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A REVIEW OF THE ANALYSIS OF ANTIHISTAMINE MEDICATION FLOATING TIMES FOR EFFICIENCY EVALUATION

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ABSTRACT

The purpose of a gastroretentive drug delivery system (GRDDS) is to increase drug absorption and bioavailability by extending the period of time that pharmaceuticals are in the stomach. This technique is especially helpful for medications with upper absorption windows digestive system or those that break down in the stomach's acidic environment. GRDDS can decrease dosage frequency and enhance therapeutic effects by prolonging a drug's gastrointestinal half-life.This review demonstrates a correlation between diminishing floating capabilities and the stomach residence time of antihistamine medications. For stomach residence and sustained release, two crucial variables are needed: total floating time and floating lag time. Among all antihistamine medications, Fexofenadine is notable for having the longest floating duration (>24 hours) and the shortest floating lag time (12.3 sec).These results suggest that among the formulations examined, Fexofenadine has the longest sustained release capacity and the best stomach residence time.

KEYWORDS: Gastro Retentive Drug Delivery Systems, floating lag time, total floating time, antihistamines, Fexofenadine, floating lag time.

INTRODUCTION

Solid oral dosage forms, including capsules and tablets, offer systemic drug concentration in the bloodstream without precise control over delivery kinetics, resulting in plasma concentration fluctuations. Oral administration stands as the most practical route for drug delivery to attain therapeutic benefits.

Controlled-release oral drug delivery systems are garnering attention owing to their advantages, such as simplified dosing regimens, enhanced patient adherence, and adaptable formulation properties. These systems are designed to prolong drug release within the gastrointestinal milieu, thereby ensuring sustained therapeutic plasma concentrations over prolonged durations.

Methods for augmenting gastric retention of solid dosage forms encompass mucoadhesion, sedimentation, flotation, modified geometric configurations, expansion, or simultaneous administration with agents impacting gastric emptying. Floating drug delivery systems (FDDS) are categorized according to these methodologies.

The compromised effectiveness of administered doses stemming from inadequate drug release from drug delivery systems (DDS) attributed to brief gastric residence time underscores the imperative for crafting oral controlled-release (CR) dosage forms endowed with gastric retention functionalities. These formulations facilitate precise control over drug delivery localization, especially pertinent for medications exhibiting absorption windows within the gastrointestinal (GI) tract or susceptibility to stability challenges, thereby presenting a multitude of benefits.

A myriad of strategies are deployed to extend gastric residence times (GRT) in the development of efficacious stomach-specific or gastroretentive drug delivery systems. These encompass hydrodynamically balanced systems (HBS), floating drug delivery systems, low-density formulations, raft systems featuring alginate gels, bioadhesive or mucoadhesive matrices, high-density configurations, super porous hydro gels, and magnetic systems.[1]

The paramount aim of oral controlled Drug Delivery Systems (DDS) lies in augmenting and reliably elevating medication bioavailability. [3]The oral pathway is favored for its simplicity, cost efficiency, and formulation adaptability, rendering it well-suited for single-dose drug delivery systems. Ideally, such systems should administer a solitary dose directly to the intended site and uphold the requisite drug concentration for an extended duration. Intensive research efforts have concentrated on crafting single-dose controlled or sustained drug release systems to enhance patient adherence and diminish dosing frequency.

Gastro Retentive Drug Delivery Systems (GRDDS) afford heightened bioavailability relative to medications primarily efficacious within the stomach milieu, such as antacids and antibiotics. GRDDS facilitate targeted drug delivery, notably advantageous for gastrointestinal disorders like gastroesophageal reflux. Gradual yet comprehensive drug release within the stomach ensues in enhanced bioavailability, diminished dosage necessities, and mitigated gastrointestinal side effects, thereby bolstering patient adherence and elongating dosing intervals.

Several techniques have been elucidated in the literature concerning the formulation of dosage forms engineered to sustain gastric retention:

Low-density systems

High-density systems

Swelling and expanding systems

Ultra-porous hydrogels

Hydrodynamically balanced systems

Gas-generating systems

Raft-forming systems

Floating systems
Ion exchange resins

Prolonged gastric retention of dosage forms confers the benefit of elongating and regulating emptying duration. Nonetheless, devising controlled-release systems to enhance absorption and bioavailability presents hurdles, such as constraining dosage form localization within the targeted gastrointestinal locale. The intricate process of drug absorption within the digestive tract is subject to multifarious influencing factors.[4] Floating systems exhibit low-density characteristics, enabling them to resist descent and persist buoyantly within the gastric milieu for prolonged durations without perturbing gastric emptying kinetics. Throughout this duration, drugs encapsulated within the system undergo gradual release at desired levels of concentration. Consequently, residual components are evacuated from the stomach, culminating in extended gastric residence time (GRT) and enhanced modulation of plasma drug concentrations. Floating systems offer particular advantages in delivering medications to the proximal segments of the gastrointestinal tract, notably antibiotics for managing Helicobacter pylori infection in peptic ulcer patients, and for drugs exhibiting poor solubility or stability in intestinal fluids.[2]

The duration of interaction between medication and the mucosal lining of the small intestine significantly impacts its absorption within the gastrointestinal tract. Therefore, the transit time through the small intestine holds paramount importance for medications that are partially absorbed. Various factors, including gastric emptying kinetics, motility patterns, and both physiological and formulation-related aspects, influence gastric emptying. Prolonged retention within the stomach proves advantageous for medications characterized by low solubility in a high pH environment, thereby enhancing bioavailability, minimizing drug wastage, and ameliorating solubility issues. This extended retention period facilitates targeted drug delivery to the stomach and adjoining segments of the small intestine, thereby fostering the emergence of innovative therapeutic avenues with substantial patient-centric advantages.[5]

Oral dosage forms present the advantages of simplicity and ease of administration, fostering heightened patient adherence. However, oral controlled drug delivery systems encounter hurdles with medications exhibiting poor absorption across the gastrointestinal tract (GIT). Modulating gastrointestinal (GI) transit time poses a significant challenge in the development of oral controlled drug delivery systems. Various methodologies have been devised to extend stomach retention and sustain plasma concentrations of medications with abbreviated half-lives, including mucoadhesion, flotation, sedimentation, expansion, modified geometric configurations, and concurrent administration of pharmacological agents that delay gastric emptying. These strategies facilitate the retention of solid dosage forms within the stomach under regulated conditions. In this study, we aim to assess the floating durations of antibacterial drugs and evaluate their overall efficacy relative to other medications within the same therapeutic class.

Methods for evaluation of floating tablets

There are several methods for evaluating the floating tablets:

Bulk density: Bulk density is calculated by dividing the mass of a powder by its volume, which is influenced by factors such as particle size distribution, morphology, and interparticle cohesion. The measurement entails transferring a defined quantity of powder into a measuring cylinder through a wide-mouthed funnel, recording the resulting volume typically in grams per milliliter (g/ml).

$$\text{Bulk density} = M/Vo$$

Where, M = mass of the powder, Vo = bulk volume of the powder.[6]

Tapped density: applied density, denoted by the ratio of a powder's mass to its tapped volume, is ascertained by Introducing 10 grams of the powder into a clean, dry 100 ml measuring cylinder. Subsequently, the cylinder undergoes 100 taps from a consistent height, and the resultant tapped volume is recorded. This parameter, expressed in grams per milliliter (g/ml), is calculated utilizing the prescribed formula.

$$\text{Tapped density} = M/Vt,$$

Where M is the powder mass and Vt is the final volume after tapping[7]

Angle of repose

The angle of repose (θ) delineates the maximum angle achievable between the surface of a heap of powder and a horizontal plane. This metric was acquired employing the fixed funnel method, wherein a funnel was secured with its apex situated at a designated height 'h' above a level horizontal surface, onto which graph paper was positioned. Powder was meticulously poured through the funnel until the apex of the resultant conical mound precisely aligned with the tip of the funnel. The angle of repose was then computed using the subsequent equation.

$$\text{Angle of repose } Ø = \tan 1(h/r)$$[8]

Hausner's ratio

Hausner's ratio, employed for predicting powder flowability, shares similarities with the compressibility index methodology. It is determined through a specific equation.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density.}$$[9]

Weight Variation test (U.S.P.)

The Weight Variation test, as outlined in the U.S. Pharmacopeia (U.S.P.), necessitates the individual weighing of 20 tablets. Subsequently, the mean weight is computed, and each tablet's weight is compared against this mean value. Adhering to the U.S.P. criteria, the test is considered acceptable if no more than 2 tablets exhibit variations exceeding the specified percentage limit, and if no tablet demonstrates a difference surpassing twice the percentage limit.[10]

Hardness

Tablet hardness and strength represent critical parameters guaranteeing the tablet's ability to withstand the shocks and pressures encountered during manufacturing, packaging, transportation, and patient handling. Various testers, such as the Monsanto tester, Strong-Cobb tester, Pfizer tester, Erweka tester, and Schleuniger tester, are employed for the assessment of tablet hardness.[11]

Dimensional Analysis

The process of dimensional analysis involves employing a vernier caliper to gauge the thickness and diameter of tablets. Twenty tablets are randomly selected from each batch, and the mean values for both dimensions are computed.[12]

Size and Shape

Tablet dimensions undergo precise characterization and regulation throughout manufacturing procedures. Among these dimensions, tablet thickness is of paramount importance. Measurement of tablet thickness can be executed utilizing a micrometer or appropriate instrumentation. It is imperative to ensure tablet thickness remains within a ± 5% deviation from the standard value to maintain rigorous quality control standards.[13]

Floating lag time (FLT) and total floating time (TFT) of floating tablets were visually assessed using a dissolution apparatus type II. In this configuration, 100 mL of 0.1 N HCl solution was utilized. The apparatus comprised a paddle rotating at 50 rpm, operating under conditions mimicking pH 1.2 at a temperature of 37 ± 0.5 °C.

Dissolution Study

The dissolution study involved in vitro assessment of drug release from the formulation using a USP dissolution apparatus type II, outfitted with a paddle. The apparatus functioned under sink conditions with a rotation speed of 50 rpm, maintaining a temperature of 37 ± 0.5 °C. The dissolution medium utilized was 900 mL of 0.1 N HCl. Samples were extracted at predetermined intervals spanning a 6-hour duration and replaced with fresh medium. The withdrawn samples underwent suitable dilution and were analyzed employing a UV/Visible spectrophotometer.

Disintegration Test

The Disintegration Test, as per U.S.P. guidelines, utilizes a device comprising six glass tubes, each 3 inches in length, with open tops and equipped with 10 mesh screens at the bottom. To evaluate disintegration time, one tablet is positioned in each tube, and the basket rack is immersed in either water, simulated gastric fluid, or simulated intestinal fluid, maintained at a controlled temperature of 37 ± 2 °C. Tablets are situated to remain 2.5 cm below the liquid surface during ascent and no closer than 2.5 cm from the bottom of the beaker during descent. The basket, housing the tablets, experiences reciprocating motion within a range of 5-6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs are positioned atop each tablet to prevent buoyancy. According to the protocol, tablets must completely disintegrate, with all fragments passing through the 10 mesh screen within the designated timeframe. Any remaining residue must exhibit a soft mass. Disintegration time ranges from 5 to 30 minutes for uncoated tablets and 1 to 2 hours for coated tablets.[14]

Swelling index

The swelling index of the tablets was evaluated employing the USP Dissolution Apparatus II, utilizing distilled water as the medium, with a volume of 900 mL, and rotation set at 50 rpm. The temperature was maintained at 37 ± 0.5 °C throughout the duration of the experiment. Following a specified time interval, the tablets were retrieved, excess water was carefully eliminated, and they were subsequently allowed to equilibrate. The tablets' swelling characteristics were quantified in terms of the percentage of water uptake (WU).[15]

$$WU(\%) = \frac{\text{Weight of the swollen tablet} - \text{Initial weight of the tablet}}{Initial weight of the tablet}$$

Buoyancy/Floating Test

The buoyancy or floating test evaluates the floating lag time and flotation time, which signify the period from tablet immersion into the medium to its ascent to the upper third of the dissolution vessel. These evaluations commonly occur in simulated gastric fluid or 0.1 mol/liter hydrochloric acid (HCl) solution, maintained at 37°C. The dissolution medium comprises 900 ml of 0.1 mol/liter HCl solution within a USP dissolution apparatus.[16]

Factors influencing gastric residence time (GRT) of floating drug delivery systems include

Density

The density of tablets is a critical factor influencing gastric retention time (GRT) in floating drug delivery systems (FDDS). To prolong GRT, the density of the dosage form should be lower than that of the gastric contents, typically ranging around 1.004 g/mL.[17]

Size and Shape

Size and shape parameters significantly impact gastric retention time (GRT) in drug delivery systems. Dosage forms with diameters surpassing 7.5 mm are preferable to those measuring 9.9 mm. Additionally, tetrahedral-shaped dosage forms and annular devices with flexural moduli of 48 and 22.5 KSI, respectively, exhibit enhanced gastrointestinal transit (GIT) performance, achieving retention rates ranging from 90% to 100%. These characteristics render them more favorable choices for floating drug delivery systems (FDDS) in comparison to alternative geometries.[18]

Viscosity

The viscosity of polymers plays a crucial role in modulating drug release and buoyancy properties within floating drug delivery systems (FDDS). Low-viscosity polymers, such as HPMC K100 LV, exhibit enhanced buoyancy characteristics, making them preferable choices for FDDS over high-viscosity polymers like HPMC K4M. Furthermore, a direct relationship exists between an elevation in polymer viscosity and a reduction in the release rate of drugs from the formulation.

Nature of the Meal

The characteristics of a meal significantly impact gastric motility patterns, particularly during the transition to a fed state induced by the ingestion of indigestible polymers or fatty acid salts. This transition leads to a deceleration in stomach emptying rate, thereby extending the release profile of medications.

Gender

Despite variations in height, weight, or body surface area, men exhibit a shorter average gastric residence time (GRT) following a meal (3.4±0.4 hours) compared to women of similar age and race (4.6±1.2 hours).

Age: Individuals aged over 70 typically experience prolonged gastric residence times (GRT).

Comparative Analysis of Floating Times among Antihistamine Drugs

These are the drugs that come under the class of Anti-histamine agents:

Bilastine

Cinnarizine HCL

Dexchlorpheniramine

Dimenhydrinate

Doxylamine

Famotidine

Fexofenadine

Lafutidine

Loratadine

Nizatidine
Omeprazole
Ranitidine

Bilastine

Bilastine, classified as a second-generation piperidine derivative, exhibits potent and selective H1-antihistamine activity, characterized by its non-sedating effects. It functions by suppressing eosinophil migration to inflamed tissues, thereby stabilizing mast cells. Its specificity for H1-receptors is notably high. In vitro studies indicate that Bilastine effectively inhibits the release of histamine, interleukin-4, and tumor necrosis factor-α from human mast cells and granulocytes, demonstrating anti-inflammatory properties.

A. Ranjeeth et al formulated bilastine in nine formulations using Micro crystalline cellulose, anhydrous lactose, HPMC K15, pullulan gum, sodium bicarbonate. The total floating duration of the formulations were (F1)>14 hours, (F2)> 15hours, (F3)> 16hours, (F4)>4 hours, (F5)>6hours, (F6)>7 hours, (F7)>11 hours, (F8, F9)>12 hours respectively. Among these F4 formulations, exhibited a floating lag time of (35±5) seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[19]

Cinnarizine-HCl

Cinnarizine is extensively utilized in the treatment of motion sickness. It is a piperazine derivative with a relatively short half-life of 4 to 6 hours and is administered in small doses. Its pharmacokinetics involve the provision of anti-histaminic and calcium channel blocking activities, attributed to its heightened affinity towards H1 and calcium channel receptors. Despite its pharmacological activities, cinnarizine experiences inconsistent and incomplete oral absorption, predominantly occurring in the proximal small intestine. This characteristic makes it a suitable candidate for formulation as a floating dosage form. Additionally, cinnarizine exhibits weakly basic properties with a lower pKa value, resulting in ionization at stomach pH levels. Consequently, it displays enhanced solubility in the stomach environment. Conversely, it remains in the un-ionized state at intestinal pH, leading to reduced solubility in the intestine.

Dhavalkumar Vekariya et al formulated cinnarizine hcl in nine formulations using Cinnarizine, HPMC K4M and PVPK 30. The total floating duration of the all nine formulations was 12 hours. Among these formulations, F9 exhibited a floating lag time of (15±0.61) seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[20]

Dexchlorpheniramine maleate

Dexchlorpheniramine maleate (DCPM), the dextrorotatory isomer of chlorpheniramine maleate, exhibits double the potency of the racemic mixture. Functioning as a histamine H1-receptor antagonist, DCPM primarily serves in the symptomatic management of allergic rhinitis. Antihistamines, including first-generation agents like pyrilamine maleate, developed circa 1940, competitively inhibit histamine action at H1-receptor sites on effector cells. Notably, these agents may elicit central nervous system (CNS) effects, manifesting as moderate sedation and impaired driving performance upon oral administration. DCPM, administered as its maleate salt, demonstrates slow gastrointestinal absorption, with peak plasma concentrations achieved within 2.5 to 6 hours post oral intake. Extensive first-pass metabolism characterizes DCPM, yielding low bioavailability (reported between 25% and 50%). Its biological half-life

averages at 6.09 ± 1.0 hours. The recommended oral dosage regimen for DCPM is 2 mg every 4 to 6 hours, not exceeding a maximum daily dose of 12 mg. Its clinical utility primarily lies in the acute treatment of urticaria, rather than its chronic management.

M.Y. Alabazi et al formulated the dexchlorpheniramine into nine formulations using HPMC K 15M Carbopol 934P. The total floating duration of all the nine formulations was 24 hours respectively. Among these formulations, F9 exhibited a floating lag time of (5.6 ±0.608) seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[21]

Dimenhydrinate

Dimenhydrinate, the diphenhydramine salt of 8-chlorotheophylline, possesses typical antihistaminic properties and primarily serves as an antiemetic for motion sickness prevention and treatment. Analogous to diphenhydramine, dimenhydrinate exhibits CNS depressant, anticholinergic, antiemetic, antihistaminic, and local anesthetic effects. Its absorption profile is favorable following oral or parenteral administration. The duration of its pharmacological action spans between 3 to 6 hours. In the context of motion sickness, an initial dose of 50–100 mg of dimenhydrinate is administered orally at least 30 minutes prior to the journey. If necessary, this dosage may be repeated every 4 hours; however, caution is advised to not exceed a total daily dose of 300 mg.

Laxmi Gupta et al formulated dimenhydrinate into 14 formulations using HPMC K15M, HPMC K4M Sodium alginate, poloxamer 188. The total floating duration of the all formulations was >10 hours. Expect D7 and D14 (<10hours) respectively. Among these formulations, D10 exhibited a floating lag time of (75.83 ± 1.50) seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[22]

Doxylamine succinate

Doxylamine succinate, an ethanolamine based H1 antihistamine, exhibits Pharmacological properties and therapeutic indications analogous to other agents within its class. Its sedative properties render it suitable for short-term management of insomnia. It finds utility in alleviating symptoms associated with hypersensitivity reactions and treating pruritic skin disorders. Additionally, it is employed in conjunction with antitussives and decongestants, such as dextromethorphan, pseudoephedrine, and phenylpropanolamine, for the temporary relief of cough and cold symptoms. Doxylamine succinate is commercially available in 25 mg tablet and 50 mg liquid-filled capsule formulations, and it is also present in combination products with antitussives and decongestants. Furthermore, it is incorporated into over 50 pharmaceutical preparations in combination with diverse therapeutic agents.

Farah Hamad et al formulated doxylamine in four formulations using varios concentrations of HPMC K4M . The total floating duration of all the four formulations was >24hours.Among these formulations, F3 exhibited afloating lag time of 80 seconds, which was lesser than that of the other formulations. They concluded that displayed sustained- release characteristics as a dosage form.[23]

Famotidine

Famotidine, a histamine H2-receptor antagonist, is commonly utilized in the treatment of various gastrointestinal conditions including gastric ulcers, duodenal ulcers, Zollinger-Ellison syndrome, and gastroesophageal reflux disease (GERD). The recommended dosage for benign gastric and duodenal ulceration is 40 mg orally once daily at bedtime

for a duration of 4 to 8 weeks. In GERD, the suggested dose is 20 mg orally twice daily for 6 to 12 weeks; for cases associated with esophageal ulceration, the dosage is increased to 40 mg twice daily for a similar duration. For short-term relief of heartburn or non-ulcer dyspepsia, a dosage of 10 mg orally up to twice daily is advised. In Zollinger-Ellison syndrome, the initial oral dose is 20 mg every 6 hours, with potential escalation up to 80 mg daily as needed. Famotidine exhibits low bioavailability (40-45%) and a short biological half-life (2.5-4.0 hours). Adverse effects such as diarrhea, dizziness, headache, and anorexia may occur, particularly with prolonged use, which can also lead to potential toxic effects.

Ravi Kumar et al formulated famotidine into 12 formulation using CP934P, HPMC K4M and HPMC K15M. The total floating duration of the formulations were F1 >`14 hours, F2 > 13 hours, (F3, F4, F5) > 12 hours, F6 >10 hours, F7 > 8 hours, F8 > 6 hours, F9 > 18 hours (F10, F11) > 20 hours, F12 > 24 hours respectively. Among these formulations, F1 exhibited a floating lag time of 25 seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[24]

Fexofenadine hydrochloride

Fexofenadine hydrochloride (Fex HCl), classified as a non-sedating antihistamine H1 blocker primarily indicated for seasonal allergic rhinitis and chronic idiopathic urticaria, exhibits limited absorption in the upper small intestine, resulting in a poor oral bioavailability of approximately 35%. Consequently, Fex HCl is regarded as a potential candidate for Gastro-Retentive Drug Delivery Systems (GRDDS). Despite this potential, research into enhancing Fex HCl oral bioavailability has been scant. In a prior investigation, a micro emulsion formulation of Fex HCl was developed with the aim of improving its absorption. Comparative analysis with conventional marketed syrup demonstrated a notable 3.76-fold increase in the drug's oral bioavailability. In this study, a novel effervescent floating GRDDS for Fex HCl was devised, representing the inaugural endeavor to replace conventional tablets. This formulation aims to regulate drug release over a 24-hour period, augment drug absorption in the proximal small intestine, and consequently, enhance its bioavailability.

May Saab et al formulated the fexofenadine in 12 formulations using HPMC K4M, HPMC K15M, HEC (Hydroxyethyl cellulose), HPMC K100LV.The total floating duration of the formulations were (F1-F3)> 24 hours respectively. Among these formulations, F1 exhibited a floating lag time of (12.3±1.5) seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[25]

Lafutidine

Lafutidine, a newly developed second-generation H2 antihistaminic blocker, demonstrates significant efficacy in the treatment of gastric and duodenal ulcers. Its mechanism involves the prevention of gastric mucosal lesions in both acute and chronic gastritis. Lafutidine exerts its therapeutic effects by penetrating the stomach wall and binding to H2 receptors, subsequently increasing blood flow to the gastric mucosa. Experimental models have confirmed its protective action in gastric mucosal tissue.

Ramdas T. Dolas et al formulated the lafutidine into 24 formulations using Sodium bicarbonate, Citric acid, PVP-K30. The total floating duration of the all 24 formulations was > 12 hours. Among these formulations, F14 exhibited a floating lag time of 33 seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[26]

Loratadine

Loratadine, a second-generation antihistamine for allergic rhinitis and chronic urticaria, is often formulated as floating tablets. These tablets are designed to float on the stomach's fluid surface, extending drug residence time and improving absorption. By addressing challenges of short gastric residence and incomplete absorption seen with immediate-release forms, loratadine floating tablets ensure controlled release over time. This approach offers benefits like enhanced bioavailability, reduced dosing frequency, and better patient compliance. Moreover, it minimizes plasma concentration fluctuations, leading to more consistent symptom management and fewer adverse effects. In summary, loratadine floating tablets hold promise in optimizing treatment outcomes by providing sustained drug release, enhancing convenience, and efficacy for patients.

Anish Kumar D et al formulated loratadine into 9 formulations using HPMC K4 M, HPMC K15 M PVK30. The total floating duration of the formulations were F1 ≥4hrs, F2 >3hrs, F3 >5hrs, F4 >3hrs, F5 >8hrs, F6 >5hrs, F7 >8hrs, F8 >6hrs, F9 >10hr respectively. Among these formulations, F9 exhibited a floating lag time of 37 seconds, which was lesser than that of the other formulations. They concluded that displayed sustained-release characteristics as a dosage form.[27]

Nizatidine

Nizatidine is a histamine H2-receptor antagonist, acts by inhibiting stomach acid production and is commonly prescribed for the treatment of peptic ulcer and gastro esophageal reflux. The recommended dosage regimen includes either 300 mg once daily at bedtime or 150 mg twice daily. With a short biological half-life of 1-2 hours and susceptibility to metabolism by colonic bacteria, nizatidine presents challenges in maintaining therapeutic levels in the body. Studies suggest that local delivery of H2-receptor antagonists can enhance stomach wall receptor site bioavailability, thereby improving the efficacy of these drugs in reducing acid secretion. Considering these factors, nizatidine emerges as a suitable candidate for a gastro retentive drug delivery system.

Gehan balata et al formulated nizatidine in eleven formulations using hydroxypropylmethylcellulose K4M (HPMC K4M), carbopol934 and sodium alginate. The total floating duration of the formulations were 8hours (F1), 12 hours (F2), 18 hours (F3), 24 hours (F4, F5, F6, F10), 16 hours (F7, F8, F9), 4 hours (F11) respectively. Among these formulations, F11 exhibited a floating lag time of (3.4 ±0.33) minutes, which was lesser than that of the other formulations. They concluded that F11 displayed sustained-release characteristics as a dosage form.[28]

Omeprazole

Omeprazole exerts its therapeutic effects by inhibiting gastric acid secretion through the blockade of the proton pump situated within the gastric parietal cells. This mechanism of action makes it a commonly utilized medication for the management of peptic ulcer disease (PUD) and gastro esophageal reflux disease (GERD). Additionally, Omeprazole is employed in conjunction with Fexofenadine and other antihistamines for the treatment of dermatological conditions such as urticaria. As the model drug in this investigation, Omeprazole serves as a histamine H2-receptor antagonist and finds extensive clinical use in the treatment of active duodenal ulcers and gastric ulcers.

Bhavna Patel et al formulated omeprazole in six formulations by using omeprazole, HPMCK4M, HPMCK15M, sodium bicarbonate, citric acid. The total floating duration of the six formulations were (F1, F3, F5) > 12 hours, (F2, F4, F6) >

10 hours respectively. Among these formulations, F5 exhibited a floating lag time of 60 seconds, which was lesser than that of the other formulations. They concluded that F5 displayed sustained-release characteristics as a dosage form.[29]

RANITIDINE

Ranitidine, an H2 receptor antagonist, is indicated for various conditions including Zollinger-Ellison syndrome, duodenal ulcers, gastric ulcers, and erosive esophagitis. Its pharmacokinetic profile reveals a short biological half-life of 2-3 hours, with absorption predominantly occurring in the proximal small intestine. However, its bioavailability is hampered by colonic metabolism. Consequently, the standard dosing regimen of 150 mg needs to be administered four times daily for the treatment of endoscopically diagnosed erosive esophagitis. This dosing frequency is necessitated by the drug's limited duration of action, which spans only 4 hours, thereby necessitating frequent administration to sustain therapeutic efficacy. Deviating from this dosing schedule risks fluctuations in plasma drug levels.

Saurabh Mandowara et al formulated ranitidine into 9 formulations using HPMC K4M, HPMC K15 M, HPMC K100M, guar gum. The total floating duration of the all formulations was > 12 hours, expect F3 5.5 hours. And the floating lag time 37 ± 0.12, 41 ± 0.2, 22.6 ± 0.22, 60 ± 0.17, 180 ± 0.11, 708 ± 0.12, 711 ± 0.2 , 200 ± 0.5, 188 ± 0.8 seconds of F1, F2, F3, F4, F5, F6, F7, F8, F9 respectively. Among these formulations, F3 exhibited a floating lag time of (22.6 ± 0.22) seconds, and is which was lesser than that of the other formulations. They concluded that F3 displayed sustained-release characteristics as a dosage form.[30]

TABULATION SHOWING FLT AND TFT OF ANTI HISTAMINE DRUGS

S. No	Drug	FLT(sec)	TFT(hr)	Formulation
1	Bilastine	35	>4	4
2	Cinnarizine HCL	15	12	9
3	Dexchlorpheniramine	5.6	>24	9
4	Dimenhydrinate	75.83	>10	10
5	Doxylamine	80	>24	3
6	Famotidine	25	>14	1
7	Fexofenadine	12.3	>24	1
8	Lafutidine	33	>12	14
9	Loratadine	37	>10	9
10	Nizatidine	186	>4	6
11	Omeprazole	60	>12	5
12	Ranitidine	22.6	5.5	3

CONCLUSION

We inferred from this review that antihistamine medication residence times lengthen as floating capacities decrease. For a medicine to meet the sustained release and stomach residence times, it must meet two crucial parameters: total floating time and floating lag time. Fexofenadine had the longest floating duration (>24)and the shortest floating lag time (12.3 seconds) of all the antihistamine medications. This implies that the greater gastric residency of the Fexofenadine of all formulations, it possesses the longest sustained release capacity.

AUTHORS CONTRIBUTIONS

All Authors have contributed equally.

CONFLICTS OF INTERESTS

All authors have none to declare.

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