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DEVELOPMENT AND CHARACTERIZATION OF SUSTAINED RELEASE METFORMIN HCL TABLETS: A NOVEL APPROACH FOR IMPROVED GLYCEMIC CONTROL

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ABSTRACT :

Metformin HCl, a first-line oral hypoglycemic agent, exhibits short half-life and requires frequent dosing, which may reduce patient compliance. The present study aims to develop and characterize sustained-release tablets (SRT) of Metformin HCl using the wet granulation method to achieve prolonged drug release, maintain steady-state plasma concentrations, and improve glycemic control. Various preformulation studies, formulation optimization, blend characterization, and in-vitro evaluation were conducted. Results revealed that formulation F5 containing HPMC K100M provided an optimal sustained release profile over 24 hours. The developed formulation demonstrated acceptable physicochemical properties, micromeritic characteristics, and in-vitro drug release, indicating its potential as a novel oral sustained release dosage form of Metformin HCl.

Keywords: Metformin HCl, Sustained Release, Wet Granulation, HPMC, Glycemic Control.

1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Metformin HCl is widely used in the management of type II diabetes mellitus due to its ability to decrease hepatic glucose production and improve insulin sensitivity. However, conventional Metformin HCl tablets require multiple daily dosing due to its short plasma half-life (4–6 hours), which can lead to poor patient adherence.

Sustained release (SR) formulations are designed to release drugs gradually, maintaining therapeutic plasma concentrations over extended periods and reducing dosing frequency. This study focuses on the development of sustained release tablets of Metformin HCl using hydrophilic matrix-forming polymers to achieve prolonged glycemic control and improved patient compliance.

2. MATERIALS AND METHODS

2.1 Materials Used:

Metformin Hydrochloride, Hydroxypropyl Methylcellulose (HPMC K100M), Guar gum, Xanthan gum, Polyvinylpyrrolidone (PVP K30), Lactose anhydrous, Magnesium stearate, Talc, Isopropyl alcohol, Phosphate buffer (pH 6.8)

2.2 Identification of Drug

2.2.1 UV-Spectrophotometric Study

UV absorption spectrum was recorded in methanol between 200–400 nm. The λmax was found at 233 nm, consistent with reported literature.

2.2.2 Melting Point Determination

Using open capillary method, the melting point of Metformin HCl was found to be 172 °C, confirming drug purity.

2.2.3 Solubility Studies

Metformin HCl was found to be readily soluble in ethanol and moderately soluble in water (5 mg/ml).

2.4 Preparation of Calibration Curve

Stock solution (100 µg/ml) of Metformin HCl in pH 6.8 phosphate buffer was prepared. Serial dilutions (5–50 µg/ml) were analyzed at 233 nm. A

calibration curve was plotted with absorbance values showing linearity.

3. Formulation of Sustained Release Tablets

Wet granulation method was employed using HPMC K4M and HPMC K100M as release-retarding polymers. The composition of formulations (F1–F8) is presented in Table 1.

Table 1: Composition of SR Tablets of Metformin HCl (mg)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Metformin HCl	500	500	500	500	500	500	500	500
HPMC K4M	20	40	60	80	-	-	-	-
HPMC K100M	-	-	-	-	20	40	60	80
PVP K30	10	10	10	10	10	10	10	10
Lactose Anhydrous	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium Stearate	5	5	5	5	5	5	5	5
Talc	3	3	3	3	3	3	3	3
Total Weight	600	600	600	600	600	600	600	600

4. Characterization of Blend

Pre-compression studies were conducted to evaluate micromeritic properties:

- **Angle of repose** (funnel method)
  The angle of repose indicates the flow property of a powder blend. It is measured using the funnel method and calculated by the formula **tan θ = h/r**. Values below 30° indicate excellent flow, while values above 45° indicate poor flow.
- **Bulk density**
  Bulk density is the ratio of powder mass to its bulk volume, including interparticulate voids. It reflects packing ability and influences die filling during tablet compression
- **tapped density**
  Tapped density represents the maximum packing of a powder after standardized tapping. It is calculated as weight divided by tapped volume and helps evaluate compressibility
- **Carr's index (% compressibility)**
  Carr's Index measures powder flowability and compressibility, calculated as [(Tapped density − Bulk density)/Tapped density] × 100. Values below 15% indicate good flow.
- **Hausner ratio**
  Hausner ratio, calculated as Tapped density/Bulk density, indicates flow property. Ratios below 1.25 suggest good flow, while higher values indicate poor flow

5. Evaluation of Tablets

Post-compression parameters evaluated:

- **General appearance**:- Tablets were examined for color, shape, size, surface texture, and presence of defects to confirm uniformity and aesthetic quality (Indian Pharmacopoeia, 1996).
- Thickness (Vernier calipers) :- The thickness of tablets was measured using a Vernier caliper to ensure uniformity. Variations should be within ±5% of the standard value.
- Hardness (Monsanto tester):- Tablet hardness was tested using a Monsanto tester and expressed in kg/cm². Three tablets were tested, and the average value was recorded to assess mechanical strength
- Weight variation (IP specifications):- Weight variation was evaluated as per IP by individually weighing 20 tablets and comparing each to the average weight. Not more than two tablets should deviate from the limit, and none should exceed twice the limit.
  % Weight Variation=Average WeightAverage Weight / Individual Weight×100
- Friability (Roche friabilator):- Friability was assessed using a Roche friabilator. Ten tablets were rotated at 25 rpm for 4 minutes (100

revolutions). Weight loss was calculated as:

$$\%F=W0 - W0/W\times100$$

- Content uniformity (UV spectrophotometry):- Five tablets were powdered, and a portion equivalent to 100 mg of drug was dissolved in phosphate buffer (pH 6.8). After filtration and dilution, absorbance was measured at 233 nm using UV spectrophotometry to ensure uniform drug content
- In-vitro drug release (USP Type II, paddle apparatus, pH 6.8 buffer, 24 h).:- A tablet was placed in 6 ml of water and the time for complete dispersion was recorded. Additionally, wetting time was determined by placing a tablet on a folded tissue soaked in water. The ratio of wet to dry weight was calculated as:

$$R=10\times Wb/Wa$$

Dissolution was performed using USP Type II (paddle) apparatus in 900 ml of pH 6.8 phosphate buffer at 37 ± 0.5°C and 50 rpm for 12 hours. Samples were withdrawn at set intervals, replaced with fresh medium, and analysed spectrophotometrically at 230 nm to determine cumulative drug release

3. RESULTS AND DISCUSSION

3.1 Identification of Drug

UV study confirmed λmax at 233 nm. Melting point (172 °C) and solubility profile were in agreement with reported values, confirming identity and purity.

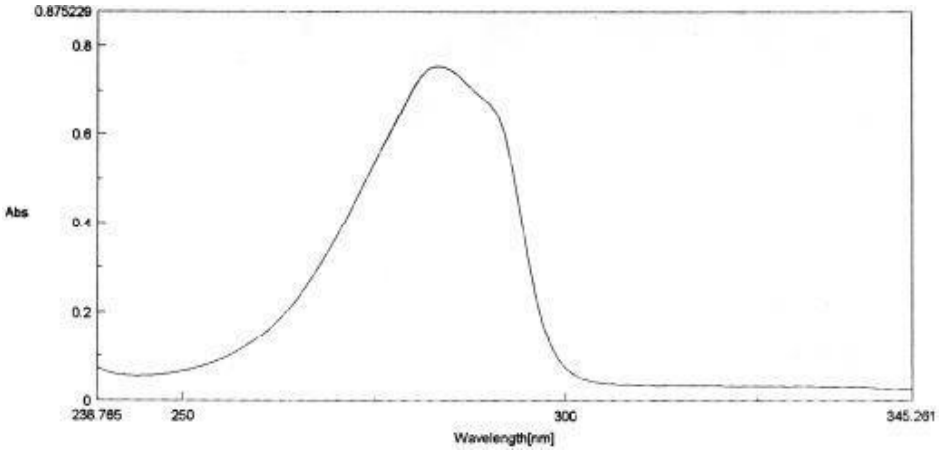

Fig 1: UV Absorption Spectrum of Metformin HCl

3.1.1 Melting Point Determination

The melting point of Metformin HCl was found to be 162°C, which is in agreement with the reported range of 171–175°C, confirming the purity and identity of the drug.

3.1.2 Solubility Studies

The solubility profile of Metformin HCl was consistent with literature values, indicating that the API meets pharmacopeial specifications for identity and quality.

3.1.3 Formulation Development of SRT

Sustained-release tablets were prepared using the wet granulation method. The drug and excipients were blended, granulated with isopropyl alcohol, and sieved (60 mesh). Lubricants and glidants were added prior to compression into tablets.

3.1.4 Characterization of Blend

Powder blends of all formulations were evaluated for pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio to assess flow properties before tablet compression.

Table 2: Result of evaluation

Formulation	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's index (%)	Hausner's Ratio	Angle of Repose
F-1	0.520±0.14	0.608±0.15	13.65±0.02	1.169±0.02	26.5±0.2
F-2	0.474±0.12	0.555±0.12	14.59±0.04	1.170±0.08	26.0±0.8
F-3	0.520±0.10	0.658±0.04	20.97±0.02	1.265±0.02	26.7±0.4
F-4	0.472±0.05	0.565±0.14	15.12±0.01	1.197±0.05	25.1±0.1

F-5	0.507±0.02	0.631±0.17	19.65±0.02	1.244±0.03	26.0±0.6
F-6	0.489±0.02	0.559±0.16	14.31±0.03	1.143±0.04	25.6±0.3
F-7	0.496±0.02	0.569±0.06	12.82±0.05	1.147±0.05	25.9±0.9
F-8	0.498±0.02	0.601±0.08	17.13±0.06	1.206±0.03	25.2±0.1

3.2 Evaluation of SRT of Metformin HCl prepared by Wet Granulation Method

3.2.1 Evaluation of physical parameters

The Prepared SRT of Metformin HCl were subjected to a variety of physical parameters as discussed below. The results are as follows:

Table 3: Characteristics of SRT of Metformin HCl

Formulation	Hardness (kg/cm^2)	Thickness (mm)	Weight Variation (mg)	Friability (%)
F-1	9.42± 0.08	3.83±0.06	201.4±1.02	0.24±0.03
F-2	9.39±0.03	3.76±0.02	203.0±1.12	0.12±0.02
F-3	9.21±0.01	3.71±0.02	201.0±1.02	0.19±0.03
F-4	8.95±0.06	3.73±0.05	201.1±1.15	0.09±0.01
F-5	7.99±0.08	3.83±0.05	199.3±1.03	0.04±0.01
F-6	9.02±0.01	4.02±0.04	198.6±1.09	0.21±0.02
F-7	8.95±0.01	3.70±0.05	201.1±1.13	0.16±0.03
F-8	7.39±0.09	3.89±0.04	200.9±1.14	0.13±0.04

3.3 In-vitro Drug Release

Calibration curve of Metformin HCl in pH 6.8 buffer showed linearity ($R^2 > 0.99$). Drug release profiles of F1–F8 indicated controlled release over 24 hours. Formulation F5 exhibited maximum drug release (96.07% at 24 h), suggesting an optimal polymer ratio for sustained release.

Table 4: Drug release study of the SRT in pH 6.8

Time (hr)	0	2	4	8	12	16	20	24
F1	0.00	6.93	26.93	42.39	65.59	73.40	79.97	93.31
F2	0.00	5.99	25.90	40.93	63.29	70.12	76.39	92.31
F3	0.00	5.32	26.3	40.63	62.32	69.91	75.21	90.35
F4	0.00	5.06	25.21	39.91	61.08	68.34	74.29	89.56
F5	0.00	5.97	26.45	45.20	65.34	71.42	84.99	96.07
F6	0.00	5.61	26.03	43.98	64.36	69.63	78.21	93.55
F7	0.00	5.31	25.49	42.69	61.56	68.64	77.10	87.44
F8	0.00	5.04	23.91	41.38	61.23	68.31	72.14	86.50

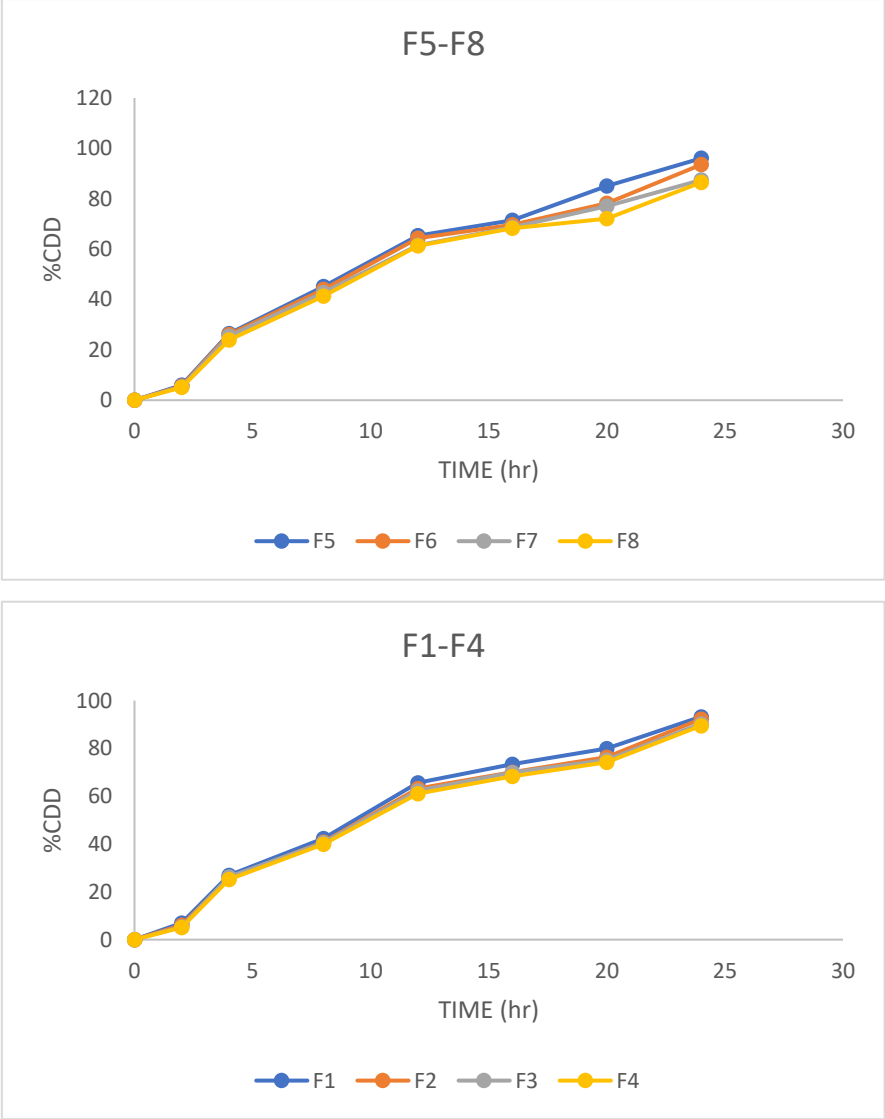

Figure 2: % Drug Release Profile of F1–F8 in pH 6.8 Buffer (Graphical representation)

4. Discussion

The present study successfully formulated sustained-release tablets of Metformin HCl using the wet granulation method with HPMC polymers as release-retarding agents. Pre-compression evaluations, including angle of repose, bulk density, and Carr's index, indicated good flow properties suitable for tablet compression. Post-compression parameters such as hardness, friability, and weight variation complied with pharmacopeial limits, ensuring mechanical integrity and uniformity. In-vitro drug release studies demonstrated controlled release over 12 hours, with formulations containing higher polymer concentrations showing slower release profiles, consistent with diffusion-controlled kinetics. The optimized batch provided a near-linear release, suggesting suitability for maintaining steady plasma drug concentrations. The use of HPMC K100M proved effective in modulating drug release compared to K4M. These findings align with previous studies on polymer-based sustained-release systems and confirm the potential of matrix tablets to enhance patient compliance by reducing dosing frequency while maintaining therapeutic efficacy.

5. CONCLUSION

The study concluded that sustained-release tablets of Metformin HCl can be effectively prepared using hydrophilic polymers such as HPMC through wet granulation. The developed formulations demonstrated acceptable pre-compression and post-compression characteristics and complied with pharmacopoeial standards. The optimized formulation exhibited controlled drug release for up to 12 hours, which can maintain therapeutic plasma levels, minimize fluctuations, and improve glycemic control in Type 2 diabetes patients. This dosage form addresses the limitations of conventional immediate-release formulations by reducing dosing frequency and improving patient adherence. The results confirmed that polymer concentration significantly influences the release rate, enabling formulation customization for desired therapeutic outcomes. Overall, this approach provides a promising, cost-

effective, and patient-friendly alternative for long-term diabetes management, supporting the concept of controlled drug delivery systems in improving clinical efficacy and safety

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