Study of Pharmacokinetic Assessment of Bilastine-Loaded Gastroretentive Floating Tablets

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Abstract: This study investigates the pharmacokinetic profile of bilastine-loaded gastroretentive floating tablets. Bilastine, an antihistamine, is utilized for its potential in managing allergic conditions. The formulation involves the development of gastroretentive tablets to enhance drug bioavailability and optimize therapeutic efficacy. The research encompasses the formulation of bilastine-loaded gastroretentive floating tablets and subsequent in vitro characterization. The pharmacokinetic evaluation is conducted through a well-designed study involving an appropriate animal model. Parameters such as maximum plasma concentration (Cmax), time to reach Cmax (Tmax), and area under the concentration-time curve (AUC) are analysed to assess the drug's absorption, distribution, and elimination. The results reveal crucial insights into the pharmacokinetic behaviour of bilastine when delivered through gastroretentive floating tablets. The discussion interprets these findings, drawing comparisons with existing literature and formulations. The study's implications for advancing drug delivery strategies and optimizing bilastine's therapeutic outcomes are explored.

Keywords: bilastine, gastroretentive, pharmacokinetic profile.

INTRODUCTION

Bilastine's efficacy is contingent upon its bioavailability, absorption, and distribution within the body. Gastroretentive drug delivery systems, designed to prolong the residence time of drugs in the stomach, offer a promising avenue for optimizing these pharmacokinetic parameters. The rationale behind this approach is to ensure a sustained release of bilastine, potentially leading to improved patient compliance and better therapeutic outcomes. Gastroretentive floating tablets, specifically tailored to achieve buoyancy in the stomach, aim to address challenges associated with conventional drug delivery systems. By prolonging gastric residence time, these tablets can enhance drug absorption and bioavailability. The study is grounded in the need to explore and understand how the unique characteristics of gastroretentive floating tablets influence the pharmacokinetics of bilastine. Moreover, the investigation aligns with the broader field of pharmaceutical research seeking innovative solutions for drug delivery. It responds to the demand for optimized formulations that can address challenges related to drug solubility, stability, and absorption. The background underscores the potential impact of this research on advancing drug delivery strategies and improving the overall effectiveness of bilastine as an antihistamine. Overall, the study's background sets the stage for exploring novel pharmaceutical formulations to elevate the therapeutic benefits of bilastine in the treatment of allergic conditions.

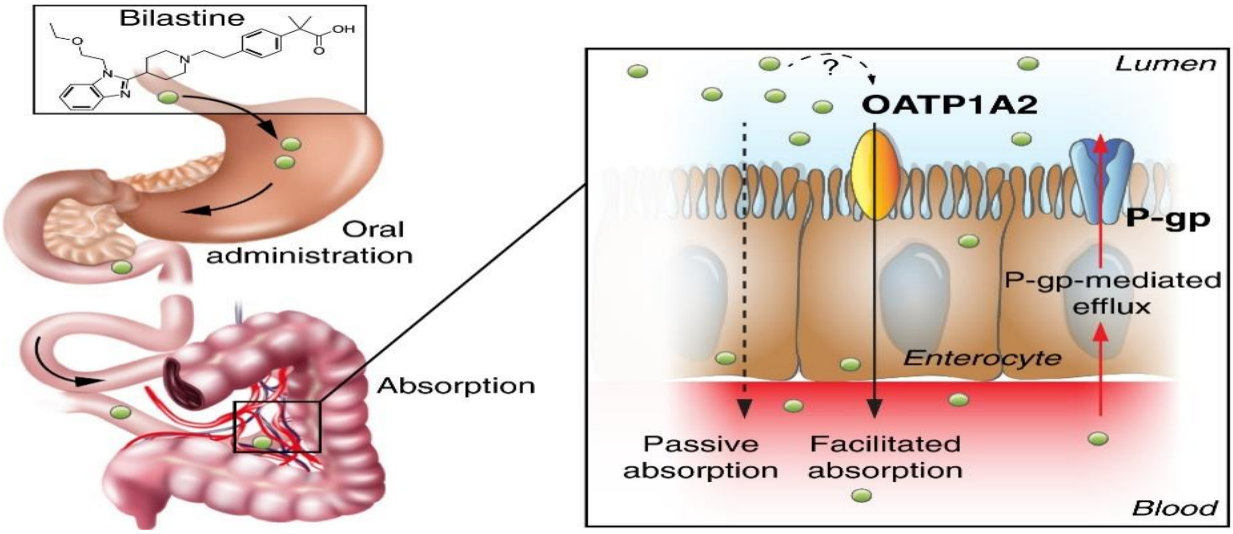
The choice of bilastine and gastroretentive floating tablets for this study is underpinned by multiple compelling reasons. Bilastine, a second-generation antihistamine, is widely recognized for its efficacy in managing allergic conditions, such as allergic rhinitis and chronic urticaria. Its non-sedative nature and minimal interactions with other medications make it a preferred choice for many patients. However, the optimization of its pharmacokinetic properties remains an area of interest, aiming to enhance its therapeutic effectiveness. Gastroretentive floating tablets have emerged as a promising drug delivery system, particularly for drugs with absorption challenges or those requiring sustained release. In the case of bilastine, which is administered orally, the bioavailability is influenced by factors like solubility and gastric residence time. Gastroretentive formulations are designed to prolong the time a drug spends in the stomach, potentially improving its absorption by overcoming solubility and permeability issues. This aligns with the goal of optimizing bilastine's bioavailability for enhanced therapeutic outcomes. Conventional drug delivery systems may

encounter limitations in sustaining drug release at levels necessary for prolonged therapeutic effects. Gastroretentive floating tablets offer a solution to these challenges by providing a controlled release mechanism. The choice of gastroretentive tablets for bilastine aims to address these limitations, ensuring a sustained and controlled release of the antihistamine over an extended period. Beyond the pharmacological considerations, patient compliance is a crucial factor in the success of any treatment.

Gastroretentive formulations have the potential to reduce the frequency of dosing, making it more convenient for patients. This aspect is particularly relevant for chronic conditions where long-term adherence to medication is essential. By choosing bilastine and gastroretentive floating tablets, the study recognizes the importance of tailoring drug delivery systems to enhance patient compliance and overall treatment efficacy.In the broader context of pharmaceutical research, the study aligns with the innovative trend of exploring novel drug delivery strategies. Gastroretentive formulations represent a cutting-edge approach that holds promise for improving the delivery of various drugs. The choice of bilastine as the active pharmaceutical ingredient in conjunction with gastroretentive floating tablets positions the study at the intersection of therapeutic optimization and advancements in drug delivery science. Overall, this research is poised to contribute valuable insights to both the specific field of antihistamine therapy and the broader landscape of pharmaceutical formulation development.

OVERVIEW OF BILASTINE AND ITS PHARMACOKINETICS:

Bilastine is a second-generation, non-sedating antihistamine that has gained prominence for its efficacy in managing allergic conditions, such as allergic rhinitis and chronic urticaria. As a member of the piperidine class of antihistamines, bilastine exerts its therapeutic effects by selectively antagonizing the H1 histamine receptors, thereby mitigating the symptoms associated with allergic responses. Pharmacokinetically, bilastine demonstrates favourable attributes contributing to its clinical utility. Notably, bilastine exhibits high oral bioavailability, with studies indicating that it reaches peak plasma concentrations within 1 to 1.5 hours after oral administration. This rapid onset of action is particularly advantageous for addressing acute allergic symptoms. Additionally, bilastine is characterized by a relatively long elimination half-life, ranging from approximately 10 to 14 hours, which supports the potential for once-daily dosing.



Crucial to its pharmacokinetic profile is the fact that bilastine undergoes minimal metabolism in the liver, primarily via carboxylesterase enzymes. Unlike some other antihistamines, bilastine is not extensively metabolized by the cytochrome P450 system, reducing the likelihood of significant drug interactions. The largely unchanged excretion of bilastine through the renal route further contributes to its predictability and safety profile. Bilastine's pharmacokinetics are also marked by a low binding affinity to plasma proteins, enhancing its free, active fraction. This characteristic may contribute to its rapid distribution to target tissues,

supporting its efficacy in managing allergic conditions. Moreover, bilastine demonstrates a low potential for central nervous system penetration due to its limited ability to cross the blood-brain barrier. This attribute contributes to the non-sedative nature of bilastine, differentiating it from earlier-generation antihistamines that often cause drowsiness. In summary, the pharmacokinetics of bilastine reflect a combination of rapid onset, sustained duration of action, minimal hepatic metabolism, and favourable distribution characteristics. These features collectively contribute to bilastine's effectiveness in treating allergic conditions and underscore its suitability for use in diverse patient populations.

GASTRORETENTIVE DRUG DELIVERY SYSTEMS AND THEIR ADVANTAGES

Gastroretentive drug delivery systems have emerged as a sophisticated approach to pharmaceutical formulation, aiming to extend the residence time of drugs in the stomach and optimize their release characteristics. One of the key advantages of these systems lies in their ability to enhance the bioavailability of drugs. By prolonging the exposure of the drug to the absorbing surfaces in the stomach, gastroretentive formulations address challenges related to solubility and permeability, ensuring a more efficient absorption process.The controlled and sustained release of drugs is a hallmark feature of gastroretentive systems, offering a distinct advantage in terms of therapeutic efficacy. This prolonged release profile contributes to a consistent and prolonged therapeutic effect, potentially reducing the frequency of dosing. Consequently, patients may experience improved compliance with their medication regimens, particularly in the case of chronic conditions where adherence to treatment is paramount. Gastroretentive formulations also play a pivotal role in enhancing drug stability. By minimizing exposure to the fluctuating and often harsh conditions of the gastrointestinal environment, these systems provide a protective microenvironment for drug molecules. This is particularly beneficial for drugs susceptible to degradation in acidic or enzymatic conditions, ensuring their integrity and effectiveness.

Furthermore, the ability of gastroretentive systems to localize drug delivery within specific regions of the gastrointestinal tract is a notable advantage. This targeted delivery is particularly relevant for drugs with site-specific actions or those requiring absorption in specific anatomical locations, allowing for optimized therapeutic outcomes. Reducing variability in plasma drug levels is another significant advantage offered by gastroretentive drug delivery systems. The controlled release they provide minimizes fluctuations in drug concentrations, contributing to a more predictable and stable pharmacokinetic profile. This can be crucial for medications where maintaining consistent plasma levels is essential for optimal therapeutic effects and to avoid potential side effects associated with peak concentrations. In addition to their pharmacokinetic benefits, gastroretentive systems offer applicability across various therapeutic classes. Their versatility in design allows for customization to the specific requirements of different drugs, making them a versatile platform for the development of advanced pharmaceutical formulations. In summary, the advantages of gastroretentive drug delivery systems encompass improved bioavailability, controlled release, enhanced stability, targeted delivery, reduced variability, improved patient compliance, and applicability to diverse therapeutic classes, collectively positioning them as a valuable tool in modern drug delivery research.

BILASTINE FORMULATIONS AND DELIVERY METHODS

Bilastine formulations encompass a variety of dosage forms designed to optimize the delivery and therapeutic effects of this second-generation antihistamine. These formulations take into account factors such as bioavailability, patient compliance, and the specific characteristics of bilastine. Conventional oral tablets are a standard and widely used formulation for bilastine. These tablets are administered orally, typically with water, and release bilastine in the gastrointestinal tract for absorption into the bloodstream. ODTs are designed to rapidly disintegrate in the mouth without the need for water. This formulation is advantageous for patients who may have difficulty swallowing traditional tablets, providing a convenient and easily administrable option. Liquid formulations, such as oral solutions, offer an alternative for patients who prefer or require liquid medication. Oral solutions can be particularly suitable for pediatric or geriatric populations with

specific dosing needs. Effervescent tablets contain a combination of a soluble acid and a carbonate or bicarbonate salt, producing effervescence when in contact with water. This formulation can enhance the solubility of bilastine and provide a fizzy and palatable dosage form. Film-coated tablets are designed with a thin layer to mask the taste or odor of the drug and improve its stability. This formulation can enhance patient acceptance and compliance. Oral suspensions involve dispersing bilastine particles in a liquid vehicle. This formulation is useful when a solid dosage form is not preferred, and it offers flexibility in adjusting doses for different patient populations. Extended-release or sustained-release formulations are designed to release bilastine gradually over an extended period. This can result in a prolonged therapeutic effect and may reduce the frequency of dosing. Bilastine can be formulated in combination with other active ingredients, such as decongestants or corticosteroids, to provide a comprehensive approach in treating allergic conditions. The choice of formulation depends on various factors, including the desired therapeutic outcome, patient preferences, and the pharmacokinetic profile of bilastine. Each formulation aims to balance effectiveness, convenience, and patient acceptability to optimize the overall treatment experience for individuals with allergic conditions.

Delivery methods for bilastine formulations encompass various routes of administration and innovative approaches to optimize drug delivery. Oral delivery is the most common and conventional method for bilastine formulations. This involves swallowing solid dosage forms, such as tablets or capsules, or taking liquid formulations by mouth. It is a convenient and widely accepted route of administration. Sublingual administration involves placing bilastine formulations, such as orally disintegrating tablets, under the tongue. This route allows for rapid absorption through the sublingual mucosa, bypassing the gastrointestinal tract and potentially leading to faster onset of action. Intravenous administration is an option for delivering bilastine directly into the bloodstream. While this route may be reserved for specific clinical scenarios, it provides rapid and complete drug absorption. Intramuscular injection of bilastine may be considered in certain situations where other routes are not feasible. However, this method is less common for antihistamines and is generally reserved for specific medical requirements. Topical formulations, such as creams or ointments containing bilastine, can be applied directly to the skin. This approach is suitable for localized allergic reactions or skin conditions and minimizes systemic exposure. Nasal sprays or nasal drops containing bilastine can be used for localized treatment of allergic rhinitis. This method allows for direct delivery to the nasal mucosa, targeting symptoms in the nasal passages. Inhalation methods, such as aerosolized formulations or dry powder inhalers, may be explored for specific respiratory conditions. This approach targets drug delivery to the lungs, making it suitable for addressing respiratory symptoms associated with allergies.

Transdermal patches containing bilastine enable drug absorption through the skin. This method provides sustained release and can be beneficial for maintaining constant therapeutic levels over an extended period. Buccal administration involves placing bilastine formulations between the cheek and gum. This method allows for absorption through the buccal mucosa, offering an alternative for patients who have difficulty swallowing or prefer non-oral routes.The choice of delivery method depends on the specific therapeutic goals, the nature of the allergic condition, and patient factors. Each method offers distinct advantages and considerations, contributing to the overall versatility of bilastine formulations in meeting diverse clinical needs.

MATERIALS AND METHODS

Formulation of gastroretentive floating tablets loaded with bilastine:

The formulation of gastroretentive floating tablets loaded with bilastine involves a meticulous process to ensure optimal drug delivery characteristics. The active pharmaceutical ingredient, bilastine, is carefully selected and characterized for its purity and stability. Choose a polymer that has excellent floating properties and provides sustained drug release. Commonly used polymers include hydroxypropyl methylcellulose (HPMC), sodium alginate, and polyethylene oxide. Incorporate a gas-generating agent, such as sodium bicarbonate or citric acid, to create gas bubbles within the tablet, promoting buoyancy. Add release modifiers like hydrophilic polymers or surfactants to control the drug release profile and enhance dissolution. Use a binder, such as

polyvinylpyrrolidone (PVP) or hydroxypropyl cellulose, to provide cohesiveness to the tablet. Include fillers like lactose or microcrystalline cellulose to achieve the desired tablet volume and aid in the compression process. Optionally, add disintegrants like crospovidone to facilitate tablet disintegration, especially if rapid drug release is desired. Incorporate lubricants like magnesium stearate to prevent tablet sticking during the manufacturing process. Consider coating the tablets with a gastro-resistant polymer to protect them from premature disintegration in the acidic environment of the stomach.

Formulation Steps:

Thoroughly mix bilastine with polymers, gas-generating agents, release modifiers, binders, fillers, and other excipients to form a homogenous blend. Granulate the blend using a suitable solvent or binder solution to form granules with optimal flow and compression properties. Compress the granules or direct blend into tablets using a tablet press. Ensure uniform tablet weight and hardness. Apply a gastro-resistant coating to protect the tablets from premature disintegration. This coating may contain polymers like Eudragit. Perform quality control tests such as weight variation, hardness, friability, and drug content to ensure the tablets meet specifications. Conduct in vitro studies to assess the floating properties of the tablets. Place them in a simulated gastric fluid and observe their buoyancy over time. Conduct dissolution studies to evaluate the drug release profile of the tablets under simulated gastric conditions. Monitor the release of bilastine over time. Adjust the formulation if needed based on the results of in vitro studies, aiming for optimal floating behaviour and sustained drug release. Once the formulation is optimized, scale up the production process for commercial manufacturing. The formulation of gastroretentive floating tablets loaded with bilastine requires a systematic and scientific approach to achieve the desired drug delivery characteristics, including prolonged gastric residence time and sustained release of the active ingredient.

CHARACTERIZATION TECHNIQUES FOR ASSESSING TABLET PROPERTIES

Characterization techniques are essential for evaluating the physical, chemical, and mechanical properties of gastroretentive floating tablets loaded with bilastine. These techniques ensure that the tablets meet the required quality standards and possess the desired characteristics for effective drug delivery. Here are common characterization techniques for assessing tablet properties:

1. Weight Variation:

Measure the weight of individual tablets to ensure uniformity. Weight variation testing helps identify any inconsistencies in the tablet manufacturing process.

2. Thickness and Diameter Measurement:

Use a digital calliper to measure the thickness and diameter of tablets. These dimensions are critical for ensuring consistent tablet size and shape.

3. Hardness Testing:

Assess tablet hardness using a hardness tester. This test helps determine the tablets' resistance to breakage and ensures they can withstand handling and transportation without crumbling.

4. Friability Testing:

Conduct friability tests to assess the tablets' ability to withstand mechanical stress. A friability tester evaluates the percentage of weight loss due to abrasion during the testing process.

5. Disintegration Test:

Employ disintegration testing to evaluate the time it takes for the tablets to disintegrate into small particles. This is particularly important for gastroretentive tablets, as their ability to float relies on the integrity of the tablet structure.

6. Floating Behaviour Assessment:

Conduct in vitro studies to assess the floating behaviour of the tablets. Place the tablets in a simulated gastric fluid and observe their buoyancy over a specified time period.

7. Drug Content Uniformity:

Analyse the drug content in individual tablets to ensure uniform distribution. High-performance liquid chromatography (HPLC) or other suitable analytical methods can be employed for drug content determination.

8. In Vitro Dissolution Studies:

Perform dissolution studies to evaluate the release profile of bilastine from the tablets. This helps assess the tablets' ability to provide sustained drug release in a controlled manner.

9. Surface Morphology Examination (Scanning Electron Microscopy - SEM):

Utilize SEM to examine the surface morphology of the tablets. This technique provides high-resolution

images, allowing for the visualization of surface characteristics and potential structural irregularities.

10. X-ray Imaging:

X-ray imaging techniques, such as X-ray computed tomography (CT), can be employed to visualize the internal structure of tablets. This is particularly useful for assessing the distribution of components within the tablet matrix.

11. Differential Scanning Calorimetry (DSC):

Use DSC to analyse the thermal properties of the tablet components. This technique helps identify potential interactions between bilastine and excipients and provides insights into the tablet's stability.

12. Fourier Transform Infrared Spectroscopy (FTIR):

Employ FTIR spectroscopy to analyse the chemical composition of tablets. This technique can identify any chemical interactions or changes that may occur during the formulation process.

These characterization techniques collectively provide a comprehensive understanding of the physical, mechanical, and chemical properties of gastroretentive floating tablets loaded with bilastine. Their application ensures the quality, stability, and efficacy of the pharmaceutical formulation.

IN VITRO DRUG RELEASE STUDIES TO EVALUATE FORMULATION PERFORMANCE

In vitro drug release studies are crucial for assessing the performance of pharmaceutical formulations, including gastroretentive floating tablets loaded with bilastine. These studies provide valuable information about the release kinetics, dissolution profile, and overall efficacy of the formulated drug. Utilize a dissolution apparatus, such as USP apparatus I or II, depending on the formulation characteristics. The apparatus should maintain sink conditions to ensure accurate drug release measurements. Prepare a dissolution medium that simulates the gastric environment. Typically, simulated gastric fluid (SGF) with appropriate pH (usually pH 1.2) is used to mimic the stomach conditions. Maintain the dissolution medium at a constant and physiologically relevant temperature, often 37 ± 0.5°C, to simulate body conditions. Use suitable containers to collect samples at predefined time intervals during the dissolution process. Employ appropriate analytical instruments, such as high-performance liquid chromatography (HPLC), to quantify the concentration of bilastine in the collected samples.

Procedure:

1. Pre-equilibration:

Pre-equilibrate the dissolution apparatus with the dissolution medium at the desired temperature.

2. Sample Collection Containers:

Place the gastroretentive floating tablets in the dissolution vessels or baskets of the apparatus. Ensure that the tablets remain buoyant throughout the study.

3. Dissolution Medium Addition:

Add the dissolution medium to the apparatus, maintaining the specified conditions.

4. Sampling Time Points:

Collect samples at predetermined time points, ensuring an adequate duration to capture the entire drug release profile. Common time points include 0.5, 1, 2, 4, 6, and 24 hours.

5. Sample Analysis:

Analyse the collected samples using suitable analytical methods (e.g., HPLC) to quantify the concentration of bilastine. This information is crucial for constructing the drug release profile.

6. Data Presentation:

Plot the cumulative percentage of drug release against time to visualize the drug release kinetics. Common representations include cumulative release curves and dissolution efficiency profiles.

7. Calculation of Release Parameters:

Calculate relevant parameters, such as the percentage of drug released at specific time points (e.g., 1 hour, 2 hours) and the dissolution efficiency at various intervals. These parameters offer insights into the formulation's performance.

8. Comparison with Reference or Control:

Compare the drug release profile of the formulated tablets with a reference or control, such as a commercially available product or a standard formulation. This aids in assessing the relative performance and efficacy of the developed formulation.

METHODS FOR SAMPLE COLLECTION, ANALYSIS, AND DETERMINATION OF PHARMACOKINETIC PARAMETERS

Sample Collection:

- ✓ Blood Sampling:

Collect blood samples at specified time points based on the drug's pharmacokinetic profile. Use venipuncture or indwelling catheters for blood collection. Use appropriate anticoagulants (e.g., EDTA, heparin) to prevent clotting.

- ✓ Plasma or Serum Separation:

Separate plasma or serum from whole blood using a centrifuge. Store plasma or serum samples at low temperatures to prevent degradation until analysis.

- ✓ Urine Collection:

Collect urine samples at predetermined intervals for drug elimination assessment. Use suitable containers with preservatives if necessary.

- ✓ Saliva Sampling:

Use specialized devices or passive drool methods for saliva collection. Collect samples at specified time points.

- ✓ Cerebrospinal Fluid (CSF) Collection:

Perform lumbar puncture for CSF collection in specific cases. Ensure aseptic conditions during the procedure.

- ✓ Tissue Biopsy (if applicable):

Collect tissue samples postmortem or during a biopsy procedure. Preserve tissues in appropriate solutions or freezing conditions.

Sample Analysis:

- ➢ High-Performance Liquid Chromatography (HPLC):

Separation and quantification of drug molecules based on their interaction with a stationary phase. Coupled with UV, fluorescence, or mass spectrometry detectors for accurate quantification.

- ➢ Gas Chromatography (GC):

Separation of volatile compounds in a sample based on their vaporization and partitioning. Suitable for volatile or thermally stable drugs.

- ➢ Liquid Chromatography-Mass Spectrometry (LC-MS):

Combines liquid chromatography with mass spectrometry for high sensitivity and specificity. Widely used for quantifying drugs in biological samples.

- ➢ Enzyme-Linked Immunosorbent Assay (ELISA):

Uses antibodies for detection and quantification of specific molecules, including drugs. Suited for drugs with specific antibodies available.

- ➢ Radioimmunoassay (RIA):

Uses radioactive isotopes to measure binding of drugs to specific antibodies. Historically used, but less common due to safety concerns.

Determination of Pharmacokinetic Parameters:

- ✓ Maximum Concentration (C_{max}):

Highest concentration of the drug in plasma after administration. Directly observed from concentration-time profiles.

- ✓ Time to Maximum Concentration (T_{max}):

Time taken to reach C_{max}.Directly observed from concentration-time profiles.

- ✓ Area Under the Curve (AUC):

Represents the total exposure to the drug over time. Obtained by integrating the concentration-time curve.

- ✓ Elimination Half-Life (t_{1/2}):

Time taken for drug concentration to reduce by half. Derived from the terminal phase of the concentration-time curve.

- ✓ Clearance (Cl):

Volume of plasma from which the drug is completely removed per unit time.Cl = Dose / AUC.

- ✓ Volume of Distribution (V_d):

Hypothetical volume into which the total drug dose would need to be uniformly distributed.V_d = Dose / (C₀ × f), where C₀ is initial plasma concentration and f is bioavailability.

- ✓ Bioavailability (F):

Fraction of administered dose reaching systemic circulation.

F = (AUC_{oral} / AUC_{iv}) × 100%.

- ✓ Steady-State Concentrations:

Concentrations reached when rate of drug input equals rate of elimination.Derived from multiple-dose pharmacokinetic studies.These methods collectively provide a comprehensive understanding of the pharmacokinetic behaviour of a drug, guiding clinical dosing and contributing to the assessment of its safety and efficacy.

RESULTS

GASTRORETENTIVE FLOATING MATRIX TABLETS OF BILASTINE

Bilastine gastric retentive matrix tablets were created to extend the drug's gastric retention duration, allowing for a controlled release of the medication

over a 16-hour period. Pullulan gum, a natural polymer, and gel-forming polymers were used to create the floating matrix tablets in order to regulate the rate of medication delivery. It is well known that HPMC K15M and Pullulan gum help to improve the buoyancy and medication release properties. In vitro and in vivo buoyant characteristics were seen when sodium bicarbonate and citric acid were combined to enhance the gas producing mixture. Talc and magnesium stearate were used because of their ability to glide and lubricate.

Standard Calibration curve of Bilastine:

Table 1: Concentration and absorbance obtained for calibration curve of Bilastine in 0.1 N hydrochloric acid buffer (pH 1.2)

S.No.	Concentration(µg/ml)	Absorbance*(at230nm)
1	5	0.232
2	10	0.456
3	15	0.601
4	20	0.819
5	25	0.926
Correlation Coefficient=0.992 Absorbancey =0.0376x +0.0436		

The UV spectrophotometric technique at max 245.0 nm in 0.1N hydrochloric acid was found to have high repeatability and was employed in the investigation. At concentrations between 5 and 25 g/ml, it was discovered that the correlation coefficient for the standard curve was closer to 1. y = 0.0376x +0.0436 was the regression equation that was produced.

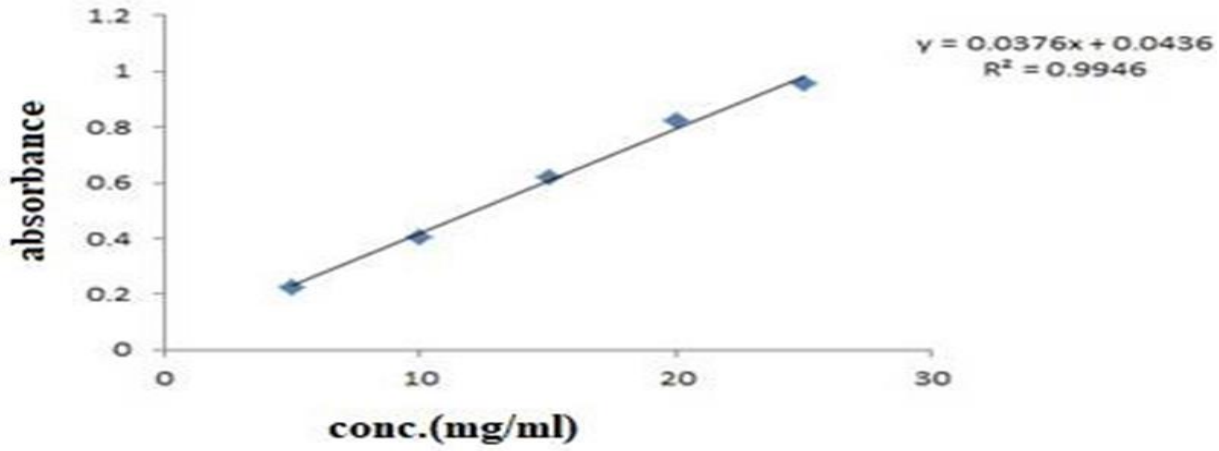


Figure 1: standard graph of Bilastine in 0.1 N HCl

Table 2: Concentration and absorbance obtained for calibration curve of Bilastine in 6.8 phosphate buffer (245nm)

S.No.	Concentration(µg/ml)	Absorbance*(at245 nm)
1	1	0.132
2	2	0.279
3	3	0.487
4	4	0.654
5	5	0.816
6	6	0.959

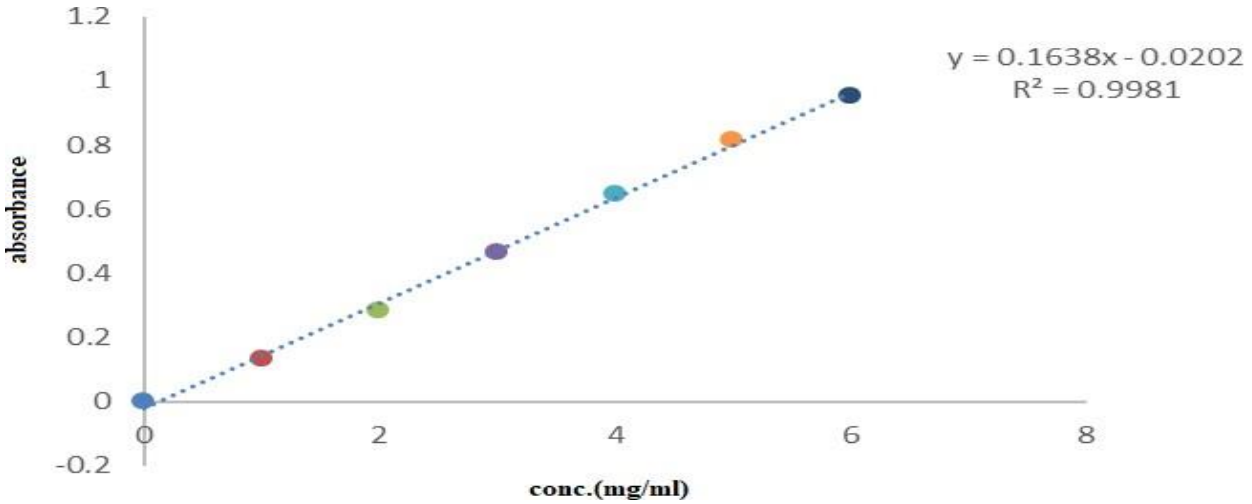
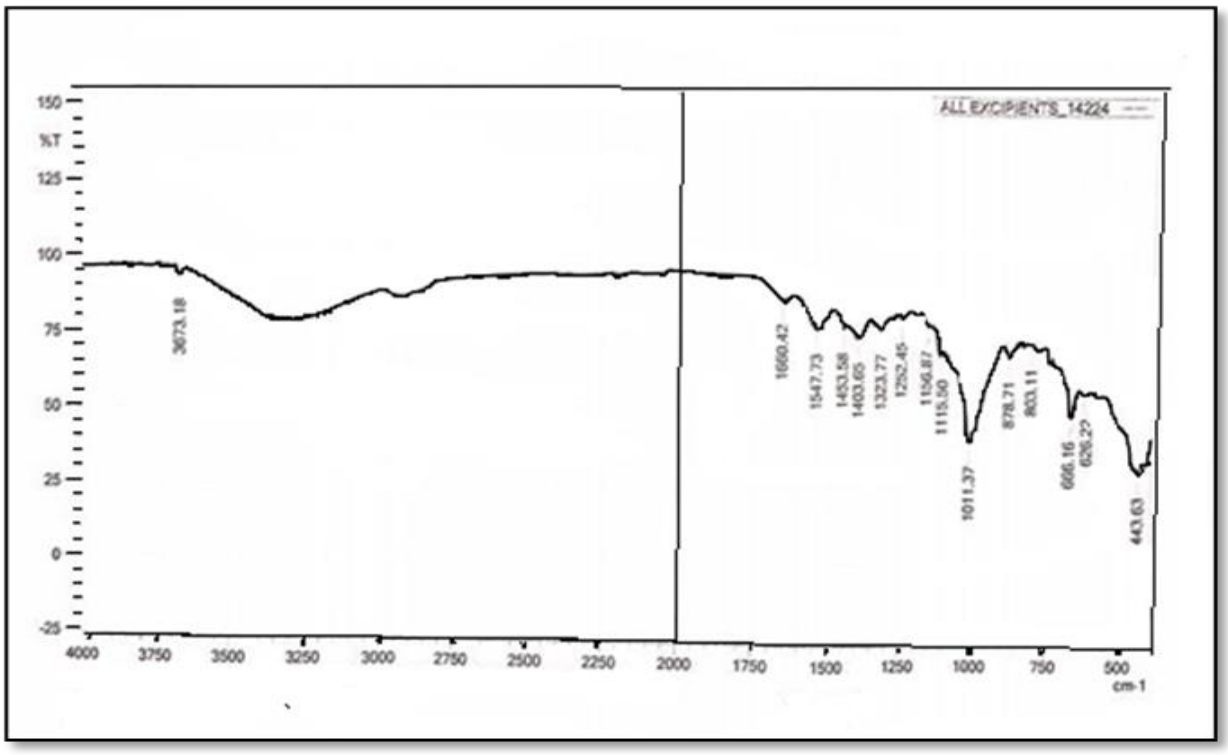


Figure 2: standard graph of Bilastine in 6.8 pH phosphate buffer

The analyses of compatibility carried out using differential scanning calorimetric and Fourier transform infrared spectroscopy. There are no pharmacological excipient interactions in the optimised formulation, according to IR spectroscopic investigations. Since all the primary peaks of the pure drug were still present in the FT-IR spectra of the optimised formulations, it was concluded that there had not been any physical or chemical interaction between Bilastine and other excipients during the formulation process.



While HPMCK15M's DSC thermogram revealed a wide endothermic peak at 62.8°C, Bilastine's thermogram displayed a sharp an endothermic peak at 181.5°C. DSC thermograms of formulations containing bilastine in combination with HPMC K15M and pullulan gum revealed endothermic peaks for bilastine at temperatures comparable to the peak for bilastine alone. This demonstrated that there were no interactions between medication excipients in the formulations. Thus, it is clear that there is no chemical interaction between the medicine and the excipients.

Studies suggested that polymers and drugs might work together.

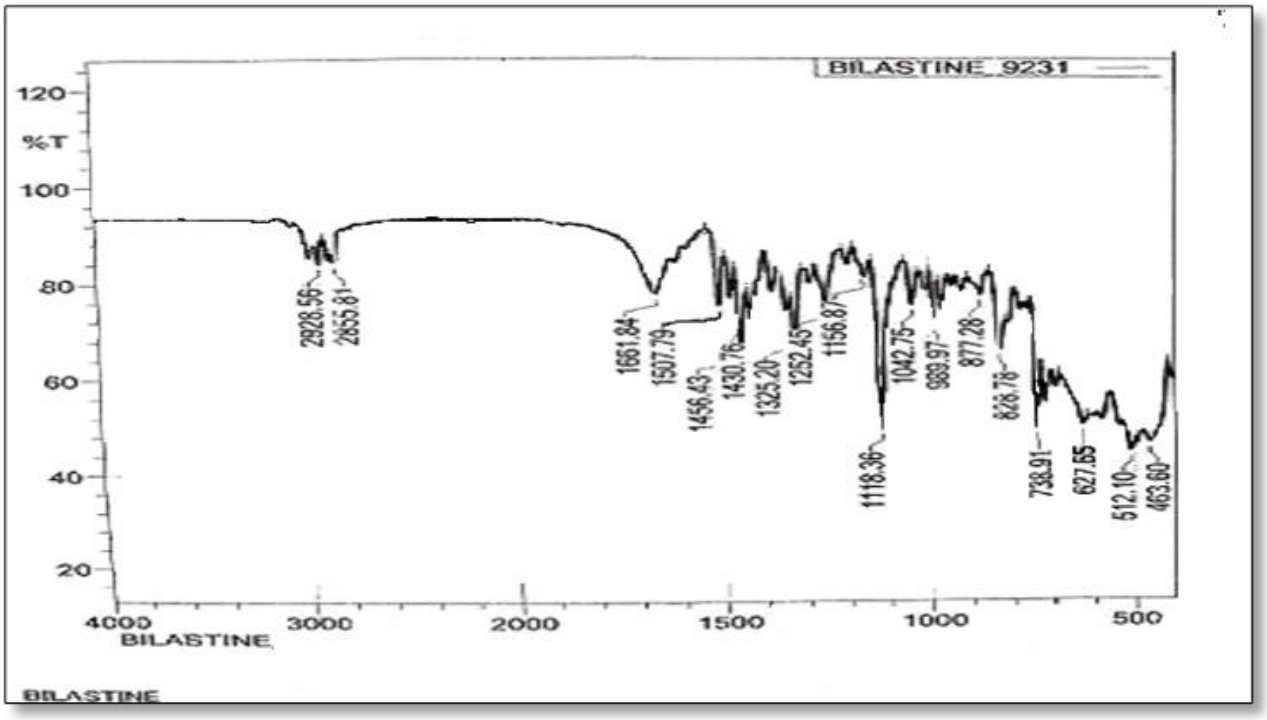


Figure No. 3: FTIR Spectrum of Bilastine + All Excipients

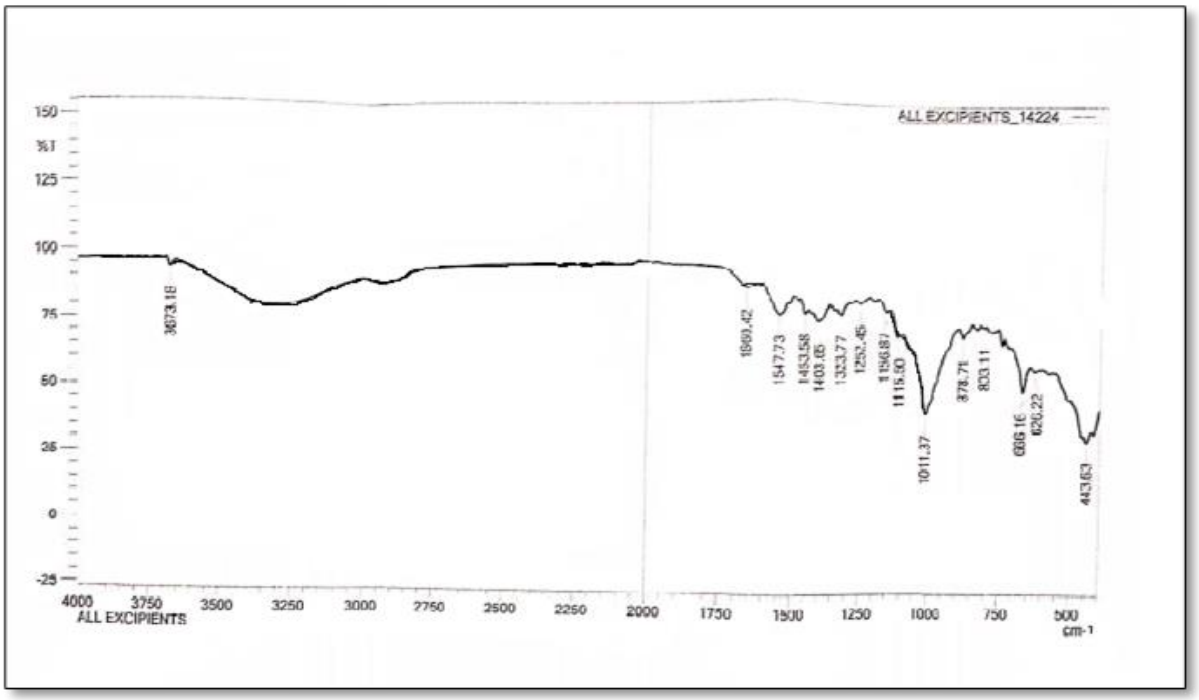
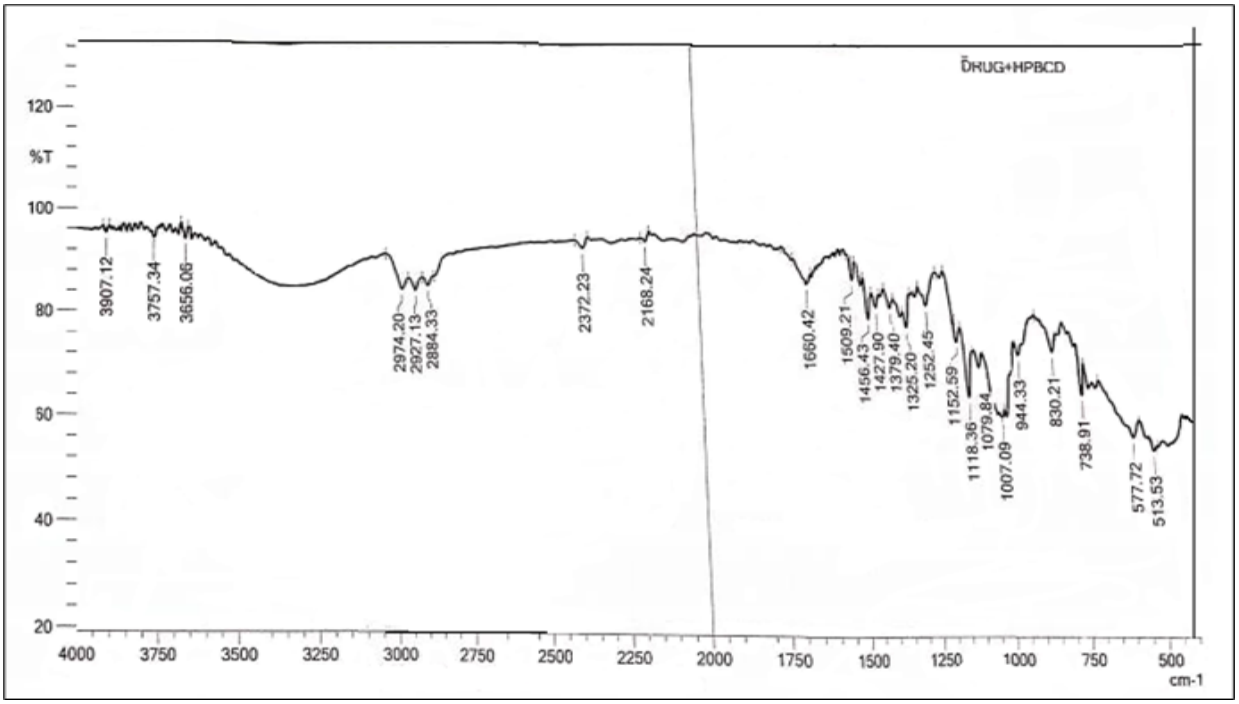


Figure No. 4: FTIR Spectrum of Bilastine



ByobservingtheabovedataitisconfirmedthatthereisnochangeintheFTIRspectrumsof thepuredrugand polymers henceconsidered compatible.

Flow Properties of Bilastine final granules

The final lubricated granules for the formulation of Bilastine floating matrix tablets were evaluated for angle of repose, Carr's index and Hausner's ratio and results were represented in table. Angle of repose was in the range of 27.4º to 30.9º with granules containing HPMC K15M, 30.1º to 32.4º with granules containing Pullulan gum and 28.6º to 29.9º with granules containing HPMC K15M & Pullulan gum, Hausner's ratio was found to be between 1.08 to 1.10 with granules of different formulations. Carr's index was in the range of 9.6 to 10.1 with granules containing HPMC K 15M, 9.9 to 10.4 with granules containing Pullulan gum and 9.8 to 9.9 with granules containing HPMC K15M & Pullulan gum. These values indicate that the prepared granules exhibited good to excellent flow properties.

Table 3: Flow characterization of Bilastine gastro retentive effervescent floating matrix tablets

Formulation	Angle of repose (θ)	Compressibility Index (%)	Hausner ratio
F1	27.4	9.6	1.08
F2	28.8	9.8	1.09
F3	30.9	10.1	1.10
F4	30.1	9.9	1.09
F5	31.3	10.2	1.09
F6	32.4	10.4	1.10
F7	28.6	9.8	1.08
F8	29.4	9.9	1.09
F9	29.9	9.9	1.09

Physico-chemical Characterization of Bilastine Effervescent Floating matrix tablets

The Bilastine floating matrix tablets were white to off-white, smooth, and round shaped in appearance. The results of physico-chemical characterizations are represented in table 14. All the batches of tablets were compressed under identical conditions to minimize processing variables. The compressed matrix tablets were further evaluated for physico-chemical parameters such as weight uniformity, hardness,

friability and drug content. These studies revealed that all the tablet formulations were found to be stable and meeting Indian Pharmacopoeia specified limits for weight variation, friability and drug content. The hardness and thickness of all the Bilastine effervescent matrix tablet formulations were in the range of 6.8 ± 0.5to7.6±0.4kpandthe3.7±0.3mmto3.9±0.3mmrespect ively. Weight uniformity of all the tablet formulations were in the range of 298.4 ± 1.12 mg to 302.4 ± 2.04 mg. Friability of the tablet formulations were negligible and were in the range of 0.1 to0.2%. Drug content estimated for all the tablet formulations were highly uniform with less than 3%variation.

Table 4: Physio-chemical characterization of Bilastine gastro retentive effervescent floating matrix tablets

Formulation	Average Weight(mg)	Thickness (mm)	Hardness (kp)	Friability (%)	Drug content (mg/tablet)
F1	299.6 ± 0.97	3.8 ± 0.1	7.1 ± 0.4	0.2	39.6 ± 0.4
F2	298.4 ± 1.12	3.9 ± 0.2	7.3 ± 0.6	0.2	40.4 ± 0.3
F3	300.2 ± 1.24	3.8 ± 0.2	7.4 ± 0.6	0.1	40.2 ± 0.3
F4	299.8 ± 1.08	3.7 ± 0.3	7.4 ± 0.6	0.2	38.8 ± 0.6
F5	298.7 ± 2.08	3.8 ± 0.3	7.5 ± 0.6	0.2	41.7 ± 0.8
F6	299.9 ± 1.04	3.8 ± 0.2	6.8 ± 0.5	0.1	40.5 ± 0.7
F7	301.2 ± 1.26	3.9 ± 0.3	7.7 ± 0.7	0.2	39.2 ± 0.8
F8	301.6 ± 1.20	3.8 ± 0.3	7.6 ± 0.4	0.2	40.3 ± 0.6
F9	302.4 ± 2.04	3.7 ± 0.4	7.2 ± 0.5	0.1	41.1 ± 0.9

CONCLUSION

In conclusion, the comprehensive evaluation of gastroretentive floating tablets loaded with bilastine involves a systematic approach that includes formulation, in vitro drug release studies, and pharmacokinetic assessments. The formulation process incorporates key excipients to achieve buoyancy and controlled release properties, ensuring optimal drug delivery. In vitro drug release studies provide insights into the tablet's performance, revealing its ability to sustain drug release over time. Overall, the integration of formulation studies, in vitro release assessments, and pharmacokinetic investigations provides a holistic understanding of the gastroretentive floating tablets loaded with bilastine. This knowledge is pivotal in advancing pharmaceutical research, optimizing drug formulations, and ultimately improving patient outcomes. Further research and clinical trials will be essential to validate the effectiveness and safety of these formulations in real-world applications.In conclusion, this research contributes valuable information to the understanding of bilastine pharmacokinetics in the context of gastroretentive floating tablets. Acknowledging limitations, the study suggests potential avenues for future research in enhancing the effectiveness of bilastine formulations. This investigation holds significance for pharmaceutical development, offering insights that could impact the design of improved antihistamine delivery systems.

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