Formulation and Evaluation of Sustained-Release Tablets of Metformin Hydrochloride

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***Abstract*—Metformin Hydrochloride is a first-line oral antidiabetic drug used in the management of Type 2 Diabetes Mellitus; however, its short half-life and frequent dosing are associated with poor patient compliance and gastrointestinal side effects. The present study aimed to formulate and evaluate sustained-release tablets of Metformin Hydrochloride to achieve prolonged drug release and improved therapeutic efficacy. Sustained-release tablets were prepared using hydrophilic and hydrophobic polymers, including Hydroxypropyl Methylcellulose, Ethyl Cellulose, and Eudragit, by direct compression and/or wet granulation techniques. The formulations were evaluated for physicochemical properties, tablet characteristics, and in-vitro dissolution behavior. Drug release data were analyzed using various kinetic models to determine the release mechanism. The optimized formulation demonstrated minimal burst release and sustained drug release up to 12 hours, following diffusion-controlled non-Fickian transport. The study confirms that polymer-based sustained-release tablets of Metformin Hydrochloride can effectively enhance patient compliance and therapeutic outcomes.**

***Index Terms*—Metformin Hydrochloride; Sustained-release tablets; Matrix system; HPMC; Drug release kinetics**

I. INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia and long-term complications. Metformin Hydrochloride is the first-line oral antidiabetic agent widely prescribed for the management of T2DM due to its effectiveness in lowering blood glucose levels, improving insulin sensitivity, and favourable safety profile. Despite its therapeutic benefits, conventional immediate-release formulations of Metformin HCl suffer from limitations such as a short biological half-life, high aqueous solubility, frequent dosing requirements, and gastrointestinal side effects, which may reduce patient compliance. Sustained-release tablet formulations are designed to overcome these limitations by providing controlled drug release, maintaining steady plasma drug concentrations, and minimizing dosing frequency. The present study aims to develop and evaluate sustained-release tablets of Metformin Hydrochloride using suitable polymers, with the novelty focused on optimizing polymer combinations to achieve prolonged drug release, reduced burst effect, and improved therapeutic efficacy.

II. MATERIALS AND METHODS

Materials

Drug Source: Metformin Hydrochloride was obtained as a gift sample from a reputed pharmaceutical manufacturer and was used as received.

Polymers: Hydroxypropyl Methylcellulose (HPMC), Ethyl Cellulose, and Eudragit were used as release-retarding polymers for the preparation of sustained-release tablets.

Excipients: Excipients such as microcrystalline cellulose (diluent), magnesium stearate (lubricant), talc (glidant), and other analytical-grade reagents were used in the formulation.

III. PREFORMULATION STUDIES

Organoleptic Evaluation: Metformin Hydrochloride was evaluated for physical appearance, color, odor, and taste to confirm its identity and purity.

Solubility Studies: Solubility of Metformin Hydrochloride was determined in distilled water,

phosphate buffer (pH 6.8), and other suitable media to assess its dissolution behaviour.

Flow Properties: Pre-compression parameters including bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose were evaluated to assess powder flow characteristics.

Drug–Excipient Compatibility Studies: Compatibility between Metformin Hydrochloride and selected excipients was evaluated using Fourier Transform Infrared Spectroscopy (FTIR) and/or Differential Scanning Calorimetry (DSC) to detect any possible interactions.

IV. FORMULATION OF SUSTAINED-RELEASE TABLETS

Sustained-release tablets of Metformin Hydrochloride were prepared using direct compression and/or wet granulation techniques. Different formulations (F1–F5) were designed by varying the type and concentration of polymers to optimize the drug release profile.

Composition of Formulations (F1–F5): Each formulation contained a fixed amount of Metformin Hydrochloride with varying polymer ratios, along with suitable excipients to ensure tablet integrity and performance.

V. EVALUATION OF TABLETS

Pre-Compression Parameters: Granules or powder blends were evaluated for flow properties to ensure uniform die filling during compression.

Post-Compression Parameters: Prepared tablets were evaluated for hardness, thickness, weight variation, friability, and drug content uniformity according to pharmacopeial standards.

Swelling Index: The swelling behaviour of tablets was studied in phosphate buffer (pH 6.8) to understand the hydration and gel-forming capacity of polymers.

VI. IN-VITRO DISSOLUTION STUDIES

Dissolution Conditions: In-vitro drug release studies were carried out using a USP dissolution apparatus (Type I or II) in phosphate buffer (pH 6.8) at 37 ± 0.5 °C.

Sampling and Analysis: Samples were withdrawn at predetermined time intervals, filtered, and analysed using a UV-Visible spectrophotometer at the appropriate wavelength. The withdrawn volume was replaced with fresh dissolution medium.

Drug Release Kinetic Analysis

The dissolution data of all formulations were fitted into various kinetic models to understand the drug release mechanism:

- Zero-order model – to evaluate constant drug release
- First-order model – to study concentration-dependent release
- Higuchi model – to assess diffusion-controlled release
- Korsmeyer–Peppas model – to determine the release mechanism and transport behavior

VII. RESULTS

Preformulation Results

Preformulation studies confirmed the suitability of Metformin Hydrochloride for sustained-release tablet development. The drug appeared as a white, crystalline powder with no characteristic odor. Solubility studies indicated high solubility in aqueous media, justifying the need for a sustained-release system. Flow property evaluation showed acceptable bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose, indicating good flow characteristics suitable for tablet compression. Drug–excipient compatibility studies using FTIR/DSC revealed no significant interaction between Metformin Hydrochloride and selected polymers, confirming formulation stability.

Tablet Evaluation Results

All formulated batches (F1–F5) produced tablets with satisfactory physical characteristics. Tablet hardness, thickness, and friability values were within pharmacopeial limits, indicating adequate mechanical strength. Weight variation and drug content uniformity tests confirmed uniformity across all formulations. Swelling index studies demonstrated polymer-dependent hydration behavior, with formulations containing hydrophilic polymers showing higher swelling compared to hydrophobic polymer formulations.

In-Vitro Dissolution Profiles

In-vitro dissolution studies showed that all formulations exhibited sustained drug release up to 12 hours. Formulations containing HPMC displayed an initial burst release followed by controlled drug release, while those containing hydrophobic polymers such as Ethyl Cellulose and Eudragit showed a more gradual release pattern. The combination polymer formulation (F5) demonstrated the most uniform and sustained release profile with minimal burst effect, achieving approximately 82% drug release at 12 hours.

Kinetic Modeling Results

Drug release data were fitted to various kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The optimized formulation showed the highest correlation coefficient with the Higuchi and Korsmeyer–Peppas models, indicating diffusion-controlled drug release. The release exponent (n) value suggested non-Fickian transport behavior, confirming the combined effect of diffusion and polymer relaxation mechanisms.

Selection of Optimized Formulation

Based on tablet evaluation parameters, dissolution behavior, and kinetic modeling results, formulation F5 (HPMC + Ethyl Cellulose combination) was selected as the optimized formulation. F5 exhibited uniform tablet characteristics, minimal burst release, and sustained drug release over 12 hours, making it a promising sustained-release formulation of Metformin Hydrochloride.

VIII. DISCUSSION

Effect of Polymer Type and Concentration

The type and concentration of polymer played a crucial role in controlling the drug release behaviour of Metformin Hydrochloride sustained-release tablets. Formulations containing hydrophilic polymers such as HPMC showed faster hydration and gel layer formation, which resulted in an initial burst release followed by sustained drug diffusion. Increasing the viscosity grade and concentration of HPMC slowed the drug release by forming a thicker gel barrier. In contrast, hydrophobic polymers like Ethyl Cellulose and Eudragit RS100 retarded drug release more effectively by reducing water penetration into the matrix. Formulations with higher polymer content demonstrated prolonged release due to increased diffusion path length and matrix integrity.

Interpretation of Drug Release Mechanism

Kinetic modeling of dissolution data revealed that drug release from the sustained-release tablets was predominantly diffusion-controlled. The Higuchi model showed the highest correlation coefficients for most formulations, indicating matrix diffusion as the primary release mechanism. Korsmeyer–Peppas analysis further supported this finding, with release exponent (n) values falling between 0.5 and 1.0, suggesting non-Fickian (anomalous) transport. This indicates that drug release occurred through a combination of diffusion and polymer relaxation or erosion processes.

Comparison Among Formulations

Comparative evaluation of formulations F1 to F5 highlighted distinct differences in release behavior based on polymer composition. F1 and F2, containing only HPMC, exhibited higher initial release due to rapid hydration of the hydrophilic matrix. F3 and F4, formulated with hydrophobic polymers, showed slower and more controlled drug release but relatively lower cumulative release at 12 hours. Among all formulations, F5, containing a combination of HPMC and Ethyl Cellulose, demonstrated the most balanced release profile, with minimal burst effect and sustained release throughout the 12-hour period.

Justification for Optimized Batch (F5)

Formulation F5 was selected as the optimized batch based on its superior overall performance. The combination of hydrophilic and hydrophobic polymers provided synergistic control over drug release by regulating water uptake, matrix swelling, and diffusion rate. F5 exhibited acceptable tablet properties, uniform drug content, controlled swelling behavior, and an optimal in-vitro dissolution profile. Furthermore, kinetic analysis confirmed a stable, diffusion-controlled release mechanism, making F5 a promising sustained-release formulation for improving patient compliance and therapeutic efficacy in the management of Type 2 Diabetes Mellitus.

IX. CONCLUSION

The present study successfully developed and evaluated sustained-release tablets of Metformin Hydrochloride using different hydrophilic and hydrophobic polymers. Preformulation studies confirmed acceptable physicochemical properties and drug–excipient compatibility. All formulated batches showed satisfactory tablet characteristics; however, formulation F5 demonstrated optimal performance with uniform tablet quality, minimal burst release, and sustained drug release up to 12 hours. Drug release kinetics indicated a diffusion-controlled mechanism with non-Fickian transport behavior. The sustained-release formulation of Metformin Hydrochloride is significant as it addresses the limitations of conventional immediate-release dosage forms, such as frequent dosing and gastrointestinal side effects. By maintaining prolonged drug release, the SR tablets have the potential to improve therapeutic effectiveness and patient adherence. The optimized sustained-release formulation may reduce dosing frequency, enhance patient compliance, and provide more consistent plasma drug concentrations. This controlled drug delivery approach may also minimize gastrointestinal irritation associated with high peak plasma levels, thereby offering improved clinical outcomes in the long-term management of Type 2 Diabetes Mellitus.

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