecum* L.: A comprehensive review. *Food Sci. Nutr.*, 13(9), e70887. <https://doi.org/10.1002/fsn3.70887>

Alamgir, A. (2018). Phytoconstituents—Active and inert constituents, metabolic pathways, chemistry and application of phytoconstituents, primary metabolic products, and bioactive compounds of primary metabolic origin. In *Therapeutic use of medicinal plants and their extracts* (Vol. 2, pp. 25–164). Springer, Cham. https://doi.org/10.1007/978-3-319-92387-1_2

Al-Asadi, J. N. (2014). Therapeutic uses of *fenugreek* (*Trigonella foenum-graecum* L.). *Am. J. Soc. Issues Humanit.*, 2, 21–36.

Berardi, A., Bisharat, L., Quodbach, J., Rahim, S. A., Perinelli, D. R., and Cespi, M. (2021). Advancing the understanding of the tablet disintegration phenomenon—an update on recent studies. *Int. J. Pharm.*, 598, 120390. <https://doi.org/10.1016/j.ijpharm.2021.120390>

Blahova, J., Martiniakova, M., Babikova, M., Kovacova, V., Mondockova, V., & Omelka, R. (2021). Pharmaceutical drugs and natural therapeutic products for the treatment of type 2 diabetes mellitus. *Pharmaceuticals*, 14(8), 806. <https://doi.org/10.3390/ph14080806>

Fasinu, P. S., Gurley, B. J., & Walker, L. A. (2015). Clinically relevant pharmacokinetic herb–drug interactions in antiretroviral therapy. *Current Drug Metabolism*, 17(1), 52–64. <https://doi.org/10.2174/1389200216666151103115053>

Garba, M. A., Aliyu, A., Mukhtar, U. D. M., Bashir, A. I.-J., and Idris, A. (2026). Herb–drug interaction and antidiabetic drug development: A spectroscopic and pharmacokinetics investigation of *Polyalthia longifolia* versus metformin. *Int. J. Sci. Glob. Sustain.* 12(2), 86–93. <https://doi.org/10.57233/ijsgs.v12i2.1090>

Giannenas, I., Sidiropoulou, E., Bonos, E., Christaki, E., and Florou-Paneri, P. (2020). The history of herbs, medicinal and aromatic plants, and their extracts: Past, current situation and future perspectives. In *Feed additives* (pp. 1–18). Elsevier. <https://doi.org/10.1016/B978-0-12-814700-9.00001-X>

Jadon, A. S., Kaushik, M. P., Anitha, K., Bhatt, S., Bhadauriya, P., and Sharma, M. (2024). Types of diabetes mellitus, mechanism of insulin resistance and associated complications. In *Biochemical immunology of diabetes and associated complications* (pp. 1–18). Elsevier. <https://doi.org/10.1016/B978-0-323-99525-8.00008-5>

Jakubowska, E., & Ciepluch, N. (2021). Blend segregation in tablet manufacturing and its effect on drug content uniformity—A review. *Pharmaceutics*, 13(11), 1909. <https://doi.org/10.3390/pharmaceutics13111909>

Khalaf, K. D., & Hassen, P. A. (2012). Spectrofluorimetric method for the determination of glibenclamide in pharmaceutical formulations. *Baghdad Science Journal*, 9(2), 296–301. <https://doi.org/10.21123/bsj.2012.9.2.296-301>

Lal, V. K., Gupta, P. P., Tripathi, P., & Pandey, A. (2011). Interaction of aqueous extract of *Trigonella foenum-graecum* seeds with glibenclamide in streptozotocin-induced diabetic rats. *Am. J. Pharmacol. Toxicol.* 6 (4), 102–106. <https://doi.org/10.3844/ajptsp.2011.102.106>

Mutombo, P. N., Kasilo, O. M. J., James, P. B., Wardle, J., Kunle, O., Katerere, D., Wambebe, C., Matsabisa, M. G., Rahmatullah, M., Nikiema, J.-B., Mukankubito, I., Sheridan, R., Sanogo, R., Nissapatorn, V., Sivakorn, C., Tripathy, S., Goyal, R., & Dhobi, M. (2023). Experiences and challenges of African traditional medicine: Lessons from COVID-19 pandemic. *BMJ Glob. Health*, 8(8), e010813. <https://doi.org/10.1136/bmjgh-2022-010813>

Nalbantova, V., Benbassat, N., & Delattre, C. (2024). *Fenugreek galactomannan and its versatile*

applications. *Polysaccharides*, 5(3), 478–492.

<https://doi.org/10.3390/polysaccharides5030027>

Pan, S.-Y., Zhou, S.-F., Gao, S.-H., Yu, Z.-L., Zhang, S.-F., Tang, M.-K., Sun, J.-N., Ma, D.-L., Han, Y.-F., & Fong, W.-F. (2013). New perspectives on how to discover drugs from herbal medicines: CAM's outstanding contribution to modern therapeutics. *Evid. -Based Complement. Altern. Med.* 2013, 627375. <https://doi.org/10.1155/2013/627375>

Rahman, A., Khidr, S. H., Samy, E. M., & Sayed, M. (2014). Enhancement of the dissolution rate of glipizide capsules using fenugreek as natural additive. *Unique J. Pharm. Biol. Sci.*, 2, 1–8.

Sabbaghi, N., Dadfarnia, S., Haji Shabani, A. M., & Farsadrooh, M. (2024). Dispersive micro solid phase extraction of glibenclamide from plasma, urine, and wastewater using a magnetic molecularly imprinted polymer followed by its determination by a high-performance liquid chromatography-photodiode array detector. *RSC Advances*, 14(19), 13168–13179. <https://doi.org/10.1039/D4RA00452C>

Stielow, M., Witczyńska, A., Kubryń, N., Fijałkowski, Ł., Nowaczyk, J., & Nowaczyk, A. (2023). The bioavailability of drugs—The current state of knowledge. *Molecules*, 28(24), 8038. <https://doi.org/10.3390/molecules28248038>

Tomlinson, B., Patil, N. G., Fok, M., Chan, P., & Lam, C. W. K. (2022). The role of sulfonylureas in the treatment of type 2 diabetes. *Expert Opin. Pharmacother.*, 23(3), 387–403. <https://doi.org/10.1080/14656566.2022.2030571>

Tran, N., Pham, B., & Le, L. (2020). Bioactive compounds in anti-diabetic plants: From herbal medicine to modern drug discovery. *Biology*, 9(9), 252. <https://doi.org/10.3390/biology9090252>

Van der Merwe, J., Steenekamp, J., Steyn, D., & Hamman, J. (2020). The role of functional excipients in solid oral dosage forms to overcome poor drug dissolution and bioavailability. *Pharmaceutics* 12(5), 393.

<https://doi.org/10.3390/pharmaceutics12050393>

Zhao, H., Yu, Y., Ni, N., Zhao, L., Lin, X., Wang, Y., Du, R., & Shen, L. (2022). A new parameter for characterization of tablet friability based on a systematic study of five excipients. *Int. J. Pharm.*, 611, 121339. [https://doi.org/10.1016/j.ijpharm.2021.121339](<https://doi.org/10.1016/j.ijpharm.2021.121339>)

