

## Research Article

# FORMULATION AND EVALUATION OF CONTROLLED RELEASE MATRIX TABLETS OF METFORMIN HYDROCHLORIDE USING HIBISCUS ROSA-SINENSIS MUCILAGE

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## ABSTRACT

**Background:** Metformin hydrochloride is a highly water-soluble biguanide used for type 2 diabetes mellitus. Its high dose and rapid dissolution make it a suitable candidate for controlled release matrix systems. Hibiscus rosa-sinensis mucilage is a natural polysaccharide-rich polymer with swelling and gel-forming properties. **Objective:** The objective of this study was to formulate and evaluate controlled release matrix tablets of metformin hydrochloride using Hibiscus rosa-sinensis mucilage as the release-retarding polymer. **Materials and methods:** Mucilage was isolated from Hibiscus rosa-sinensis leaves by aqueous extraction followed by alcohol precipitation. Nine tablet batches (F1-F9) were prepared by wet granulation using a constant dose of metformin hydrochloride and increasing mucilage concentration. Granules were evaluated for flow properties, and tablets were evaluated for weight variation, hardness, thickness, friability, drug content, swelling index, matrix integrity and in vitro drug release. Dissolution was performed using USP Apparatus II in 0.1 N HCl followed by phosphate buffer pH 6.8. Statistical comparison and release kinetic modeling were performed. **Results:** All batches showed acceptable pre-compression and post-compression characteristics. Increasing mucilage concentration improved matrix integrity, increased swelling and reduced the release rate. Batch F6 containing 175 mg mucilage showed balanced release with 61.8% cumulative release at 6 hours and 97.2% release at 12 hours. Kinetic analysis showed highest fitting with the Higuchi model ( $R^2 = 0.986$ ) and anomalous transport using the Korsmeyer-Peppas model ( $n = 0.63$ ). **Conclusion:** Hibiscus rosa-sinensis mucilage can act as an effective natural release-retarding polymer for metformin hydrochloride controlled release matrix tablets. F6 was selected as the optimized batch because it provided acceptable tablet quality and controlled release over 12 hours.

**Keywords:** Metformin hydrochloride; Hibiscus rosa-sinensis; mucilage; controlled release; matrix tablets; natural polymer; wet granulation; Higuchi model.

## INTRODUCTION

Metformin hydrochloride is a widely used oral antihyperglycaemic biguanide for the management of type 2 diabetes mellitus. It improves glycaemic control mainly by reducing hepatic glucose production and improving insulin sensitivity. The drug is highly water soluble, has incomplete and variable gastrointestinal absorption and is commonly administered in high doses, which creates formulation challenges for oral controlled release delivery.<sup>1,2</sup>

Controlled release dosage forms are designed to deliver drug at a predetermined rate so that therapeutic concentration can be maintained for an extended period. Oral controlled release tablets can reduce dosing frequency, reduce peak-trough fluctuation and improve patient convenience during long-term therapy.

Pharmaceutically, such systems must provide reproducible release without dose dumping and must also satisfy physical tablet quality requirements.<sup>3,4</sup>

Hydrophilic matrix tablets are among the simplest and most practical controlled release systems. After exposure to dissolution medium, the polymer hydrates and swells to form a gel barrier. Drug release then occurs through water penetration, diffusion through the hydrated layer and gradual erosion of the matrix. Higuchi and Korsmeyer-Peppas models are commonly applied to interpret such release mechanisms.<sup>5,6</sup>

Natural polymers have received attention as pharmaceutical excipients because they are generally available, economical, biodegradable and capable of functional roles such as binding, swelling, film formation and release retardation. Plant mucilages are polysaccharide materials that absorb water and form viscous hydrated structures, which may retard drug diffusion in matrix tablets.<sup>7,8</sup>

Hibiscus rosa-sinensis mucilage has swelling and gel-forming characteristics that make it relevant for sustained and controlled drug release. Earlier work has indicated its usefulness in metformin and ketoprofen matrix systems, where polymer concentration influenced release rate. The present study was therefore designed to formulate metformin hydrochloride controlled release tablets using Hibiscus rosa-sinensis mucilage and to identify an optimized batch based on tablet quality and in vitro release performance.<sup>9,10,11</sup>

## **MATERIALS AND METHODS**

### **Materials**

Metformin hydrochloride was used as the active pharmaceutical ingredient. Hibiscus rosa-sinensis mucilage was used as the natural release-retarding polymer. Microcrystalline cellulose was selected as diluent and compression aid, PVP K30 as binder, talc as glidant, magnesium stearate as lubricant, alcohol as mucilage precipitating solvent and distilled water as extraction and granulation medium. The excipient roles were selected according to standard tablet formulation principles.<sup>12</sup>

### **Isolation of Hibiscus rosa-sinensis mucilage**

Fresh Hibiscus rosa-sinensis leaves were washed, shade dried and powdered. The powder was soaked in distilled water and heated mildly with intermittent stirring to extract mucilage. The dispersion was filtered through muslin cloth, and the filtrate was treated with alcohol to precipitate the mucilage. The precipitated mucilage was separated, washed with alcohol, dried at controlled temperature, powdered, passed through sieve and stored in a well-closed container. The extraction procedure was kept uniform to reduce variability in polymer behaviour.<sup>9</sup>

### **Preformulation and analytical method development**

Preformulation studies included organoleptic evaluation, solubility screening, mucilage hydration observation and physical drug-excipient compatibility by observation for colour change, liquefaction, lump formation or odour development. A UV spectrophotometric method was developed for metformin hydrochloride estimation. Standard solutions were prepared, absorbance was measured at 233 nm and a calibration curve was constructed. The method was used for assay and dissolution sample analysis in line with the principle that analytical procedures should be suitable for their intended purpose.<sup>13,14,15</sup>

### **Formulation of matrix tablets**

Nine batches were prepared by wet granulation. Metformin hydrochloride, Hibiscus rosa-sinensis mucilage and microcrystalline cellulose were sieved and mixed geometrically. PVP K30 binder solution was added gradually to form a coherent wet mass. The wet mass was passed through sieve, dried, resized and blended with talc and

magnesium stearate before compression into tablets. Compression force was adjusted to obtain tablets with adequate hardness and low friability.<sup>16,17</sup>

**Table 1. Formula design of trial batches**

| Batch | Metformin (mg) | HCl | HRS (mg) | mucilage | MCC (mg) | PVP K30 (mg) | Talc (mg) | Mg stearate (mg) | Total weight (mg) |
|-------|----------------|-----|----------|----------|----------|--------------|-----------|------------------|-------------------|
| F1    | 500            |     | 50       |          | 250      | 30           | 10        | 10               | 850               |
| F2    | 500            |     | 75       |          | 225      | 30           | 10        | 10               | 850               |
| F3    | 500            |     | 100      |          | 200      | 30           | 10        | 10               | 850               |
| F4    | 500            |     | 125      |          | 175      | 30           | 10        | 10               | 850               |
| F5    | 500            |     | 150      |          | 150      | 30           | 10        | 10               | 850               |
| F6    | 500            |     | 175      |          | 125      | 30           | 10        | 10               | 850               |
| F7    | 500            |     | 200      |          | 100      | 30           | 10        | 10               | 850               |
| F8    | 500            |     | 225      |          | 75       | 30           | 10        | 10               | 850               |
| F9    | 500            |     | 250      |          | 50       | 30           | 10        | 10               | 850               |

### Evaluation of granules and tablets

Granules were evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. Compressed tablets were evaluated for appearance, average weight, hardness, thickness, friability, drug content, swelling index and matrix integrity. In vitro drug release was studied using USP Apparatus II. Dissolution was carried out in 900 mL of 0.1 N HCl for the first 2 hours followed by phosphate buffer pH 6.8 for the remaining period at  $37 \pm 0.5$  °C and 100 rpm. Samples were withdrawn at 1, 2, 4, 6, 8, 10 and 12 hours, filtered, diluted and analysed spectrophotometrically.<sup>13</sup>

Descriptive statistics were used for formulation results. An independent t-test compared 6-hour release between a low-polymer batch and optimized batch, while one-way ANOVA compared 12-hour release among selected low, optimized and high-polymer batches. The optimized batch was fitted to zero-order, first-order, Higuchi and Korsmeyer-Peppas models for mechanism interpretation.<sup>5,6,18</sup>

## RESULTS

### Preformulation and calibration curve

Metformin hydrochloride was observed as a white, odourless crystalline powder that was freely soluble in water. Hibiscus rosa-sinensis mucilage appeared as a light brown to brown powder and showed marked hydration in water, supporting its matrix-forming potential. Physical compatibility observations showed no visible colour change or liquefaction in drug-excipient mixtures. Calibration data showed a linear increase in absorbance with concentration at 233 nm, with regression equation approximately  $y = 0.0529x + 0.0013$  and  $R^2 = 1.0000$ .

### Pre-compression evaluation

**Table 2. Pre-compression evaluation of granules**

| Batch | Bulk density (g/mL) | Tapped density (g/mL) | Carr index (%) | Hausner ratio | Angle of repose (degree) |
|-------|---------------------|-----------------------|----------------|---------------|--------------------------|
| F1    | 0.49                | 0.57                  | 14.0           | 1.16          | 28.1                     |
| F2    | 0.50                | 0.58                  | 13.8           | 1.16          | 28.6                     |
| F3    | 0.50                | 0.59                  | 15.3           | 1.18          | 29.0                     |
| F4    | 0.51                | 0.60                  | 15.0           | 1.18          | 29.4                     |
| F5    | 0.51                | 0.60                  | 15.8           | 1.19          | 29.8                     |
| F6    | 0.52                | 0.61                  | 14.8           | 1.17          | 30.1                     |
| F7    | 0.52                | 0.61                  | 15.6           | 1.18          | 30.5                     |
| F8    | 0.52                | 0.62                  | 16.1           | 1.19          | 30.9                     |
| F9    | 0.53                | 0.63                  | 15.9           | 1.19          | 31.2                     |

All batches showed acceptable flow properties for laboratory compression. Slight increases in angle of repose at higher mucilage concentration reflected the cohesive nature of the natural polymer, but the values remained suitable after granulation and addition of glidant.

### Post-compression evaluation

**Table 3. Post-compression evaluation of tablets**

| Batch | Average weight (mg) | Hardness (kg/cm <sup>2</sup> ) | Thickness (mm) | Friability (%) | Drug content (%) |
|-------|---------------------|--------------------------------|----------------|----------------|------------------|
| F1    | 848.6 ± 3.4         | 6.1 ± 0.3                      | 6.42 ± 0.04    | 0.52           | 98.1             |
| F2    | 849.2 ± 3.8         | 6.2 ± 0.2                      | 6.45 ± 0.05    | 0.49           | 98.5             |
| F3    | 850.5 ± 3.2         | 6.4 ± 0.3                      | 6.48 ± 0.03    | 0.45           | 99.0             |
| F4    | 851.1 ± 3.1         | 6.5 ± 0.3                      | 6.50 ± 0.04    | 0.42           | 99.3             |
| F5    | 849.8 ± 2.9         | 6.7 ± 0.2                      | 6.52 ± 0.05    | 0.39           | 99.1             |
| F6    | 850.4 ± 2.7         | 6.8 ± 0.2                      | 6.55 ± 0.04    | 0.36           | 100.2            |
| F7    | 851.3 ± 3.0         | 6.9 ± 0.3                      | 6.58 ± 0.05    | 0.35           | 99.7             |
| F8    | 852.0 ± 2.8         | 7.0 ± 0.2                      | 6.60 ± 0.04    | 0.33           | 100.5            |
| F9    | 852.4 ± 2.6         | 7.1 ± 0.3                      | 6.63 ± 0.05    | 0.32           | 100.7            |

All tablet batches possessed acceptable average weight, mechanical strength, thickness, friability and drug content. Friability values below 1% indicated adequate resistance to abrasion, and drug content values close to label claim indicated satisfactory distribution of metformin hydrochloride.

### Swelling and in vitro dissolution

Swelling index increased with mucilage concentration. F9 showed the highest swelling due to the highest polymer level; however, excessive swelling was associated with incomplete drug release at 12 hours. F6 showed sufficient swelling to maintain matrix integrity while allowing near-complete release.

**Table 4. In vitro dissolution profile of selected formulations**

| Time (h) | F1 (%) | F3 (%) | F6 Optimized (%) | F9 (%) | Marketed ER (%) |
|----------|--------|--------|------------------|--------|-----------------|
| 0        | 0.0    | 0.0    | 0.0              | 0.0    | 0.0             |
| 1        | 36.4   | 28.6   | 18.6             | 12.4   | 22.0            |
| 2        | 58.2   | 44.7   | 29.8             | 22.6   | 36.4            |
| 4        | 82.1   | 65.3   | 46.4             | 35.9   | 55.2            |
| 6        | 96.2   | 79.8   | 61.8             | 50.7   | 70.1            |
| 8        | 99.1   | 89.2   | 76.5             | 64.2   | 84.3            |
| 10       | 100.0  | 96.1   | 88.7             | 75.8   | 94.0            |
| 12       | 100.0  | 99.0   | 97.2             | 84.9   | 99.1            |

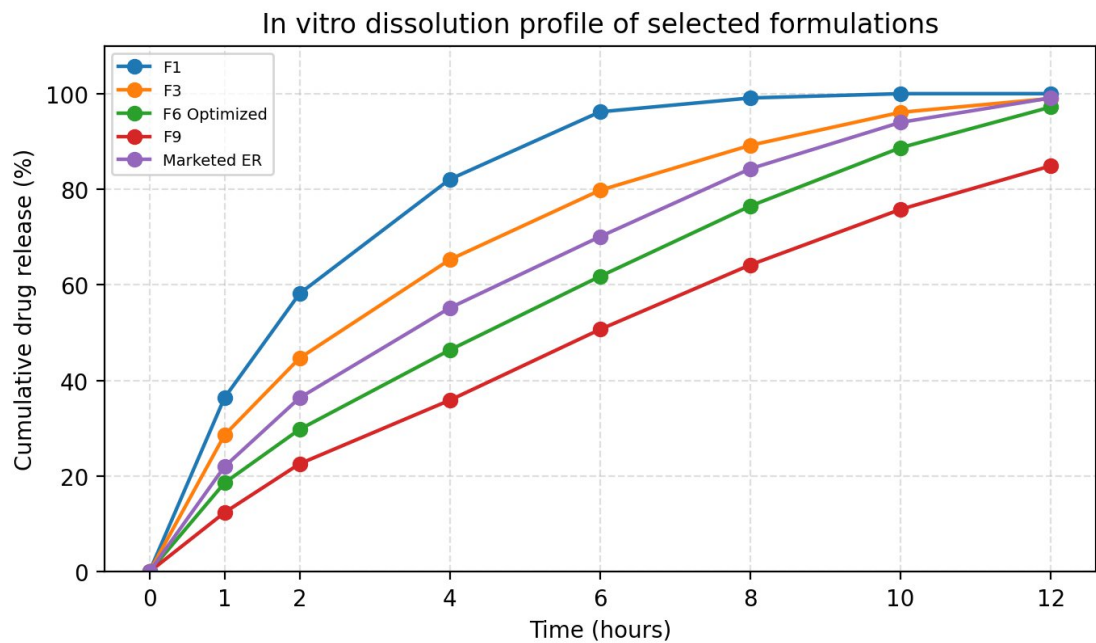


Figure 1. In vitro dissolution profile of selected formulations

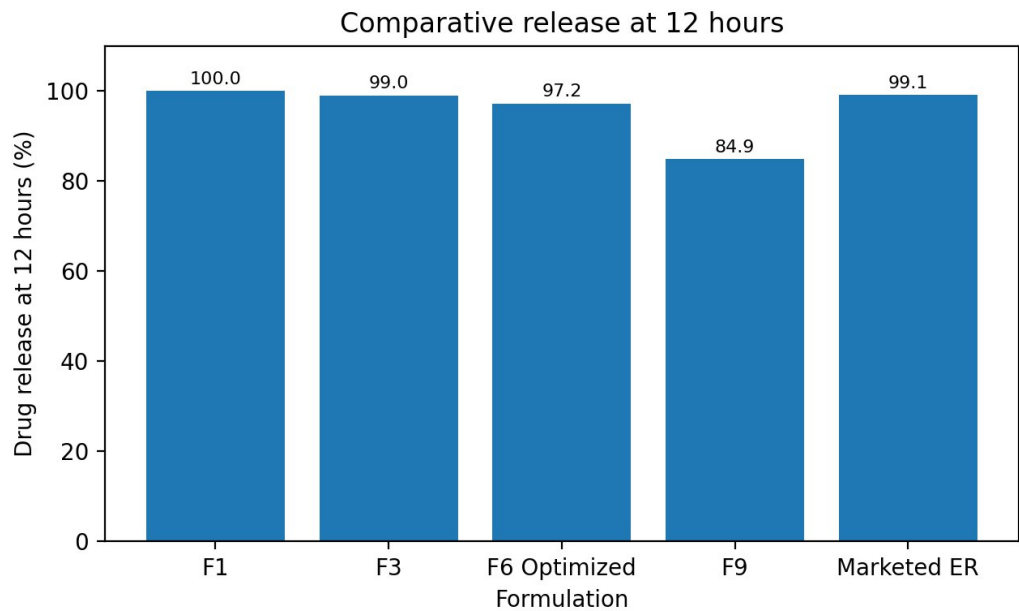


Figure 2. Comparative drug release at 12 hours

The dissolution profile showed the concentration-dependent effect of Hibiscus rosa-sinensis mucilage. F1 released the drug rapidly, indicating insufficient polymer level. F9 retarded release excessively and released only 84.9% drug at 12 hours. F6 showed a balanced controlled release pattern with 61.8% release at 6 hours and 97.2% release at 12 hours.

Statistical and kinetic analysis

Table 5. Statistical and kinetic summary

| Analysis | Comparison/Batch | Value | Inference |
|----------|------------------|-------|-----------|
|----------|------------------|-------|-----------|

|                        |                                                                    |                            |                                                                     |
|------------------------|--------------------------------------------------------------------|----------------------------|---------------------------------------------------------------------|
| t-test at 6 h          | F6: $61.80 \pm 1.05$ vs F1: $96.27 \pm 0.71$                       | $t = -12.36$ ; $p < 0.001$ | Significant reduction in mid-phase release by higher mucilage level |
| ANOVA at 12 h          | F1: $99.83 \pm 0.29$ ; F6: $97.20 \pm 0.92$ ; F9: $84.90 \pm 0.82$ | $F = 112.46$ ; $p < 0.001$ | Significant difference among selected polymer levels                |
| Zero-order model       | Optimized F6                                                       | $R^2 = 0.973$              | Release not purely constant over time                               |
| First-order model      | Optimized F6                                                       | $R^2 = 0.941$              | Some concentration-dependent contribution present                   |
| Higuchi model          | Optimized F6                                                       | $R^2 = 0.986$              | Best fitting; diffusion through hydrated matrix likely              |
| Korsmeyer-Peppas model | Optimized F6                                                       | $R^2 = 0.972$ ; $n = 0.63$ | Anomalous transport by diffusion and erosion                        |

## DISCUSSION

The present study demonstrated that metformin hydrochloride can be formulated as controlled release matrix tablets using Hibiscus rosa-sinensis mucilage. The major challenge was controlling the release of a highly water-soluble, high-dose drug. A weak matrix failed to retard drug release sufficiently, while an excessive polymer concentration produced incomplete release by 12 hours. Thus, optimization required a balance between polymer concentration, swelling, gel strength, matrix erosion and drug diffusion.

Preformulation results confirmed the need for a hydrophilic matrix system. The drug dissolved readily in water, whereas the mucilage swelled in aqueous medium. This swelling behaviour is essential because it creates a hydrated barrier that controls water entry and drug diffusion. These findings are in agreement with previous reports describing Hibiscus rosa-sinensis mucilage as a swelling, film-forming and release-retarding natural polymer.<sup>9,11</sup>

Granulation produced blends with acceptable flow and compressibility. Although higher mucilage levels slightly increased cohesiveness, all batches remained suitable for laboratory compression. This indicates that Hibiscus mucilage can be incorporated into a wet granulated tablet system when supported by appropriate excipients and lubrication.

Post-compression results showed acceptable hardness, friability, thickness, weight variation and drug content. These findings are important because a controlled release product must satisfy mechanical and uniformity requirements in addition to dissolution performance. The optimized batch F6 had hardness of 6.8 kg/cm<sup>2</sup>, friability of 0.36% and drug content of 100.2%, indicating satisfactory tablet quality.

Dissolution data showed that polymer concentration was the critical formulation variable. F1 released drug too rapidly because the gel barrier was insufficient. F9 showed excessive retardation because the higher mucilage level created a stronger, thicker hydrated barrier. F6 was optimized because it achieved gradual release up to 12 hours without substantial drug retention. This pattern correlates with earlier reports in which increasing Hibiscus mucilage concentration reduced drug release rate in matrix tablets.<sup>10,11</sup>

The best fit of F6 to the Higuchi model supports diffusion through a hydrated matrix as the dominant mechanism. The Korsmeyer-Peppas exponent of 0.63 indicates anomalous transport, suggesting that release was governed by both diffusion and erosion. This mechanism is consistent with hydrophilic matrix theory, where the outer hydrated layer erodes while the inner matrix continues to hydrate and release drug.<sup>5,6,18</sup>

Overall, Hibiscus rosa-sinensis mucilage functioned as a promising natural release-retarding polymer for metformin hydrochloride. The study also supports the broader pharmaceutical relevance of plant-derived mucilages as economical and functional excipients for oral controlled release dosage forms. Further work should focus on detailed mucilage characterization, microbial quality testing, accelerated stability, scale-up and in vivo correlation.<sup>7,8,19</sup>

## CONCLUSION

It can be concluded from this study that Hibiscus rosa-sinensis mucilage is an effective natural polymer for controlled release matrix tablets of metformin hydrochloride. Increasing mucilage concentration improved swelling and release retardation. The optimized formulation F6 containing 175 mg mucilage showed acceptable granule flow, tablet strength, low friability, uniform drug content and controlled release over 12 hours, with 97.2% drug release at the final time point. Release kinetics suggested Higuchi-type diffusion with anomalous transport involving both diffusion and erosion.

## FUTURE SCOPE

- Detailed physicochemical characterization of Hibiscus rosa-sinensis mucilage using FTIR, DSC, XRD and rheological evaluation.
- Microbial limit testing and standardization of mucilage extraction yield.
- Optimization by factorial design or response surface methodology.
- Comparison with established polymers such as HPMC K100M and sodium alginate.
- Accelerated and long-term stability testing under ICH conditions.
- In vivo pharmacokinetic and pharmacodynamic evaluation after suitable ethical approval.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## FUNDING

No external funding was received for this work.

## ETHICAL APPROVAL

Not applicable, as the study was limited to laboratory-based formulation and in vitro evaluation.

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