# Development And In-Vitro Characterisation of Xanthan Gum-Based Gastroretentive Floating Matrix Tablets for Sustained Delivery of Metformin Hydrochloride

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***Abstract*—Metformin hydrochloride (MET HCl), a BCS Class III antidiabetic agent, carries a short elimination half-life of 1.5–3 h, making multiple daily doses unavoidable with conventional tablets and undermining long-term patient adherence. This study developed effervescent gastroretentive floating matrix tablets of MET HCl using xanthan gum as the hydrophilic matrix polymer. Nine batches (F-XG1 to F-XG9) were manufactured by wet granulation following a $3^2$ full factorial design, with xanthan gum (100–150 mg) and $NaHCO_3$ (100–150 mg) as independent variables. The optimised formulation, F-XG6 (xanthan gum 125 mg, $NaHCO_3$ 150 mg), displayed excellent granule flow (angle of repose 22.4° ± 1.2°; Carr's index 15.8 % ± 0.9 %) and satisfactory tablet quality (hardness 8.5 ± 0.4 kg/cm²; friability 0.28 % ± 0.05 %). Tablets floated within 3.2 ± 0.8 min and remained buoyant for more than 12 h in 0.1 N HCl. Cumulative drug release reached 92.4 % ± 2.1 % at 12 h. Korsmeyer–Peppas analysis of the early-time release data (Q < 60 %) yielded n = 0.99 ($R^2$ = 0.9994), indicating near Case-II transport governed primarily by polymer erosion and matrix relaxation. The dissolution profile was comparable to that of Glucophage XR® ($f_2$ = 72.1). Six-month accelerated stability at 40°C/75 % RH confirmed no significant change in drug content, hardness, or release profile (p > 0.05). The formulation represents a practical twice-daily sustained-release strategy for improving glycaemic control in type 2 diabetes.**

***Index Terms*—Floating tablets; Gastroretention; Korsmeyer–Peppas model; Metformin HCl; Sustained release; Xanthan gum.**

## I. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent non-communicable diseases worldwide. The International Diabetes Federation reported roughly 463 million adults living with the condition as of 2021 — a figure projected to reach 700 million by 2045 — placing sustained pressure on healthcare systems and demanding formulations that patients can maintain across years of therapy [1].

Metformin hydrochloride (MET HCl) remains the cornerstone pharmacological treatment for T2DM owing to its well-established efficacy, long-term safety record, and affordability. Its principal pharmacokinetic limitation is a short elimination half-life of approximately 1.5–3 h; conventional immediate-release tablets therefore require dosing two or three times daily. In patients on multiple medications, this polypharmacy burden substantially impairs adherence, and lapses in metformin therapy directly erode glycaemic control. Moreover, intestinal absorption of metformin is largely restricted to the proximal small intestine, so a tablet that exits the stomach and upper gut too rapidly delivers much of its payload to regions of diminishing permeability [2].

Gastroretentive floating drug-delivery systems address this problem by prolonging residence of the dosage form in the stomach, feeding drug steadily into the proximal intestine at a rate commensurate with its absorption capacity [3]. Effervescent systems achieve buoyancy through in-situ $CO_2$ generation: sodium bicarbonate reacts with gastric acid on tablet immersion, trapping gas within the swelling polymer network and reducing apparent bulk density below 1 g/cm³. This approach is amenable to conventional wet-granulation equipment and is therefore well suited for scale-up.

Xanthan gum was selected as the matrix-forming polymer for this formulation on account of its rapid hydration, robust gel formation at low concentrations,

pharmacopoeial recognition as safe, and documented mucoadhesive properties that can augment gastric retention [4]. Because the interplay between gel strength and $CO_2$ generation governs both floating performance and drug-release rate, a $3^2$ full factorial design was employed to map the effects of xanthan gum and $NaHCO_3$ concentration systematically and identify the optimal combination.

The objectives were: (i) to develop effervescent gastroretentive floating matrix tablets of MET HCl using xanthan gum; (ii) to optimise the formulation through factorial design; (iii) to characterise the optimised batch for flow properties, floating behaviour, dissolution kinetics, and accelerated stability; and (iv) to compare the in-vitro dissolution profile with that of the reference product Glucophage XR®.

## II. MATERIALS AND METHODS

### *A. Materials*

MET HCl (purity 99.8 %) was supplied as a gift sample. Hyderabad. Xanthan gum, sodium bicarbonate, PVP K-25, microcrystalline cellulose (MCC PH-102), colloidal silicon dioxide (Aerosil 200), and magnesium stearate were obtained from Sigma-Aldrich and Loba Chemie Pvt. Ltd. All materials were of pharmaceutical grade and used as received.

### *B. UV Analytical Method*

A UV spectrophotometric method was developed at 232 nm using 0.1 N HCl as the dissolution medium. Linearity was confirmed over 5–50 µg/mL ($R^2$ = 0.9994). Accuracy (recovery 98.5–101.2 %) and precision (RSD < 2.0 %) were validated per ICH Q2(R1) before any dissolution measurements were undertaken.

### *C. Factorial Design and Granulation*

Nine batches (F-XG1 to F-XG9) were formulated using a $3^2$ full factorial design with xanthan gum (Factor A: 100, 125, 150 mg) and $NaHCO_3$ (Factor B: 100, 125, 150 mg) as the two variables. The primary response was percentage cumulative drug release at 12 h ($\%Q_{12h}$). The batch composition is presented in Table I.

MET HCl and xanthan gum were dry-mixed in a mortar, then kneaded with a 5 % w/w PVP K-25 solution in isopropyl alcohol until a coherent wet mass formed. Granules were dried at 50°C for 12 h, sieved through a #20 mesh, and blended with Aerosil 200 and magnesium stearate for 5 min. Tablets were compressed on a 10-station rotary press using 13 mm flat-faced punches; target fill weight ranged from 751 to 851 mg across batches

TABLE I. $3^2$ FACTORIAL DESIGN BATCH COMPOSITION (MG/TABLET)

| Batch | MET HCl (mg) | Xanthan Gum (mg) | $NaHCO_3$ (mg) | PVP K-25 (mg) | MCC (mg) | Aerosil 200 (mg) | Mg Stearate (mg) | Total (mg) |
|---|---|---|---|---|---|---|---|---|
| F-XG1 | 500 | 100 | 100 | 15 | 25 | 7.5 | 3.5 | 751 |
| F-XG2 | 500 | 100 | 125 | 15 | 25 | 7.5 | 3.5 | 776 |
| F-XG3 | 500 | 100 | 150 | 15 | 25 | 7.5 | 3.5 | 801 |
| F-XG4 | 500 | 125 | 100 | 15 | 25 | 7.5 | 3.5 | 776 |
| F-XG5 | 500 | 125 | 125 | 15 | 25 | 7.5 | 3.5 | 801 |
| F-XG6 | 500 | 125 | 150 | 15 | 25 | 7.5 | 3.5 | 826 |
| F-XG7 | 500 | 150 | 100 | 15 | 25 | 7.5 | 3.5 | 801 |
| F-XG8 | 500 | 150 | 125 | 15 | 25 | 7.5 | 3.5 | 826 |
| F-XG9 | 500 | 150 | 150 | 15 | 25 | 7.5 | 3.5 | 851 |

### *D. Characterisation Methods*

Pre-compression: angle of repose (fixed-funnel method), bulk density, tapped density, Carr's index (CI), and Hausner ratio (HR) were measured on dried granules from all batches.

Post-compression: tablets were evaluated for weight variation (IP 2022 limits), hardness (Pfizer tester), friability (Electrolab EF-2; 100 rpm, 4 min, n = 20), drug content (n = 6; UV at 232 nm), and floating

parameters (floating lag time and total floating time) in 900 mL 0.1 N HCl at 37 ± 0.5°C.

Dissolution: USP Apparatus II (Electrolab TDL-08L), 50 rpm, 37 ± 0.5°C, 900 mL 0.1 N HCl, n = 6. Samples of 5 mL were withdrawn at 0, 1, 2, 4, 6, 8, 10, and 12 h with equal-volume medium replacement to maintain sink conditions. Absorbance was read at 232 nm and concentrations derived from the validated calibration curve.

Kinetic modelling: cumulative dissolution data were fitted to zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models. For the Korsmeyer–Peppas model, only data at Q < 60 % were used, as required for a disc-shaped matrix geometry. Model selection was based on the highest $R^2$ [7]. Profile similarity to Glucophage XR® was assessed with the $f_2$ factor (FDA criterion: $f_2 \geq 50$), calculated from time points at which the reference had not yet exceeded 85 % release.

Stability: the optimised batch F-XG6 was stored in sealed HDPE bottles at 40°C/75 % RH per ICH Q1A(R2) [6]. Drug content, hardness, and $Q_{12h}$ were assessed at 0, 3, and 6 months.

## III. RESULTS AND DISCUSSION

### *A. Factorial Optimisation*

The contoured response surface (Fig. 1) shows that $NaHCO_3$ concentration exerted the greater influence on both buoyancy and $\%Q_{12h}$, while xanthan gum concentration primarily governed gel strength and diffusional resistance. At the highest xanthan gum level (150 mg), the dense gel retarded drug release below the 12 h target. At the lowest level (100 mg), the matrix eroded prematurely and buoyancy was inconsistent across replicates. The combination of 125 mg xanthan gum with 150 mg $NaHCO_3$ — batch F-XG6 — yielded the best balance of sustained release and reliable buoyancy.

### *B. Micromeritic and Tablet Properties*

All flow parameters for F-XG6 fell within the excellent' to 'good' category (Table II), ensuring uniform die fill at the high active dose of 500 mg per unit. Drug content of 98.7 ± 1.2 %, hardness of 8.5 ± 0.4 kg/cm², and friability of 0.28 ± 0.05 % all met IP acceptance limits comfortably.

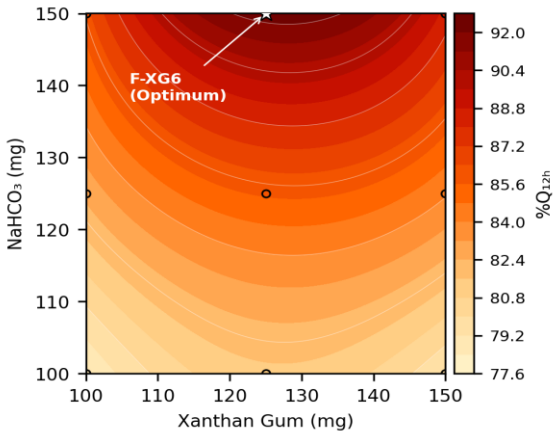


*Fig. 1. Response surface plot showing the effect of xanthan gum and $NaHCO_3$ concentration on $\%Q_{12h}$. The optimised region (F-XG6, marked) corresponds to xanthan gum 125 mg and $NaHCO_3$ 150 mg.*

TABLE II. EVALUATION PARAMETERS OF F-XG6

| Parameter | Result | Criterion |
|---|---|---|
| Angle of Repose (°) | 22.4 ± 1.2 | < 25 (Excellent) |
| Carr's Index (%) | 15.8 ± 0.9 | 13–16 (Good) |
| Hardness (kg/cm²) | 8.5 ± 0.4 | 4–10 |
| Friability (%) | 0.28 ± 0.05 | < 1.0 |
| Drug Content (%) | 98.7 ± 1.2 | 95–105 |
| Float Lag Time (min) | 3.2 ± 0.8 | < 5 |
| Total Float Time (h) | > 12 | ≥ 12 |

### *C. Floating Behaviour*

When F-XG6 contacted the acidic dissolution medium, $CO_2$ generated by the $NaHCO_3$ reaction was rapidly entrapped within the swelling xanthan gel, reducing apparent bulk density to approximately 0.92 g/cm³ and making the tablet buoyant within 3.2 ± 0.8 min. Phase III of the migrating motor complex can sweep unfloated objects from the fasting stomach within 2–4 h, so a floating lag time under 5 min substantially reduces the risk of premature gastric emptying before meaningful drug release has occurred [5].

### *D. Dissolution Profile and Similarity Factor*

F-XG6 released drug progressively over 12 h (Fig. 2; Table III). The 0–6 h phase averaged 11.2 %/h,

consistent with rapid initial hydration and $CO_2$-assisted pore opening. A transient plateau occurred at 6–8 h (rate 2.5 %/h), attributed to formation of a compact secondary gel layer as the outer matrix became fully hydrated, temporarily impeding diffusion. Between 8 and 10 h, release recovered to 6.8 %/h as progressive swelling-induced erosion disrupted this barrier. Cumulative release reached 92.4 ± 2.1 % at 12 h, meeting the target for a twice-daily formulation.

The $f_2$ similarity factor was calculated from five time points at which the reference had not yet exceeded 85 % release (t = 1, 2, 4, 6, and 8 h), in accordance with FDA guidance. The resulting value of $f_2$ = 72.1 comfortably exceeds the minimum threshold of 50, confirming that the dissolution behaviour of F-XG6 is similar to that of Glucophage XR® and providing a rational basis for advancing to in-vivo bioequivalence evaluation.

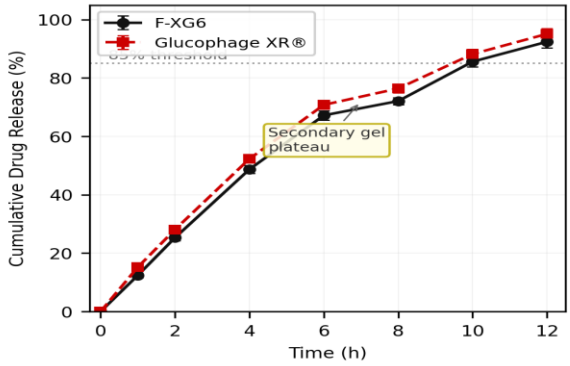


*Fig. 2. Comparative dissolution profiles of F-XG6 and Glucophage XR® in 0.1 N HCl at 37°C (USP Apparatus II, 50 rpm, n = 6; $f_2$ = 72.1). The dashed horizontal line marks the 85 % threshold used for $f_2$ calculation.*

*E. Release Kinetics*

Table IV presents the kinetic parameters derived directly from the dissolution data in Table III. Of the five models evaluated, the Korsmeyer–Peppas model gave the best fit to the early-time region (Q < 60 %; t = 1, 2, 4 h; $R^2$ = 0.9994). The diffusional exponent n = 0.99 approximates Case-II transport (n = 1.00 for a disc geometry), indicating that drug release was governed predominantly by polymer chain relaxation and matrix erosion rather than simple Fickian diffusion. The Hixson–Crowell model also produced a satisfactory fit ($R^2$ = 0.9937), confirming the contribution of surface erosion to the overall release pattern. The Korsmeyer–Peppas analysis was confined to the early-time data as is standard practice for swelling disc matrices.

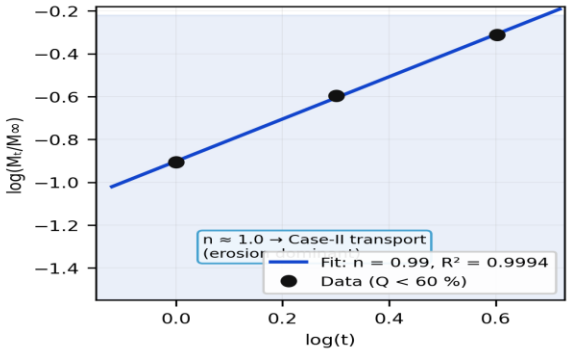


*Fig. 3. Korsmeyer–Peppas kinetic plot for F-XG6 (log $M_t/M_\infty$ vs. log t, Q < 60 % data; n = 0.99, $R^2$ = 0.9994). The value n ≈ 1.0 indicates near Case-II transport.*

*F. Accelerated Stability*

After six months at 40°C/75 % RH, all evaluated attributes of F-XG6 remained within specification (Table V; Fig. 4). Drug content declined by 1.5 percentage points (98.7 → 97.2 %), well within the 95–105 % limit, and the change was not statistically significant (paired t-test, p > 0.05). Hardness dropped by only 0.2 kg/cm², and the dissolution profile at 6 months was essentially superimposable on the baseline profile ($Q_{12h}$ 91.8 vs. 92.4 %). These findings confirm physicochemical compatibility between MET HCl, xanthan gum, and the excipient mixture, and indicate that HDPE packaging with desiccant is adequate for the proposed storage conditions. Initial granulation trials encountered some surface stickiness, which was resolved by extending drying time from 10 to 12 h and adding Aerosil 200 at 0.9 % w/w; the published formulation reflects these optimised parameters

TABLE III. DISSOLUTION DATA: F-XG6 VS. GLUCOPHAGE XR® (N = 6, MEAN ± SD)

| Time (h) | F-XG6 (%) | Glucophage XR® (%) |
|---|---|---|
| 0 | 0.0 | 0.0 |
| 1 | 12.4 ± 0.8 | 15.2 ± 0.9 |
| 2 | 25.3 ± 1.0 | 28.1 ± 1.1 |
| 4 | 48.7 ± 1.4 | 52.3 ± 1.3 |
| 6 | 67.2 ± 1.6 | 70.8 ± 1.5 |
| 8 | 72.1 ± 1.2 | 76.4 ± 1.4 |
| 10 | 85.6 ± 1.8 | 88.2 ± 1.7 |
| 12 | 92.4 ± 2.1 | 95.1 ± 1.9 |

TABLE IV. RELEASE KINETICS PARAMETERS FOR F-XG6

| Model | Equation | $R^2$ | Mechanism |
|---|---|---|---|
| Zero Order | Q = 7.71t + 9.00 | 0.9514 | Constant rate |
| First Order | ln (100 − Q) = −0.21t + 4.71 | 0.9776 | Concentration-dependent |
| Higuchi | Q = 33.03√t − 19.33 | 0.9903 | Fickian diffusion |
| Korsmeyer–Peppas* | log (Mt/M∞) = 0.99·log(t) − 0.90 | 0.9994 | Case-II/erosion |
| Hixson–Crowell | Ks = 0.220 | 0.9937 | Surface erosion |

**Fitted to Q < 60 % data points (t = 1, 2, 4 h); n = 0.99 ± 0.01 (mean ± SE).*

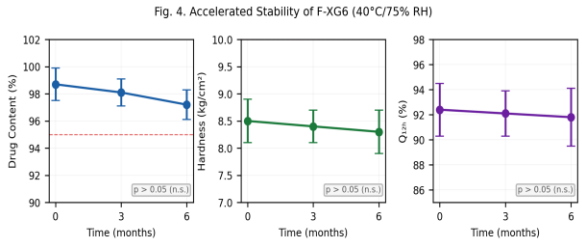


*Fig. 4. Accelerated stability profiles of F-XG6 at 40°C/75 % RH: (left) drug content, (centre) hardness, (right) cumulative 12 h release ($Q_{12h}$) at 0, 3, and 6 months. Error bars = SD (n = 3). Red dashed lines denote specification limits. All changes were non-significant (p > 0.05, paired t-test).*

TABLE V. ACCELERATED STABILITY DATA FOR F-XG6 (40°C/75 % RH; MEAN ± SD, N = 3)

| Parameter | 0 Months | 3 Months | 6 Months |
|---|---|---|---|
| Drug Content (%) | 98.7 ± 1.2 | 98.1 ± 1.0 | 97.2 ± 1.1 |
| Hardness (kg/cm²) | 8.5 ± 0.4 | 8.4 ± 0.3 | 8.3 ± 0.4 |
| $Q_{12h}$ (%) | 92.4 ± 2.1 | 92.1 ± 1.8 | 91.8 ± 2.3 |

## IV. CONCLUSION

Gastroretentive floating matrix tablets of MET HCl based on xanthan gum were successfully developed and optimised through a systematic $3^2$ factorial approach. The selected formulation F-XG6 met all targeted performance criteria: it achieved buoyancy within 5 min, maintained floating for over 12 h, and released 92.4 % of the drug in 12 h. Release kinetics followed near Case-II transport (Korsmeyer–Peppas n = 0.99), reflecting the dominant contribution of polymer relaxation and matrix erosion — a mechanism consistent with the pronounced swelling observed during dissolution testing. The in-vitro dissolution profile was similar to that of Glucophage XR® ($f_2$ = 72.1), and physicochemical stability was confirmed over six months under accelerated conditions.

Moving from conventional thrice-daily dosing to a twice-daily sustained-release regimen is a clinically meaningful gain in a chronic disease where patient adherence directly determines HbA1c reduction and long-term complication risk. The data presented here provide a scientific foundation for pilot-scale manufacturing, followed by in-vivo pharmacokinetic evaluation and formal in-vitro–in-vivo correlation analysis to determine whether the promising dissolution data translate to equivalent systemic exposure.

## ACKNOWLEDGMENT

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