FORMULATION AND CHARACTERIZATION OF HYDRODYNAMICALLY BALANCED DELIVERY SYSTEM OF MIGLITOL FOR PROLONGED GASTRIC RETENTION IN TYPE-2 DIABETES

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ABSTRACT

The objective of the current study was to create and assess a hydrodynamically balanced system (HBS) for miglitol in order to achieve sustained drug release and extended stomach retention. Five formulations (HBSF1 to HBSF5) were prepared using Modified Methylcellulose Hydrogel (MMCH) and Xanthan Gum (XG) as hydrophilic polymers, ensuring controlled drug release and enhanced buoyancy. The micromeritic properties of the formulations were evaluated, demonstrating excellent flowability, compressibility, and uniform weight distribution, with Carr's Index (≤3.48%), Hausner Ratio (~1.02–1.03), and an Angle of Repose below 25°, ensuring efficient capsule filling and manufacturing reproducibility. Due to the development of a stable colloidal hydrogel matrix, the in vitro flotation investigation verified that all formulations maintained their buoyancy for more than 12 hours without experiencing a floating lag period. The drug content uniformity ranged between 98.88% and 100.10%, ensuring consistency in drug distribution. According to the in vitro drug release research, HBSF3 achieved a cumulative drug release of 92.23% at 12 hours, indicating a sustained and regulated release. With an n-value of 0.8670, the release kinetics study showed that HBSF3 adhered to the Korsmeyer-Peppas model (R2 = 0.9937), indicating anomalous diffusion-controlled release via polymer swelling and erosion mechanisms. The zero-order model (R^2 = 0.9821) further confirmed a steady and prolonged release pattern. Overall, HBSF3 was identified as the optimized formulation, offering prolonged gastric retention, enhanced bioavailability, and controlled drug release, making it a promising candidate for sustained-release Miglitol therapy in diabetes management. The study concludes that HBS formulations can significantly improve drug efficacy and patient compliance by reducing dosing frequency.

KEYWORDS: Miglitol Sustained Release, In Vitro Drug Release, Hydrodynamically Balanced System (HBS), Micromeritic Properties, Release Kinetics Models

INTRODUCTION

Persistent hyperglycaemia is a hallmark of diabetes mellitus, a chronic metabolic disease brought on by either insulin resistance, inadequate insulin production, or both. Among the available therapeutic strategies, α-glucosidase inhibitors such as Miglitol play a crucial role in delaying carbohydrate digestion and absorption, thereby preventing postprandial glucose spikes. However, Miglitol's quick intestinal absorption and short biological half-life (~2 hours) need frequent dosage, which may result in decreased patient compliance and erratic plasma drug levels. In order to overcome these obstacles, a hydrodynamically balanced system (HBS) for miglitol was created, which offers regulated drug release and extended stomach retention, improving the medication's therapeutic effectiveness (Bantounou et al., 2024; Patel et al., 2024; S et al., 2024).

A gastro-retentive drug delivery system (GRDDS) that is hydrodynamically balanced (HBS) is made to stay afloat in the stomach for a long time, guaranteeing both site-specific drug release and prolonged gastric retention. An HBS formulation can greatly increase drug bioavailability by keeping the medication inside its absorption window, as miglitol is mainly absorbed in the upper gastrointestinal tract. Floating drug delivery systems (FDDS) achieve buoyancy through gas-generating, swelling, or low-density polymeric approaches, where hydrophilic polymers form a gel-like matrix that remains afloat in gastric fluids. By extending the gastric residence time (GRT), such systems provide controlled drug release, reduced dosing frequency, and improved patient adherence (Patel et al., 2024).

An oral α-glucosidase inhibitor called miglitol is used to treat type 2 diabetic mellitus (T2DM). It functions by delaying carbohydrate digestion and absorption in the small intestine, thereby preventing postprandial hyperglycaemia (PPHG). Unlike insulin secretagogues, Miglitol does not stimulate insulin release, reducing the risk of hypoglycaemia and making it a safe option for diabetic patients, particularly those prone to hypoglycaemia, such as the elderly or those on multiple antidiabetic drugs (Singh & Kim, 2000). In the upper gastrointestinal tract, miglitol is quickly absorbed, reaching peak plasma concentrations in two to three hours. However, its short biological half-life (~2 hours) necessitates frequent dosing (three times daily with meals), which can lead to reduced patient adherence and fluctuating plasma drug levels. Additionally, its low bioavailability (~40%) and site-specific absorption in the small intestine limit its therapeutic potential, making conventional dosage forms suboptimal for sustained glucose regulation (Reddy & Murthy, 2002).

In order to ensure longer drug release and extended gastric retention time (GRT), a hydrodynamically balanced system (HBS) is a gastro-retentive drug delivery system (GRDDS) that is made to stay buoyant in stomach fluids for an extended amount of time. Since the upper gastrointestinal tract is where miglitol is mainly absorbed, an HBS formulation can greatly increase its bioavailability by extending the period of the drug's absorption window, enabling controlled drug release and prolonged therapeutic activity.

The need for HBS in Miglitol delivery arises due to several pharmacokinetic and therapeutic challenges. Miglitol is absorbed mainly in the proximal small intestine, and conventional formulations rapidly transit through the stomach, limiting its absorption. An

HBS retains the drug in the stomach, gradually releasing it at an optimal rate, enhancing drug uptake and bioavailability. Furthermore, Miglitol has a short half-life (~2 hours), necessitating frequent dosing (three times daily), leading to poor patient compliance. An HBS formulation ensures sustained drug release over 12 hours, reducing the need for multiple daily doses and providing better glycemic control (Erni & Held, 1987).

Additionally, postprandial glucose spikes are a major concern in diabetes management, as Miglitol is most effective when continuously available in the stomach and upper intestine to inhibit α-glucosidase enzymes, preventing rapid glucose absorption. An HBS system allows for sustained drug release, maintaining steady plasma concentrations and minimizing fluctuations. Another advantage is avoiding dose dumping and gastrointestinal side effects, as a sustained-release HBS formulation prevents the high peak plasma concentrations seen with immediate-release tablets, thereby reducing gastrointestinal discomfort such as bloating and diarrhea, which are common with α-glucosidase inhibitors. The incorporation of hydrophilic polymers, particularly Modified Methylcellulose Hydrogel (MMCH) and Xanthan Gum (XG), plays a crucial role in ensuring buoyancy and controlled release. These polymers provide a low-density system that floats in stomach juices while delivering the medication gradually. They do this by absorbing water, swelling, and forming a gel-like matrix. This optimized release pattern ensures that Miglitol remains bioavailable in the stomach for a prolonged period, making it ideal for gastro-retentive formulations (Erni & Held, 1987). In assumption, formulating Miglitol as an HBS-based GRDDS effectively addresses the limitations associated with its short half-life, site-specific absorption, and frequent dosing requirements. An HBS formulation can optimise Miglitol therapy by guaranteeing prolonged stomach retention, sustained drug release, and greater bioavailability. This will improve glycaemic control, patient compliance, and overall therapeutic outcomes in the management of diabetes (Erni & Held, 1987). This study aimed to develop and evaluate multiple Miglitol HBS formulations to identify the most optimized formulation for sustained drug release. The formulations were systematically characterized based on micromeritic properties, which are crucial for ensuring uniform capsule filling, optimal flowability, and physical stability of the dosage form. To ensure consistent dosing, weight uniformity and drug content uniformity tests were conducted across all formulations. Additionally, to evaluate each formulation's potential for sustained release, 12-hour in vitro drug release tests were conducted. To identify the main drug release mechanism controlling the release of miglitol, the observed drug release profiles were examined using mathematical kinetic models, such as zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell models. The main goal of this study was to create a hydrodynamically balanced system (HBS) that could maintain gastric retention for an extended period of time while guaranteeing a steady and regulated release of miglitol. By increasing miglitol's bioavailability, lowering dosage frequency, and enhancing glycaemic control, this formulation strategy seeks to improve treatment outcomes for individuals with type 2 diabetes mellitus (T2DM).

MATERIAL AND METHODS

Every chemical and substance used in this investigation was of analytical quality and was sourced from reputable vendors. Zendoz Pharmaceuticals in Baddi, Himachal Pradesh,

provided the miglitol. Sigma Aldrich provided the Medium Molecular Mass Chitosan and Xanthan Gum. Loba Chemical Private Limited provided the lactose, talc, magnesium stearate, and barium sulphate. Kumar Traders, located in Kolkata, India, provided the size 000 empty hard gelatin capsules. Any extra materials were exclusively bought commercially from reliable and verified suppliers.

Preparation of Miglitol Floating HBS Capsules

Using the direct compression approach, the hydrodynamically balanced system (HBS) formulations of miglitol were created. To guarantee a consistent particle size distribution, the necessary amounts of lactose, xanthan gum (XG), modified methylcellulose hydrogel (MMCH), and miglitol were precisely weighed and run through a #60 sieve. To create a uniform slurry, the powders were vigorously combined for 15 minutes using the tumble process. To guarantee the right flow characteristics, the lubricants—magnesium stearate and talc—were added to the mixture after it had been blended and stirred for five more minutes. To ensure consistent weight distribution across the various formulation codes (HBSF1 to HBSF5), the finished blend was manually packed into firm gelatin capsules of size "0." After that, the capsules were kept at room temperature in sealed containers until they could be examined further. To determine their appropriateness for gastro-retentive drug delivery, the produced formulations underwent pre-compression and post-compression evaluations that included flow characteristics, weight variation, drug content, in vitro buoyancy experiments, swelling index, and in vitro drug release investigations.

Table 1: Composition of Miglitol (HBS Formulation) Capsules

	Formulation Code				
Ingredients (mg)	**HBSF1**	**HBSF 2**	**HBSF 3**	**HBSF 4**	**HBSF 5**
Miglitol	100	100	100	100	100
MMCH (Modified Methylcellulose Hydrogel)	20	40	60	80	100
XG (Xanthan Gum)	100	80	60	40	20
Lactose	80	80	80	80	80
Talc	5	5	5	5	5
Magnesium Stearate	12	12	12	12	12

Determination of Micromeritic Properties

A crucial stage in the creation of Hydrodynamically Balanced System (HBS) capsules is determining the micromeritic properties, especially to guarantee the effective handling and processing of powders such excipients, polymers, the active medication (Miglitol), and their mixes. The micromeritic properties of the Miglitol HBS formulation powder blends were evaluated to assess their flowability and compressibility, which are critical for ensuring uniform capsule filling and batch-to-batch consistency. The following parameters were determined (Mohapatra, Satyavani, & Sahoo, 2020):

1. Bulk Density (BD) and Tapped Density (TD)

A graduated measuring cylinder method was used to determine the powder blends' bulk and tapped densities. A 50 mL graduated cylinder was filled with a known weight (W) of the powder, and the initial volume (V_0) was recorded in order to calculate bulk density using the following formula:

Bulk Density=W/V0

The final volume (Vf) was then recorded after the cylinder was mechanically tapped 100 times. The calculation of taped density was done using:

Tapped Density=W/Vf

2. Compressibility Index (Carr's Index, CI)

Using the following formula, the compressibility index was calculated to evaluate the powder's capacity to consolidate:

Carr's Index (%) = Tapped Density−Bulk Density/Tapped Density×100

Excellent flow characteristics are indicated by a lower CI value (< 15%), while poor flow characteristics are suggested by a higher value (> 25%).

3. Hausner's Ratio (HR)

The following formula was used to determine Hausner's ratio, a measure of inter-particulate friction:

Hausner's Ratio = Tapped Density/Bulk Density

A value close to 1.00–1.25 indicates good flowability, while values above 1.50 suggest poor flow.

4. Angle of Repose (θ)

The fixed funnel method was used to further evaluate the powder's flowability. The powder was allowed to freely flow through a funnel that was fixed at a height and onto a level surface, creating a conical heap. After measuring the heap's height (h) and radius (r), the angle of repose was computed using the following formula:

$\theta = \tan -1(h/r)$

An angle of repose below 30° indicates good flowability, while values above 40° indicate poor flow.

These micromeritic studies ensured that the prepared formulation blends had suitable flow properties, essential for efficient capsule filling and consistent weight variation (Mohapatra et al., 2020).

Determination of Weight Uniformity

The weight uniformity of the Miglitol HBS formulation capsules was determined to ensure consistency in drug content and compliance with pharmacopeial standards. From each formulation batch (HBSF1 to HBSF5), twenty capsules were chosen at random and weighed separately using an analytical balance. The contents of each capsule were carefully removed, and the empty capsule shells were weighed separately to determine the net fill weight. Each weight was compared to the average weight of the capsule contents, which was determined by calculating the mean weight of the contents. According to the USP guidelines, capsules weighing ≤ 300 mg should not deviate by more than ±10% from the average weight, while those weighing more than 300 mg should not exceed ±7.5% variation. If more than two capsules deviated from the prescribed limits or if a single capsule exceeded twice the permissible variation, the batch was considered non-compliant.

This test was essential for ensuring dose uniformity and maintaining formulation consistency, thereby guaranteeing reliable therapeutic efficacy. Capsules that passed the weight uniformity test proceeded to further quality evaluations (A. Verma, Dubey, Verma, & Nayak, 2017).

Evaluation of Drug Content Uniformity

To guarantee uniform drug distribution throughout all capsules in compliance with pharmacopeial standards, the drug content uniformity of the Miglitol HBS formulation capsules was assessed. Ten capsules were randomly selected from each formulation batch (HBSF1 to HBSF5), and their contents were accurately weighed and dissolved in a suitable solvent. After 15 minutes of sonication to guarantee the drug's full solubility, the produced solutions were filtered through a 0.45 µm membrane filter. A UV-visible spectrophotometer was used to analyse the filtrate at the predefined wavelength of miglitol after it had been suitably diluted. The absorbance readings were then compared to a standard calibration curve. The percentage drug content in each capsule was calculated using the formula:

Drug Content (%) = (Observed Concentration / Theoretical Concentration) × 100

According to pharmacopeial specifications, the drug content of individual capsules should fall within 90% to 110% of the labeled claim. If more than one capsule deviated beyond this range, or if any single capsule exceeded ±15% variation, the batch was considered non-compliant. The results of this test ensured uniformity in drug distribution, minimizing dosage variations and ensuring therapeutic efficacy. Capsules that met the drug content uniformity criteria were considered suitable for further evaluation.

In Vitro Drug Release and Kinetic modelling

In order to assess the drug's release profile under simulated gastrointestinal conditions, an in vitro drug release study of the Miglitol HBS formulation capsules was carried out utilising a USP dissolution equipment II (paddle type). The trial was conducted at 37 ± 0.5°C with a paddle rotation speed of 50 rpm in 900 mL of simulated gastric fluid (pH 1.2) for the first two hours and simulated intestinal fluid (pH 6.8) for the remaining hours. To maintain sink conditions, aliquots of 5 mL were taken out and replaced with an equivalent volume of new dissolving liquid at prearranged intervals. After passing through a 0.45 µm membrane filter and being suitably diluted, the samples were examined at the specified wavelength of miglitol using a UV-visible spectrophotometer. To create the release profile, the percentage cumulative drug release was computed and plotted against time.

The acquired drug release data were fitted into a number of mathematical models, including as zero-order, first-order, Higuchi, and Korsmeyer-Peppas models, in order to comprehend the release kinetics and mechanism. The equation $Q = k_0 t$, where Q is the cumulative amount of medication released, k_0 is the zero-order release rate constant, and t represents time, was used to evaluate the zero-order model, which depicts drug release at a constant rate. Using the formula $\log C = \log C_0 - k_1 t/2.303$, where C is the concentration at time t, C_0 is the initial concentration, and k_1 is the first-order rate constant, the first-order model—which postulates that the release rate is concentration-dependent—was assessed. $Q = k\_H\ t^{1/2}$, where k_H is the Higuchi dissolving constant, was used to analyse the Higuchi model, which represents drug release from a matrix system. The equation $Mt/M\infty = k\ t^n$, where

Mt/M∞ is the fraction of drug released at time t, k is a release rate constant, and n is the release exponent reflecting the mechanism of drug release, was used to use the Korsmeyer-Peppas model to ascertain the release mechanism. Each model's regression coefficient (R2) was calculated, and the model with the highest correlation value was found to be the best fit. By shedding light on the drug release mechanism, the kinetic modelling results made sure the formulation had the appropriate controlled-release properties (Nayak, Das, & Maji, 2013; A. Verma et al., 2017).

Characterization by FTIR: Drug-Excipient Interaction study

Fourier Transform Infrared (FTIR) spectroscopy was used in the drug-excipient interaction investigation for Miglitol HBS formulations in order to evaluate any possible chemical interactions between the drug and excipients. The potassium bromide (KBr) pellet method was used to record the FTIR spectra of pure miglitol, individual excipients (MMCH, xanthan gum, lactose, talc, and magnesium stearate), and the physical mixture of the optimised formulation. Under hydraulic pressure, precisely weighed samples were combined with dry KBr in a 1:100 ratio and compacted into thin pellets. An FTIR spectrophotometer was used to scan the produced pellets in the 4000–400 cm^{-1} spectral region.

The spectra of the physical mixture were compared with the distinctive peaks of miglitol, which included those that corresponded to functional groups such -OH stretching, C-H stretching, and C-O bending. Any significant shifts, disappearance, or appearance of new peaks were analyzed to determine possible interactions between the drug and excipients. The absence of major spectral changes confirmed the compatibility of Miglitol with the selected excipients, ensuring the stability of the formulation. This study was crucial for ensuring that no chemical degradation or unfavourable interactions occurred, which could compromise the drug's efficacy and stability in the final HBS formulation.

In Vitro Floatation

To ensure longer stomach retention, the buoyancy of the Miglitol HBS formulation capsules under simulated gastric circumstances was assessed using an in vitro floating research. A USP dissolving apparatus II (paddle type) with 900 mL of simulated gastric fluid (SGF, pH 1.2) kept at 37 ± 0.5°C and a paddle rotation speed of 50 rpm was used to conduct the test. After the capsules were carefully inserted into the dissolving solvent, their ability to float was noted. The time it took for the capsule to ascend to the surface was measured and called the floating lag time (FLT). Additionally, the total floating time (TFT), representing the duration for which the capsules remained buoyant without sinking, was monitored. The formulations were considered suitable for gastro-retentive drug delivery if they exhibited a floating time of at least 12 hours. The incorporation of hydrophilic polymers such as MMCH and xanthan gum facilitated hydration and gel formation, contributing to buoyancy by entrapping air within the matrix. The floating behaviour of different formulations (HBSF1 to HBSF5) was compared to assess the influence of polymer concentration on floatation. An optimal balance between swelling and density reduction was required to ensure prolonged gastric retention and controlled drug release. The results of this study helped in optimizing the formulation for effective hydrodynamically balanced system (HBS) performance (A. Verma et al., 2017).

Statistical Analysis

Along with the mean and standard deviation (SD) of several independent calculations, the formulations' release data and additional experimental data have been provided. The statistical program GraphPad Prism Version 8 and the unpaired "t" test were used to determine whether the differences were significant. A significance criterion of $p < 0.05$ was established.

RESULTS AND DISCUSSION

Micromeritic Properties

The micromeritic properties of the different HBS formulations of Miglitol were evaluated to assess their flow characteristics and compressibility, which are essential for ensuring uniform capsule filling and consistent formulation quality. All formulations' bulk and tapped densities were within a reasonable range, suggesting that the powder blend had minimum void space and good packing. The Carr's Index (CI) values ranged between 2.00% and 3.48%, suggesting excellent flow properties with minimal interparticle friction. These findings were further supported by the Hausner Ratio (HR) values, which were close to 1.02–1.04, confirming low compressibility and optimal blend characteristics suitable for direct compression.

The angle of repose (AOR), a critical parameter for evaluating powder flowability, ranged from 17.76° to 23.57°, indicating good to excellent flow properties across all formulations. The lowest AOR value was observed for HBSF1 (17.76°), which suggests superior flowability, while HBSF4 (23.57°) exhibited slightly higher resistance to flow. This variation in AOR values might be attributed to differences in polymer concentrations, which could influence powder cohesiveness and flow characteristics. Overall, all formulations demonstrated favorable micromeritic properties, ensuring efficient capsule filling and minimal processing challenges. These results indicate that the selected excipients and formulation strategies effectively contribute to the optimized flow and compressibility of the HBS Miglitol capsules, making them suitable for further evaluation and development.

Table 2: Micromeritic Properties of Different HBS Capsules of Miglitol

Formulation Code	Bulk Density (BD) (g/cm³)	Tapped Density (TD) (g/cm³)	Carr's Index (CI) (%)	Hausner Ratio (HR)	Angle of Repose (AOR) (°)
HBSF1	0.587	0.599	2.00	1.020	17.76
HBSF2	0.489	0.506	3.36	1.035	20.68
HBSF3	0.499	0.517	3.48	1.036	21.89
HBSF4	0.574	0.589	2.55	1.026	23.57
HBSF5	0.559	0.571	2.10	1.021	22.97

Note: Data are presented as mean values, n = 3. All formulations are part of the Hydrodynamically Balanced System (HBS) for Miglitol.

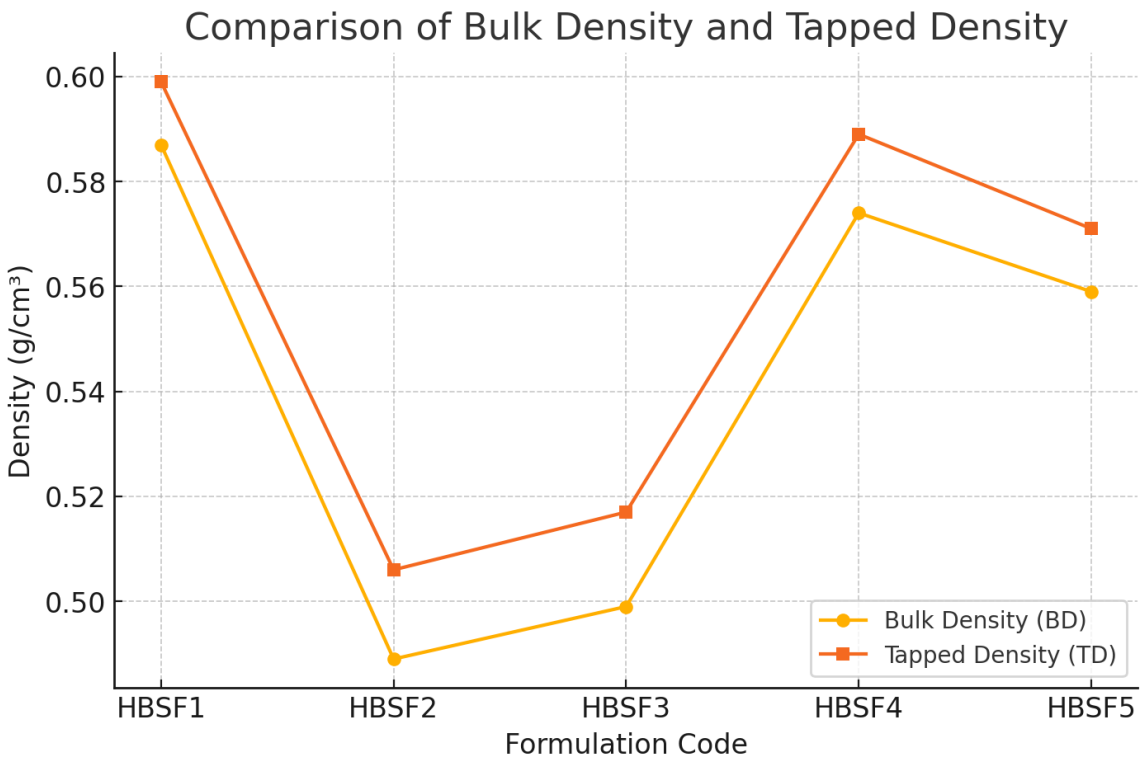

Figure 1. Bulk Density (BD) and Tapped Density (TD)

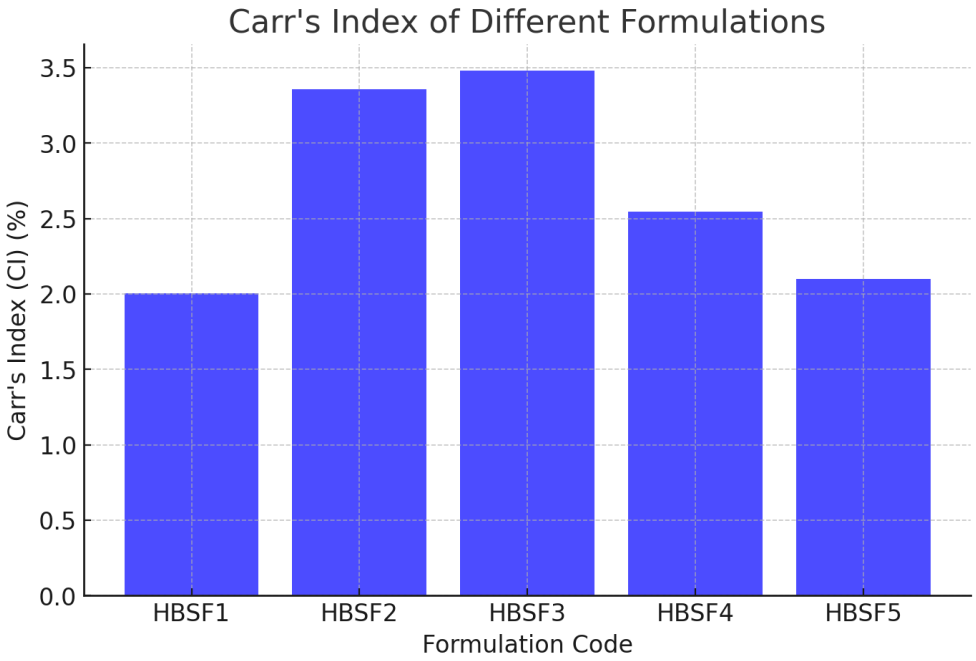

Figure 2. Carr's Index

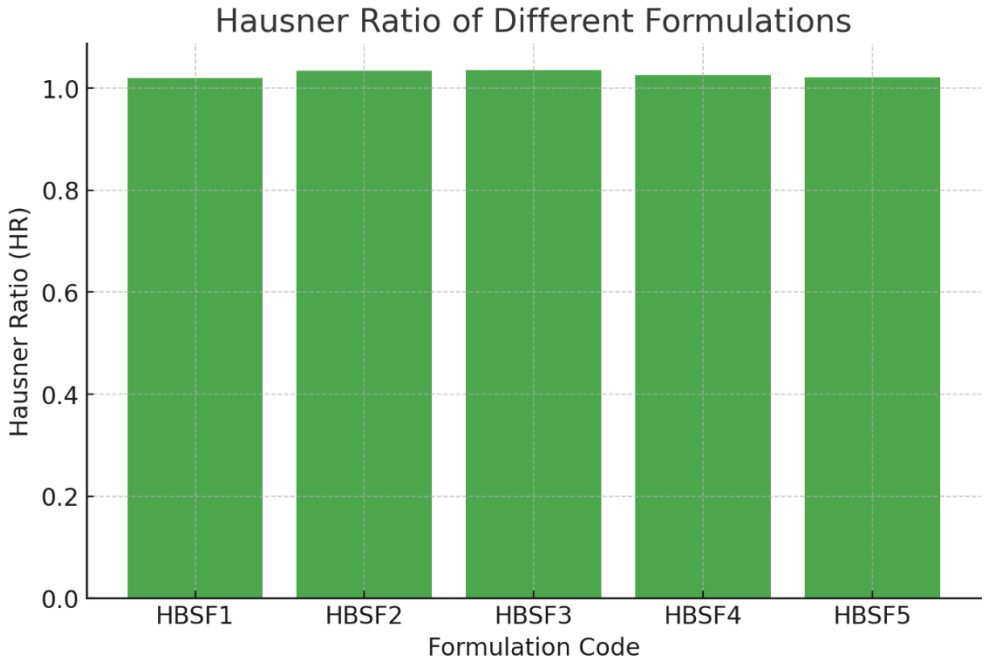

Figure 3. Hausner Ratio of Different Formulations

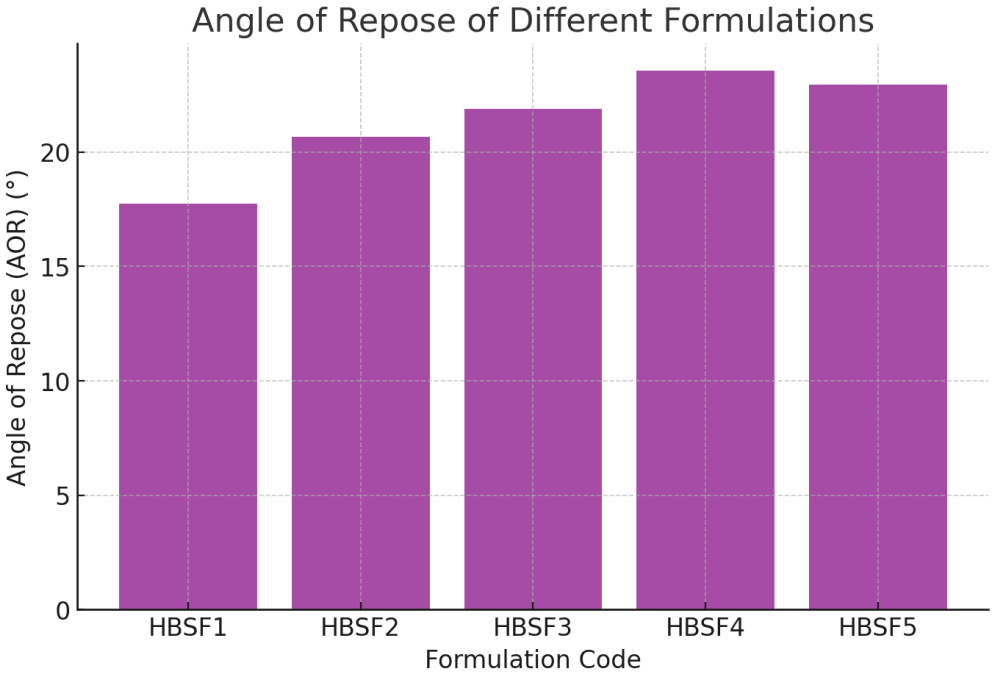

Figure 4. Angle Of Repose of Different Formulations

Weight Uniformity Test and Coefficient of Variation (%)

The weight uniformity test was conducted to ensure consistent formulation filling and minimal variation among the HBS capsules of Miglitol. The results demonstrated that the mean capsule weights across all formulations ranged from 785.78 mg to 794.84 mg, with standard deviations within an acceptable range, indicating a uniform distribution of the formulation components. The coefficient of variation (CV%) values, which measure the relative variability in weight, ranged from 1.28% to 1.92%, suggesting minimal weight fluctuations within the tested formulations.

Among all formulations, HBSF2 exhibited the lowest coefficient of variation (1.28%), indicating the highest uniformity in capsule weight. Conversely, HBSF5 showed the highest CV% (1.92%), although still within acceptable pharmacopeial limits, implying slightly higher weight variability. The observed variations may be attributed to differences in polymer compositions affecting blend flowability and capsule filling efficiency. Nevertheless, all formulations complied with pharmacopeial weight variation limits, confirming their suitability for further processing and evaluation. These findings underscore the reliability of the HBS formulation strategy, ensuring consistent dosage accuracy, which is crucial for maintaining the desired therapeutic efficacy of Miglitol capsules.

Table 3: Weight Uniformity Test and Coefficient of Variation (%) of Different HBS Capsules of Miglitol

Formulation Code	Weight Uniformity (Mean± SD) *	Coefficient of Variation (%)
HBSF1	785.78 ± 13.58	1.40
HBSF2	786.98 ± 13.76	1.28
HBSF3	793.42 ± 12.36	1.87
HBSF4	787.65 ± 13.67	1.81
HBSF5	794.84 ± 12.56	1.92

Drug Content Uniformity

To make sure that every formulation of Miglitol HBS capsules contained the desired drug concentration within allowable bounds, a drug content uniformity test was carried out. The findings showed uniform drug distribution, with the drug concentration ranging from 98.88% to 100.10% across all formulations. The standard deviation values remained low, confirming minimal variability within each batch. Among all formulations, HBSF1 exhibited the highest drug content (100.10% ± 1.99%), indicating precise formulation and mixing efficiency. The lowest drug content was observed in HBSF3 (98.88% ± 1.98%), though still within pharmacopeial acceptance limits of 90%–110% for drug content uniformity. The variations observed across the formulations could be attributed to minor differences in blend homogeneity, polymer interaction, or slight inconsistencies in mixing and capsule filling. Overall, all formulations complied with the regulatory requirements for content uniformity, ensuring consistent dosing and therapeutic efficacy. The results further validate the HBS formulation approach as a reliable delivery system for Miglitol, ensuring uniform drug distribution and stability across different formulations.

Table 4: Result of Drug Content Uniformity for All Formulations of Miglitol

Formulation Code	Drug Content Uniformity (%)
HBSF1	100.10 ± 1.99
HBSF2	99.45 ± 2.24
HBSF3	98.88 ± 1.98
HBSF4	99.76 ± 2.32
HBSF5	98.99 ± 2.19

Data are given as mean ± SD, n = 3.

Compatibility study by FTIR

The compatibility study between Miglitol and excipients in the HBS formulations was conducted using Fourier Transform Infrared (FTIR) spectroscopy to detect potential interactions that could affect drug stability and formulation integrity. FTIR spectra of pure Miglitol, individual excipients (MMCH, xanthan gum, lactose, talc, and magnesium stearate), and the physical mixture of the optimized formulation were recorded to analyze characteristic functional group peaks and any possible shifts, disappearance, or formation of new peaks. Pure miglitol's FTIR spectra showed clear, distinctive peaks that corresponded to its functional groups, such as C–OH stretching (~3330 cm^{-1}), C–H stretching (~2890 cm^{-1}), C=O stretching (~1635 cm^{-1}), and C–O bending (~1030 cm^{-1}). The distinctive peaks of miglitol did not significantly move or acquire new peaks when compared to the spectra of the physical mixture, suggesting that there were no strong interactions or signs of chemical breakdown. Additionally, the peaks corresponding to excipients such as MMCH and xanthan gum were also present in the physical mixture, confirming that the drug remained stable and compatible with the selected formulation components. The minor variations in peak intensities were attributed to physical interactions, such as hydrogen bonding, rather than chemical incompatibilities. Overall, the Miglitol and the excipients included in the formulation did not interact significantly, according to an FTIR compatibility investigation. This finding supports the stability and integrity of the hydrodynamically balanced system (HBS) for Miglitol, ensuring optimal performance, controlled drug release, and long-term formulation stability.

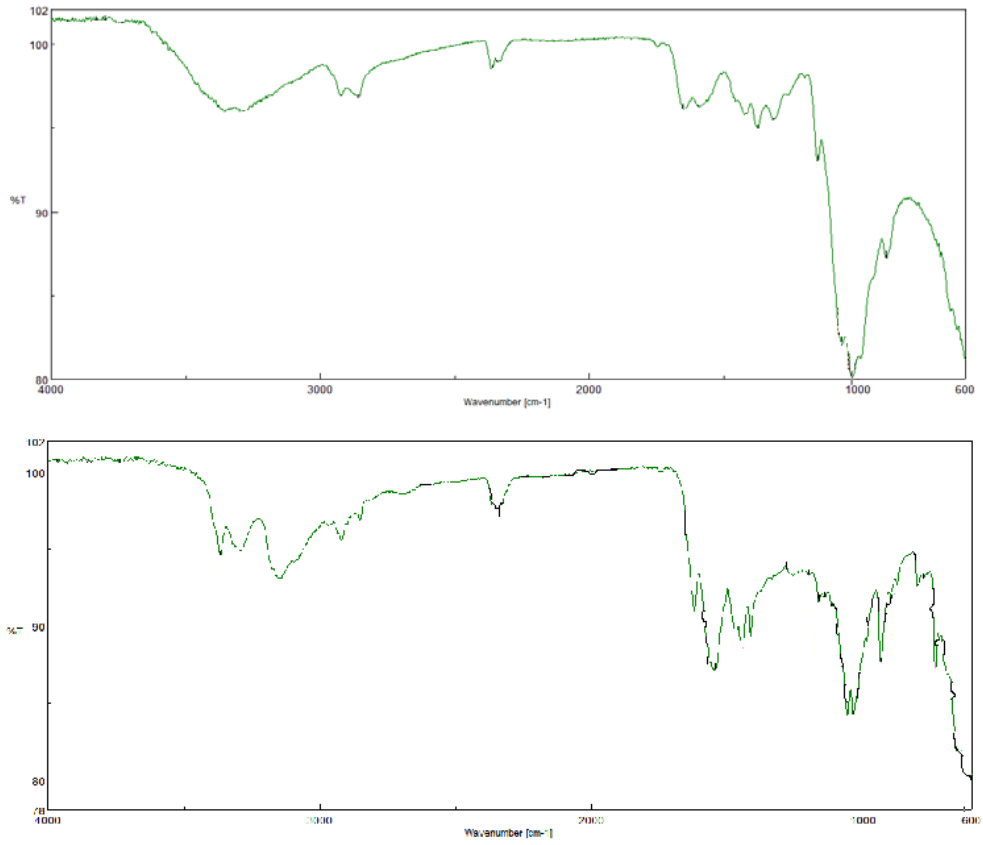

Figure 5. The FTIR spectra of HBSF3 (HBS capsule) and miglitol show a high degree of compatibility between the constituents and no discernible interaction.

In vitro drug release study

To assess the controlled release behaviour of the Miglitol HBS formulations (HBSF1–HBSF5) over a 12-hour period, an in vitro drug release study was carried out. The cumulative drug release data indicated a gradual and sustained release profile, with variations observed among the different formulations. At the 1-hour mark, drug release ranged from 13.91% (HBSF4) to 16.86% (HBSF1), indicating that all formulations exhibited an initial release phase suitable for gastro-retentive drug delivery. By the 4-hour time point, the formulations maintained a steady release rate, with drug release values between 33.79% (HBSF4) and 35.93% (HBSF2), demonstrating controlled diffusion. At 8 hours, the drug release was above 60% for all formulations, with HBSF1 showing the highest release (63.69%) and HBSF4 the lowest (60.57%). By the 12-hour mark, the cumulative drug release ranged from 89.34% (HBSF5) to 95.91% (HBSF1), confirming that all formulations successfully achieved a sustained release profile. Among all formulations, HBSF1 exhibited the highest cumulative drug release, suggesting that the polymer ratio in this formulation facilitated faster hydration and diffusion of the drug. In contrast, HBSF4 and HBSF5 showed slightly lower drug release, possibly due to a higher concentration of modified methylcellulose hydrogel (MMCH), which might have increased the gel strength, thereby slowing drug diffusion. Overall, the findings show that the hydrodynamically balanced system (HBS) for miglitol effectively maintained drug release for 12 hours, guaranteeing controlled drug administration and extended stomach retention. The differences in release profiles across formulations highlight the influence of polymer

composition on drug diffusion, with HBSF1 being the most rapidly releasing formulation and HBSF5 exhibiting the slowest but controlled release behavior. These results underline the potential of HBS formulations to improve patient compliance, lower dosage frequency, and sustain a longer therapeutic benefit in the treatment of diabetes.

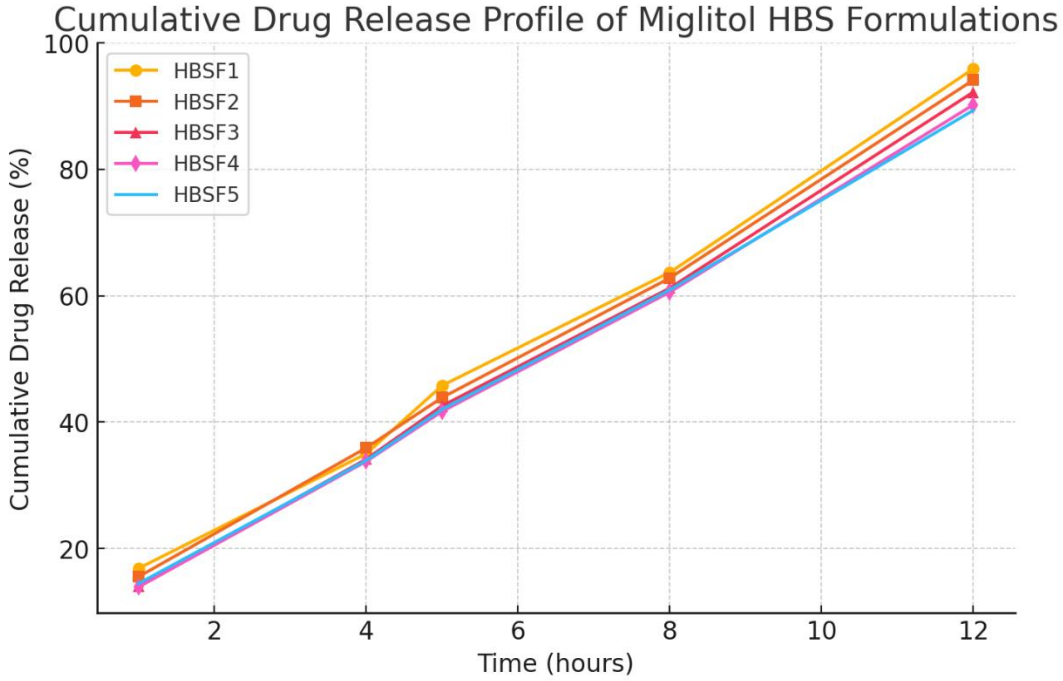

Figure 6. *In vitro* release of Miglitol from the HBS capsules.

In Vitro Release Kinetics Modelling

To identify the drug release mechanism and mathematical model that best captures the dissolution profile, the in vitro release kinetics data of the Miglitol HBS formulations (HBSF1–HBSF5) were examined. According to the findings, the Korsmeyer-Peppas model had the greatest R2 values (0.9871–0.9944) of any formulation. This suggests that anomalous (non-Fickian) transport, which combines diffusion and erosion mechanisms, was the main mechanism for drug release. The zero-order model (R^2 = 0.9690–0.9821) also showed a strong correlation, particularly for HBSF3 and HBSF4, indicating a consistent and controlled drug release profile. This implies that the rate of drug release from these formulations was almost constant, which is ideal for dosage forms with sustained release. The correlation values of the first-order model (R2 = 0.9112–0.9390) were marginally lower than those of the zero-order model, suggesting that drug release was not totally reliant on the residual drug concentration. The Higuchi model (R^2 = 0.8689–0.8815) showed the lowest fit among all models, suggesting that diffusion alone was not the dominant release mechanism. However, its relatively high values indicate that diffusion still plays a role in the release process. The n values from the Korsmeyer-Peppas model (0.8376–0.8670) suggest an anomalous transport mechanism, meaning that both polymer relaxation (erosion) and Fickian diffusion contribute to the drug release.

The formulations that fit the zero-order and Korsmeyer-Peppas models the best were HBSF3 and HBSF4, indicating the ideal ratio of controlled polymer swelling to prolonged release. HBSF5 exhibited the highest R^2 value for the first-order model (0.9390), indicating that it may have a slightly concentration-dependent release compared to the other

formulations. The Miglitol HBS formulations successfully accomplish prolonged drug release via a combination of diffusion-controlled and polymer matrix erosion processes, according to the release kinetics data overall. The findings confirm that the selected hydrophilic polymers in the formulation successfully modulate drug release, making the hydrodynamically balanced system (HBS) an effective approach for controlled drug delivery.

Table 5: Data on In Vitro Release Kinetics for Every Miglitol Formulation

Formulation Code	R^2 Value (Zero Order)	R^2 Value (First Order)	R^2 Value (Higuchi)	R^2 Value (Korsmeyer-Peppas)	n value (Korsmeyer-Peppas)
HBSF1	0.9690	0.9112	0.8755	0.9871	0.8380
HBSF2	0.9740	0.9226	0.8789	0.9918	0.8395
HBSF3	0.9821	0.9263	0.8689	0.9937	0.8670
HBSF4	0.9810	0.9336	0.8730	0.9944	0.8584
HBSF5	0.9759	0.9390	0.8815	0.9943	0.8376

***In vitro* floatation**

Miglitol HBS capsules' in vitro flotation testing showed that formulation HBSF3 exhibited no floating lag time and remained buoyant for more than 12 hours in an acidic environment (pH 1.2). This enhanced buoyancy was attributed to the formation of a colloidal hydrogel, driven by the rapid hydration and swelling of two hydrophilic polymers, namely Modified Methylcellulose Hydrogel (MMCH) and Xanthan Gum (XG). These polymers facilitated the development of a polymeric drug matrix gel, which increased the viscosity of the medium, ensuring prolonged floatation. The structural integrity of the gel matrix maintained the capsule's buoyancy, allowing for sustained drug release and extended gastric retention, essential characteristics for an effective hydrodynamically balanced system (HBS) (Nayak et al., 2013; Anurag Verma, Bansal, Ghosh, & Pandit, 2012; A. Verma et al., 2017).

The optimized formulation

Among the five formulations (HBSF1–HBSF5), HBSF3 was identified as the best formulation based on its superior in vitro flotation performance, micromeritic properties, weight uniformity, drug content uniformity, drug release profile, and kinetic modelling. In simulated stomach fluid (pH 1.2), the formulation demonstrated sustained buoyancy for more than 12 hours without any floating lag time. The presence of Modified Methylcellulose Hydrogel (MMMCH) and Xanthan Gum (XG) facilitated the formation of a colloidal hydrogel matrix, ensuring consistent floatation and controlled drug release. With a bulk density of 0.499 g/cm³ and a tapped density of 0.517 g/cm³, HBSF3's micromeritic characteristics were ideal, suggesting good powder flowability. Excellent compressibility was confirmed by the Carr's Index (3.48%) and Hausner Ratio (1.036), and the formulation's appropriate flow characteristics for uniform capsule filling were indicated by the Angle of Repose (21.89°). The weight uniformity test showed a mean weight of 793.42

mg with minimal variation (CV% = 1.87%), ensuring batch-to-batch consistency. Similarly, the drug content uniformity was within acceptable pharmacopeial limits (98.88% ± 1.98%), confirming uniform drug distribution. The in vitro drug release study demonstrated a sustained release profile, with 92.23% cumulative drug release at 12 hours, indicating its suitability for prolonged therapeutic action. Kinetic modelling further supported its optimized performance, with the highest R^2 value (0.9937) in the Korsmeyer-Peppas model, suggesting that drug release followed an anomalous (non-Fickian) diffusion mechanism involving both polymer swelling and matrix erosion. The zero-order kinetics (R^2 = 0.9821) confirmed that the drug release was independent of the drug concentration, ensuring a steady and controlled release profile. Furthermore, the n-value (0.8670) in the Korsmeyer-Peppas model supported a combination of diffusion and polymer relaxation-controlled release. In conclusion, HBSF3 was identified as the best formulation due to its prolonged gastric retention, excellent micromeritic properties, uniform drug distribution, sustained drug release, and well-fitted kinetic model. This formulation effectively provided controlled drug release and enhanced bioavailability of Miglitol, making it an ideal candidate for further development in hydrodynamically balanced system (HBS) drug delivery applications.

CONCLUSION

The creation and assessment of hydrodynamically balanced Miglitol capsules addressed the requirement for controlled-release formulations in the treatment of diabetes by showing the possibility of extended stomach retention and sustained drug release. The incorporation of Modified Methylcellulose Hydrogel (MMMCH) and Xanthan Gum (XG) facilitated the formation of a colloidal hydrogel matrix, ensuring buoyancy for over 12 hours and enhancing drug retention in the stomach. Among the five formulations, HBSF3 was identified as the best, as it exhibited excellent micromeritic properties, ensuring smooth processing and uniform weight distribution. The in vitro drug release study confirmed that HBSF3 followed a sustained-release pattern, with 92.23% drug release at 12 hours, effectively prolonging the drug's therapeutic effect. Kinetic modelling revealed that HBSF3 adhered to the Korsmeyer-Peppas model (R2 = 0.9937, n = 0.8670), suggesting an unusual diffusion-controlled mechanism in which polymer relaxation and diffusion both influenced drug release. The strong correlation with the zero-order model (R^2 = 0.9821) further confirmed a steady and controlled release, independent of drug concentration. The findings suggest that HBS formulations are an effective strategy for improving the bioavailability of Miglitol, ensuring sustained drug action and reduced dosing frequency, which can enhance patient compliance and therapeutic outcomes. The optimized formulation (HBSF3) holds significant potential for clinical applications in diabetes treatment, supporting further research and development in gastro-retentive drug delivery systems.

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