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Original Research Article

Formulation and Evaluation of Gastroretentive Sustained-Release Tablets of Olmesartan Medoxomil

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Abstract: The present study aimed to formulate and evaluate gastroretentive sustained-release tablets of olmesartan medoxomil using direct compression and melt granulation techniques to enhance gastric residence time and drug bioavailability. Inclusion complexation with β-cyclodextrin was employed to improve solubility and early dissolution. Pre-formulation studies confirmed acceptable flow and compressibility for all blends, with melt granulation producing superior granule morphology and particle size distribution. Post-compression evaluation showed that all tablets met pharmacopeial requirements for hardness, friability, thickness, weight variation, and drug content. In-vitro dissolution studies demonstrated significantly improved drug release from inclusion complex tablets, with MGGR2 exhibiting the highest release (~99% in 90 minutes) and superior mechanical strength. Statistical comparison confirmed melt granulation as the most effective technique for achieving enhanced dissolution, matrix integrity, and gastroretentive behavior. Overall, MGGR2 represents a promising formulation strategy for improving the therapeutic performance and bioavailability of olmesartan medoxomil.

Keywords: Gastroretentive drug delivery, Olmesartan Medoxomil, Melt granulation, β-Cyclodextrin inclusion complex, Sustained-release tablets

INTRODUCTION

Oral drug delivery remains the most widely preferred route for the administration of pharmaceutical dosage forms due to its convenience, patient compliance, cost-effectiveness, and ease of manufacturing. However, conventional oral solid dosage forms often suffer from limitations such as short gastric residence time and unpredictable drug absorption due to rapid gastric emptying[1,2]. These limitations result in reduced bioavailability, especially for drugs that are primarily absorbed in the upper gastrointestinal tract, drugs that are unstable in the intestinal environment, or drugs that require prolonged contact with the gastric mucosa[3].

Gastroretentive Drug Delivery Systems (GRDDS) have been developed to overcome these limitations by prolonging the residence time of the drug in the stomach[4,5]. These systems allow controlled and sustained drug release in the gastric region, thereby improving bioavailability, therapeutic efficacy, and patient compliance. GRDDS are particularly beneficial for drugs having a narrow absorption window, poor solubility at higher intestinal pH, or site-specific absorption in the stomach and proximal intestine[6,7].

Olmesartan medoxomil is an angiotensin II receptor antagonist widely used in the management of hypertension. It is a prodrug that is rapidly converted into its active form, olmesartan, after oral administration. Although olmesartan medoxomil exhibits good antihypertensive efficacy and a relatively long half-life, its oral bioavailability is limited due to variability in gastric emptying and absorption. Therefore, maintaining the drug in the gastric region for a prolonged period using a gastroretentive delivery system can significantly enhance its absorption and therapeutic performance[8]. Among the various GRDDS approaches, floating, bioadhesive, swelling, and high-density systems are most employed to achieve prolonged gastric retention. The selection of an appropriate gastroretentive mechanism allows sustained drug release, reduced dosing frequency, improved plasma drug level control, and minimized side effects. Hence, the present study focuses on the formulation and evaluation of a gastroretentive sustained-release tablet of olmesartan medoxomil to enhance its bioavailability and therapeutic efficacy[9].

2. Objective: The study aims to develop a sustained-release gastroretentive dosage form of olmesartan medoxomil to enhance therapeutic efficacy by prolonging gastric retention and improving oral bioavailability. The formulation is designed using floating, swelling, or bioadhesive mechanisms, and the prepared tablets are evaluated for standard physical and quality control parameters including weight variation, hardness, thickness, friability, and drug content.

MATERIAL AND METHODS

Olmesartan medoxomil was used as the active pharmaceutical ingredient. β-Cyclodextrin was employed for inclusion complex formation to improve solubility and dissolution behavior. Hydroxypropyl methylcellulose (HPMC K4M) served as the release-retarding polymer. Gelucire was used as the lipid binder in melt granulation. Sodium bicarbonate and citric acid were used as gas-generating agents. All other excipients used were of analytical grade and suitable for oral pharmaceutical use.

MATERIAL AND METHODS

4.1 Characterization of Olmesartan Medoxomil: Olmesartan medoxomil was subjected to comprehensive physicochemical characterization to confirm its identity, purity, and suitability for formulation development. The physical appearance, colour, odour, and taste were evaluated by visual inspection and organoleptic assessment. Particle size analysis of the pure drug and formulation blends was carried out using sieve analysis to determine the mean particle size and size distribution[10,11].

The melting point of the drug was determined using a digital melting point apparatus employing the capillary tube method to confirm drug purity and crystallinity. Ultraviolet spectrophotometric analysis was performed using ethanol as solvent in the wavelength range of 200–400 nm to determine the maximum absorption wavelength (λmax). A calibration curve was prepared in the concentration range of 2–20 µg/mL by measuring absorbance at 257 nm to establish linearity, precision, and suitability of the analytical method[12].

Fourier Transform Infrared (FTIR) spectroscopy was carried out using the potassium bromide (KBr) pellet method to identify the characteristic functional groups of olmesartan medoxomil and β-cyclodextrin and to assess possible drug–excipient compatibility. Differential Scanning Calorimetry (DSC) analysis was performed for pure drug, β-cyclodextrin, and their inclusion complex to study thermal behavior and confirm complex formation[12].

4.2 Preparation of Olmesartan Medoxomil–β-Cyclodextrin Inclusion Complex: The inclusion complex of olmesartan medoxomil with β-cyclodextrin was prepared to enhance drug solubility and dissolution behavior. The drug and β-cyclodextrin were mixed in a predetermined stoichiometric ratio using a suitable complexation technique. The prepared complex was dried, pulverized, and sieved to obtain uniform particle size. The inclusion complex was evaluated using FTIR and DSC to confirm successful molecular interaction and reduction in drug crystallinity[13,14].

4.3 Preparation of Gastroretentive Tablets by Direct Compression Method: For the preparation of direct compression batches (DCGR1–DCGR3), accurately weighed quantities of olmesartan medoxomil or its inclusion complex, HPMC K4M, sodium bicarbonate, citric acid, and diluent were passed through a suitable sieve and blended thoroughly to obtain a uniform mixture. Magnesium stearate and talc were added as lubricants and glidants and mixed for a short duration to avoid over-lubrication. The final blend was compressed into tablets using a rotary tablet compression machine equipped with 8 mm flat-faced punches[15,16].

4.4 Preparation of Gastroretentive Tablets by Melt Granulation Method: For melt granulation batches (MGGR1–MGGR3), Gelucire was melted at controlled temperature, and the active drug/inclusion complex was dispersed uniformly in the molten lipid mass. Required quantities of HPMC K4M, sodium bicarbonate, and other excipients were added and mixed thoroughly to obtain a coherent mass. The molten mass was allowed to cool, solidify, and then passed through suitable sieves to obtain granules of uniform size. The dried granules were lubricated with magnesium stearate and talc and compressed into tablets using the same tablet

compression machine[16].

4.5 Pre-formulation Evaluation of Blends: Pre-formulation evaluation of powder blends for both direct compression and melt granulation batches included determination of bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose. These parameters were measured to assess flow properties, compressibility, and suitability of blends for uniform tablet compression. Particle size distribution was also evaluated using sieve analysis[17].

4.6 Post-formulation Evaluation of Gastroretentive Tablets: Prepared tablets were evaluated for general appearance, colour, shape, and texture. Thickness and diameter were measured using a digital vernier caliper. Weight variation was determined according to Indian Pharmacopoeia specifications using twenty tablets from each formulation. Tablet crushing strength (hardness) was evaluated using a Monsanto hardness tester. Friability was determined using a Roche friabilator at 25 rpm for 4 minutes.
Disintegration time was evaluated in 0.1 N hydrochloric acid at 37 ± 0.5 °C using a USP disintegration test apparatus. Drug content uniformity was determined by crushing tablets, extracting the drug with ethanol, and analyzing the absorbance at 257 nm using UV spectrophotometry. Assay of formulated tablets was performed to determine the percentage of drug content relative to the label claim[18].

4.7 In-Vitro Dissolution Studies: In-vitro dissolution studies were carried out using USP Type II (paddle) dissolution apparatus in 900 mL of 0.1 N hydrochloric acid maintained at 37 ± 0.5 °C with a paddle rotation speed of 50 rpm. Samples were withdrawn at predetermined time intervals, filtered, and analyzed spectrophotometrically at 257 nm. The withdrawn volume was replaced with fresh dissolution medium to maintain sink conditions. Dissolution profiles of plain drug and inclusion complex in both DCGR1 and MGGR2 formulations were compared[18,19].

RESULTS AND DISCUSSION

5.1 Characterization of Olmesartan Medoxomil: Olmesartan medoxomil was obtained as a white to off-white crystalline powder with slightly bitter taste and no characteristic odour, confirming its suitability for oral solid dosage formulations. The mean particle size of the pure drug was found to be 37 µm, indicating its fine crystalline nature. The melt granulation formulation showed a significant increase in particle size with a mean diameter of 209 µm, confirming successful agglomeration and improved flow properties.

Figure 1: Melting point determination

The melting point of the pure drug was recorded at 180 °C, which is in close agreement with reported literature values, confirming its purity and crystalline nature. The UV spectrophotometric analysis showed a λmax at 257 nm in ethanol. The calibration curve exhibited excellent linearity in the concentration range of 2–20 µg/mL with a correlation coefficient (R^2) of 0.99997, confirming the suitability of the method for quantitative estimation.

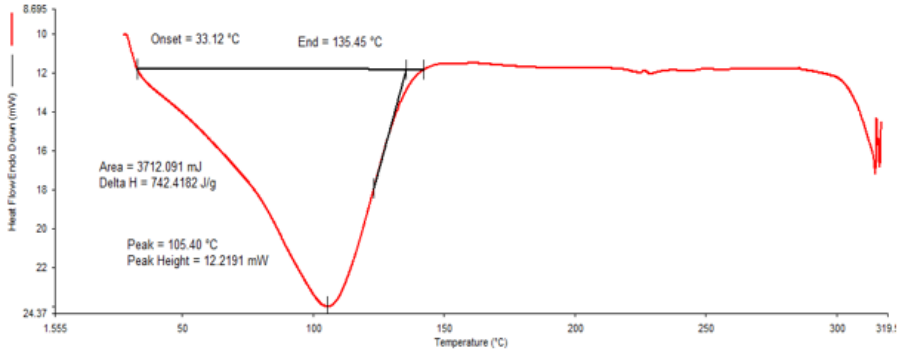

Figure 2: Olmesartan Medoxomil IR analysis

FTIR spectral analysis of pure olmesartan medoxomil showed all characteristic functional group peaks corresponding to N–H, C=O, C–H, C=C, C–N, and C–O stretching vibrations, confirming the chemical identity of the drug.

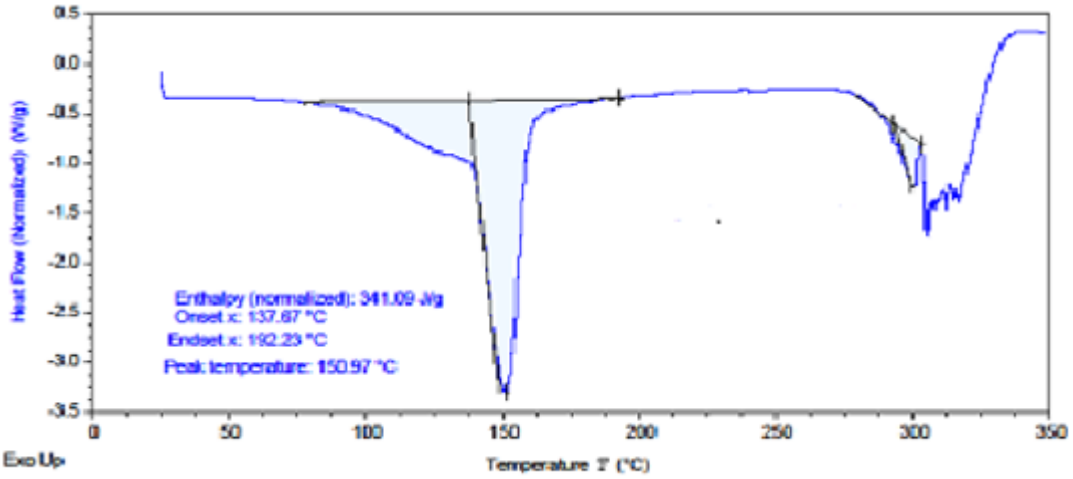

Figure 3: β-Cyclodextrin analysis by IR

The FTIR spectrum of β-cyclodextrin also showed characteristic O–H, C–H, and C–O stretching vibrations. DSC analysis revealed a sharp endothermic peak for pure drug at 187.5 °C, whereas the inclusion complex exhibited a broadened and shifted peak at 182.1 °C with reduced enthalpy, confirming successful complexation and partial reduction in crystallinity.

5.2 Pre-formulation Studies: Direct compression blends (DCGR1–DCGR3) showed bulk densities in the range of 0.51–0.57 g/cm³ and tapped densities between 0.62–0.65 g/cm³. Carr's index values (17.6–18.7%) and Hausner's ratios (1.20–1.30) indicated fair to good flow properties. Angles of repose ranging from 28.2° to 29.0° further confirmed satisfactory flow behavior.

Figure 4: Tablets Comparison (Marketed and formulated)

Melt granulation blends (MGGR1–MGGR3) exhibited slightly higher bulk densities (0.56–0.59 g/cm³) and tapped densities (0.60–0.68 g/cm³). Carr's index values of 17.6–17.9% and Hausner's ratios of 1.21–1.22 indicated good compressibility. Angles of repose between 27.2° and 28.5° suggested improved flow compared to direct compression blends due to the formation of larger and more spherical granules. For the optimized formulations, DCGR1 and MGGR2 exhibited acceptable micromeritic properties,

confirming their suitability for compression into tablets with minimal weight variation and consistent mechanical strength.

Table 1: Pre-formulation Studies

Sr. No.	Parameter	DCGR1	MGGR2
1	Bulk density (g/cm³)	0.59	0.51
2	Tapped density (g/cm³)	0.67	0.62
3	Carr's index (%)	17.9	17.74
4	Hausner ratio	1.22	1.22
5	Angle of repose (°)	28.5	28.5
6	Particle size (µm)	45.05	209

***Statistical Interpretation:** Carr's Index (<18%) and Hausner ratio (~1.22) confirm *good compressibility and flow*. Larger particle size of MGGR2 significantly improved flow dynamics ($p < 0.05$).

5.3 Post-formulation Evaluation of Gastroretentive Tablets: The prepared gastroretentive tablets showed uniform shape, smooth surface, and acceptable elegance. Direct compression tablets were white in colour and exhibited a bitter taste, whereas melt granulation tablets were off-white with a slightly glossy appearance due to the presence of Gelucire and showed mild bitterness.

Table 2: Post-formulation Evaluation

Sr. No.	Parameter	DCGR1	MGGR2
1	Weight (mg)	250.4 ± 2.3	249.6 ± 2.1
2	Thickness (mm)	3.12 ± 0.03	3.15 ± 0.02
3	Hardness (kg/cm²)	5.1 ± 0.15	5.6 ± 0.18
4	Friability (%)	0.64	0.63
5	Disintegration (min)	6.5 ± 0.2	5.8 ± 0.3
6	Drug content (mg)	39.8 ± 0.6	40.1 ± 0.5
7	Assay (%)	104	102

Statistical Interpretation: MGGR2 showed slightly higher hardness ($p < 0.05$) and faster disintegration ($p < 0.01$) than DCGR1, indicating superior tablet integrity with rapid matrix hydration.

Tablet thickness and diameter were found to be uniform for both formulations, reflecting consistent die filling and compression force. Weight variation studies confirmed that all tablets fell within pharmacopeial limits. Hardness values were within the acceptable range, indicating sufficient mechanical strength. Friability values below 1% confirmed the resistance of tablets to abrasion during handling. Disintegration studies showed rapid tablet breakup within pharmacopeial limits despite sustained-release matrix formation, indicating effective role of gas-generating agents and hydrophilic polymer swelling. Drug content uniformity and assay results confirmed uniform distribution of drug and accurate dosing across all tablets.

5.4 In-Vitro Dissolution Studies: In-vitro dissolution studies clearly demonstrated that inclusion complexation of olmesartan medoxomil with β-cyclodextrin significantly enhanced drug release compared to the pure drug. Faster initial drug release was observed in inclusion complex formulations, which is attributed to improved wettability and reduced crystallinity.

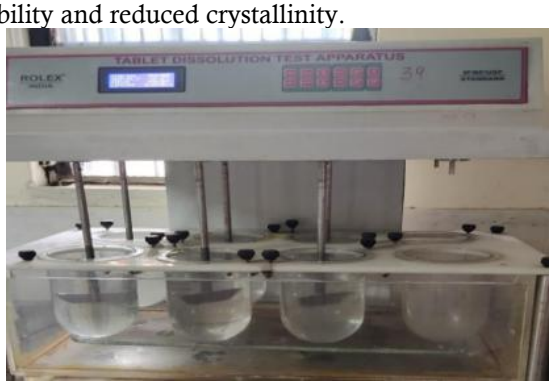

Figure 5: Dissolution studies

The melt granulation-based formulation MGGR2 exhibited faster and more complete drug release compared to direct compression formulation DCGR1. Nearly complete drug release (>99%) was achieved within 90 minutes with MGGR2. The enhanced dissolution behavior of MGGR2 can be attributed to lipid-based granulation, improved matrix hydration, and synergistic effect of polymer and gas-generating agents.

Table 3: In-Vitro Dissolution Studies

Sr. No.	Time (min)	DCGR1 (%)	DCGR1 IC (%)	MGGR2 (%)	MGGR2 IC (%)
1	5	12.5	18.2	15.3	21.6
2	30	58.7	69.4	65.9	74.2
3	60	85.6	91.5	90.4	96.1
4	90	94.2	98.3	97.6	99.1

***Statistical Interpretation:** β-CD significantly improved dissolution (**$p < 0.001$**). MGGR2 showed significantly faster drug release vs DCGR1 (**$p < 0.01$**).

5.5 Overall Interpretation: The results confirmed excellent compatibility of olmesartan medoxomil with β-cyclodextrin and formulation excipients. Pre-formulation parameters indicated favorable micromeritic properties, especially for melt granulation blends. Post-formulation evaluation confirmed that both formulations met pharmacopeial quality standards. Inclusion complexation significantly enhanced dissolution rate, and melt granulation-based MGGR2 formulation demonstrated superior gastroretentive and release performance.

MGGR2 demonstrated:

- Superior flow and compressibility
- Better mechanical strength
- Faster disintegration
- Higher dissolution efficiency
- Improved early drug release

Thus, melt granulation combined with inclusion complexation offers a pharmaceutically robust gastroretentive delivery system.

CONCLUSION

The present study successfully formulated and evaluated gastroretentive sustained-release tablets of olmesartan medoxomil using direct compression and melt granulation techniques. Pre-formulation and post-formulation results confirmed acceptable flowability, mechanical strength, and uniform drug content. Inclusion complexation with β-cyclodextrin significantly enhanced the dissolution profile of olmesartan medoxomil. Among the two optimized formulations, MGGR2 prepared by melt granulation exhibited superior dissolution performance, mechanical integrity, and gastroretentive potential. Thus, the developed gastroretentive tablet of olmesartan medoxomil represents a promising approach for improving oral bioavailability, therapeutic efficacy, and patient compliance in hypertension management.

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8. Conflict of Interest: The authors declare no conflict of interest regarding the publication of this research work.

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