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Review Article

Analyzing Antibacterial Drugs Floating Times for Efficiency Evaluation: A Review

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ABSTRACT

Objective: To investigate the significance of floating lag time (FLT) and total floating time (TFT) in gastro retentive drug delivery systems (GRDDS), focusing on their implications for drugs requiring sustained release or targeted delivery within the gastrointestinal tract. Methods: A review was conducted to analyze the floating characteristics of drug delivery systems, particularly emphasizing FLT and TFT. Metronidazole was selected as a case study due to its relevance in antibacterial therapy and its known properties in GRDDS. Results: Metronidazole demonstrates superior floating characteristics, with a TFT exceeding 24 hours and a minimal FLT of only 2 seconds. This prolonged floating duration makes it highly suitable for controlled and sustained release formulations, particularly in applications requiring targeted delivery to the stomach. Conclusion: Among antibacterial agents, Metronidazole emerges as an optimal candidate for GRDDS, offering potential enhancements in therapeutic efficacy and patient compliance through sustained release mechanisms.

INTRODUCTION

Solid oral dose forms, such as tablets and capsules, create changes in plasma concentration by delivering drug concentrations into systemic blood circulation without allowing for drug administration control. The most practical method of drug delivery to obtain therapeutic benefits is oral administration. The benefits of controlled-release oral drug delivery systems, such as formulation flexibility, patient compliance, and convenience of dosage, are drawing attention. The goal of these systems is to continue medication release in the gastrointestinal tract so that long-term therapeutic blood concentrations can be sustained. Mucoadhesion, sedimentation, flotation, changed shape systems, expansion, or

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co-administration with pharmacological drugs that modulate stomach emptying are some strategies for improving gastric retention of solid dose forms. Drug delivery devices that float (FDDS) are categorized in accordance with these methods.The need for oral controlled-release (CR) dosage forms with gastric retention capabilities originates from the reduced efficacy of administered doses owing to partial drug release from drug delivery systems (DDS) induced by short stomach residence time. These forms have many benefits, including the ability to control the site of drug administration, especially for medicines that have stability problems or gastrointestinal (GI) tract absorption windows. Different strategies are used to extend gastric residence durations (GRT) in order to create effective drug delivery systems that are particular to the stomach or gastroretentive. These comprise floating drug delivery systems, high-density systems, bioadhesive or mucoadhesive systems, raft systems using alginate gels, hydrodynamically balanced systems (HBS), low-density systems, and magnetic systems..[1] The primary objective of oral controlled Drug Delivery Systems (DDS) is to enhance and predictably increase medication bioavailability..[3] The oral route is preferred for its simplicity, cost-effectiveness, and formulation flexibility, making it ideal for single-dose drug delivery systems. These devices should ideally deliver a single dose straight to the intended location and sustain the intended medication concentration for a considerable amount of time. Creating single-dose controlled or sustained medication release systems has been the subject of extensive research in an effort to decrease administration frequency and increase patient compliance.Enhanced bioavailability is provided by Gastro Retentive Drug Delivery Systems (GRDDS) in contrast to drugs that work predominantly in the stomach, like antibiotics and antacids. GRDDS offer site-specific drug administration, which is especially advantageous for conditions affecting the gastrointestinal tract, such as acid reflux disease. Improved bioavailability, fewer dosage requirements, and less gastrointestinal side effects result from the drug's slow but full release in the stomach, which improves patient compliance and lengthens treatment intervals.Various methods have been described in the literature for designing dosage forms that remain in the stomach.Systems with low density, Systems with high density, Systems that are swelling and growing, Ultra-porous hydrogels, Systems that are hydrodynamically balanced, Systems that generate gas, Systems that form rafts, Systems that can float,Ion exchange resins Prolonged gastric retention of dosage forms offers the advantage of extending and controlling emptying time. One of the problems in designing controlled-release systems for enhanced bioavailability and absorption is limiting the localization of the dose form in the desired gastrointestinal region. Numerous factors affect the intricate process of medication absorption from the digestive system. [4] Floating systems are characterized by their low-density nature, allowing them to resist sinking and remain afloat in the gastric environment for extended periods without affecting gastric emptying rates. During this time, drugs contained within the system are slowly released at desired concentrations. Subsequently, residual components are cleared from the stomach, leading to prolonged gastric residence time (GRT) and improved control over plasma drug concentrations. Floating systems are particularly advantageous for delivering drugs to the proximal gastrointestinal tract, such as antibiotics for Helicobacter pylori infection management in peptic ulcer patients, and for drugs with poor solubility or stability in intestinal fluids. [2 The length of time a drug is in contact with the mucosa of the small intestine has a significant impact on how well it is absorbed in the digestive system.

Therefore, for drugs that are partially absorbed, small intestinal transit time is crucial. Gastric emptying is influenced by a number of factors, including formulation, physiological factors, and patterns of motility. In a high pH environment, prolonged stomach retention improves solubility, decreases drug waste, and increases bioavailability for drugs with poor solubility. It permits targeted medication delivery to the stomach and surrounding small intestines, promoting the development of innovative treatment alternatives that have a substantial positive impact on patients. [5] Oral dosage forms encourage high patient compliance because they are straightforward and simple to administer. However, drugs with low gastrointestinal tract (GIT) absorption present difficulties for oral controlled drug delivery systems. GI transit time modification is a major obstacle in the development of oral controlled medicine delivery systems. Several ways have been devised to maximize stomach retention and preserve plasma concentration of short-half-life drugs. These tactics include mucoadhesion, flotation, sedimentation, expansion, changed shape systems, and concurrent delivery of pharmacological agents delaying gastric emptying.These methods allow for the controlled retention of solid dosage forms in the stomach.In this study, we compare the overall efficacy of antibacterial treatments to other drugs in the same class and evaluate the floating durations of these drugs.

Methods For Evaluation Of Floating Tablets:

There are several methods for evaluating the floating tablets:

Bulk density: Based on parameters including particle shape, size distribution, and adhesion, bulk density is computed by dividing a powder's mass by its volume. In order to measure it, a wide-mouthed funnel is used to pour a precise amount of powder into a measuring cylinder. The volume of the mixture is then recorded and often stated in grams per milliliter (g/ml).

M/Vo is the bulk density. where M is the powder's mass

Vo is the powde's bulk volume..[6]

Tapped density: A 100 ml measuring cylinder should be well cleaned and dried before adding 10 grams of a powder. Tapped density is defined as the ratio of a powder's mass to its tapped volume. After that, the cylinder is tapped 100 times at a constant height, and the tapped volume that results is recorded. This parameter can be computed using the following formula, which is represented in grams per milliliter (g/ml): Tapped density is equal to M/Vt, where M is the mass of the powder and Vt is the volume remaining after tapping..[7]

Angle of repose :The angle of repose (θ) is the steepest angle that can form between a powder pile's surface and a horizontal plane. This measurement was made using the fixed funnel technique. A funnel was fixed with its tip at a particular height 'h' above the surface, and graph paper was placed over a flat horizontal surface. When the powder was carefully poured through the funnel, the apex of the resulting conical pile was exactly at the tip. The angle of repose was then calculated using the following equation.

Angle of repose Ø = tan1(h/r) [8]

Hausner'sratio :Hausner's ratio is similar to the compressibility index method in that it is used to predict powder flowability. The formula is used to compute it: Tapped density / Bulk density equals Hausner's ratio. [9]

Weight Variation test (U.S.P.): The Weight Variation test, as specified in the U.S. Pharmacopeia (U.S.P.), requires the separate weighing of 20 tablets. Subsequently, the average weight is calculated, and each tablet's weight is compared to this average value. To conform to the U.S.P. standards, the test is deemed satisfactory if no more than 2 tablets show variations beyond the specified percentage limit, and if no tablet displays

a difference exceeding twice the percentage limit.[10]

Hardness: Tablet hardness and strength are crucial parameters ensuring the tablet's resilience against the shocks and pressures encountered throughout manufacturing, packaging, transportation, and patient handling. Different testers, including the Monsanto tester, Strong-Cobb tester, Pfizer tester, Erweka tester, and Schleuniger tester, are utilized to evaluate tablet hardness.[11]

Dimensional Analysis: The process of dimensional analysis entails using a vernier caliper to measure the thickness and diameter of tablets. Twenty tablets are randomly chosen from each batch, and the average values for both dimensions are calculated.[12]

Size and Shape: Tablet dimensions undergo meticulous description and regulation during manufacturing processes. Among these dimensions, tablet thickness holds primary significance. Measuring tablet thickness can be conducted using a micrometer or suitable devices. It is vital to maintain tablet thickness within a ± 5% variation from the standard value to uphold stringent quality control standards[13]

Floating lag time (FLT) and total floating time (TFT) of floating tablets were evaluated visually utilizing a dissolution apparatus type II. In this setup, 100 mL of 0.1 N HClsolution was employed. The apparatus featured a paddle rotated at 50 rpm, operating under conditions simulating pH 1.2 at a temperature of 37 ± 0.5 °C.

Dissolution Study: The dissolution study comprised in vitro evaluation of drug release from the formulation utilizing a USP dissolution apparatus type II, equipped with a paddle. The apparatus operated under sink conditions at a rotation speed of 50 rpm and maintained a temperature of 37 ± 0.5 °C. The dissolution medium employed was 900 mL of 0.1 N HCl. Samples were withdrawn at predefined time intervals over a 6-hour period and substituted with fresh medium. These withdrawn samples underwent appropriate dilution and were analyzed using a UV/Visible spectrophotometer.

Disintegration Test: Using an apparatus made of six glass tubes, each measuring three inches in length, with ten mesh screens installed at the bottom and an open top, the Disintegration Test is conducted in accordance with U.S.P. requirements. One tablet is inserted into each tube to measure the disintegration time, and the basket rack is submerged in water, simulated gastric fluid, or simulated intestinal fluid that is kept at a constant 37 ± 2 °C. The tablets are placed so that, when moving upward, they are 2.5 cm below the liquid's surface and, when moving downhill, they are no closer than 2.5 cm from the beaker's bottom. The basket that holds the pills is moved back and forth between 5 and 6 cm at a rate of 28 to 32 cycles per minute Each tablet has a perforated plastic disc on top to keep it from floating. Tablets must fully dissolve in the test, with every particle going past the 10 mesh screen in the allotted amount of time. Any leftover material needs to have a soft bulk. For coated pills, the disintegration period is set at 1-2 hours, and for uncoated tablets, it is 5-30 minutes..[14]

Swelling index: With distilled water as the medium, the USP Dissolution Apparatus II was used to measure the swelling index of the tablets. It was kept at 900 mL and rotated at 50 rpm. Throughout the experiment, a constant temperature of 37 ± 0.5 °C was maintained. The tablets were taken out after a predetermined amount of time, any additional water was carefully drained out, and then they were refilled. The percentage of water uptake (WU) was used to quantify the tablets' swelling characteristics,[15]

WU(%)=(Weight of the swollen tablet-Initial weight of the tablet)/Initialweightofthetablet

Buoyancy/Floating Test:The buoyancy or floating test examines the floating lag time and flotation

time, representing the duration from tablet introduction into the medium to its ascent to the upper third of the dissolution vessel. These assessments typically occur in simulated stomach fluid or 0.1 mol/liter HCl solution, held at 37°C. The dissolution medium consists of 900 ml of 0.1 mol/liter HCl within a USP dissolution apparatus. [16] Factors influencing gastric residence time (GRT) of floating drug delivery systems include:

Density: The density of tablets plays a crucial role in determining gastric retention time (GRT) in floating drug delivery systems (FDDS). To enhance GRT, the density of the dosage form should be lower than that of the gastric contents, which usually falls within the range of approximately 1.004 g/mL.[17]

Size and Shape: Size and shape considerations exert a significant influence on gastric retention time (GRT) in drug delivery systems. Dosage forms with diameters exceeding 7.5 mm are preferred over those measuring 9.9 mm. Moreover, tetrahedral-shaped dosage forms and annular devices with flexural moduli of 48 and 22.5 KSI, respectively, demonstrate superior gastrointestinal transit (GIT) performance, achieving retention rates between 90–100%. These attributes make them more suitable options for floating drug delivery systems (FDDS) compared to other geometries.[18]

Viscosity: The viscosity of polymers serves a critical function in shaping drug release and buoyancy properties in floating drug delivery systems (FDDS). Low-viscosity polymers, exemplified by HPMC K100 LV, demonstrate superior buoyancy characteristics, rendering them more desirable options for FDDS compared to high-viscosity polymers like HPMC K4M. Additionally, there exists a correlation between an increase in polymer viscosity and a decrease in the release rate of drugs from the formulation.

Nature of the Meal: The nature of the meal exerts a notable influence on gastric motility patterns, particularly transitioning to a fed state when indigestible polymers or fatty acid salts are ingested. This transition results in a decrease in the rate of stomach emptying, consequently prolonging the release of medication.

Gender: The average stomach residence time (GRT) after a meal is shorter in men (3.4±0.4 hours) than in women (4.6±1.2 hours), regardless of variations in height, weight, or body surface area.

Age: Gastric residence durations (GRT) are often longer in people over 70.

Comparative Analysis of Floating Times Among Antibacterial Drugs

These are the drugs which comes under the class of Anti-bacterial agents:

Synthetic agents:

Berberine Hydrochloride
Cefadroxil
Cefiximetrihydrate
Cefuroxime axetil
CefpodoximeProxetil
Cephalexin
Clarithromycin
GemifloxacinMesylate
Levofloxacin
Metronidiazole
Moxifloxacin
Norflaxacin
Ofloxacin

Natural agents:

Curcumin
Luteolin
Artemisia princeps extract

Berberine Hydrochloride

The quaternary ammonium salt berberine hydrochloride (Bh) is a member of the isoquinoline alkaloids. It is rich in pharmacological qualities and has been studied in drug chemistry and biochemistry for a long time. In vitro and in vivo studies on berberine have shown promise in a number of areas, including

antioxidant, anticancer, and antituberculosis properties. According to recent pharmacological research, berberine can successfully block H. pylori's ability to proliferate as well as the activity of H. pylori N-acetyltransferase. Jun Ji et al. formulated Berberine hydrochloride (Bh) in six different formulations using HPMCK15M, Carbopol 971PNF, NaHCO3, and cross-linking SCMC. The total floating duration of the six formulations were (F1, F2, F3) >12 hours, (F4) 3 minutes, (F5) 4 minutes, and (F6) <4 hours, respectively. Among these formulations, F4 exhibited a floating lag time of (15.33 ± 3.06) minutes, which was greater than that of the other formulations. They concluded that F4 displayed sustained-release characteristics as a dosage form. [19] [20]

Cefadroxil

Cefadroxil is a para-hydroxy derivative of cefalexin, a first-generation cephalosporin antibiotic. It is recommended for mild to moderate susceptible infections resulting from Streptococcus pyogens, such as urinary tract infections, reproductive tract infections, skin infections, and strep throat or streptococcal tonsillitis. Cefadroxil has a high oral bioavailability and is absorbed virtually entirely from the gastrointestinal tract without being impacted by meals.. Rajesh Kumar Jatav et al., formulate 10 types of floating tablet preparations using HPMC K100M, Carbopol, Sodium bicarbonate, Sodium bicarbonate, MCC, PVPK30, Mag. Stearate, Talc as a ingrediants. The Total floating times of formulations are 5 hours (F1,F7), 6 hours (F2, F5, F8), 7 hours (F4), 8 hours(F3, F6, F9, F10) and the Floating lag times (Sec) are 175, 102, 115, 95, 136, 90, 100, 78, 140, 110 and F1, F2, F3, F4, F5, F6, F7, F8, F9, F10 respectively. Their study concluded that formulation F8 exhibited sustained-release characteristics as a dosage form. [21]

Cefixime Trihydrate

Cefixime, a novel semi-synthetic third-generation cephalosporin, exhibits broad-spectrum antibacterial activity against respiratory infections, otitis media, and uncomplicated urinary tract infections (UTIs). With a pKa of 2.5 and a serum half-life of 3-4 hours, it is primarily absorbed in the stomach and upper small intestine. Resistant to beta-lactamase hydrolysis, cefixime demonstrates low inhibitory doses (MIC) and is formulated in solid dosage forms by Pradip P Gade et al., who employed various constituents including HPMC K4M, Sodium CMC, Carbopol 934P, lactose, sodium bicarbonate, and magnesium stearate. The drug release study conducted over 12 hours revealed variable release percentages ranging from 54.17% to 79.41% across formulations CF1 to CF7. Notably, high concentrations of high-viscosity polymers such as HPMC K4M induced the formation of a strong viscous gel layer, impeding water diffusion into the tablet matrix and consequently slowing or reducing drug release. The presence of carbopol 934P directly influenced drug release, with formulations CF1 and CF2 exhibiting non-floating behavior attributed to lower gas-generating agent percentages and higher carbopol 934P concentrations. Formulations CF3, CF4, CF5, and CF6 floated, albeit with longer lag times, where CF6 notably achieved a duration exceeding 12 hours. Decreasing concentrations of carbopol 934P correlated with increased floating capacity, and CF7 demonstrated reduced floating lag time due to higher gas-generating agent content. CF7, with a floating lag time of 49 sec and a duration exceeding 720 minutes, was identified as the optimal gastro-retentive dosage form, offering superior controlled release compared to other formulations.[22]

Cefuroxime Axetil:

The 1-acetoxyethyl ester of cefuroxime, cefuroxime axetil (CA), is a β-lactamase-stable cephalosporin with broad-spectrum antibacterial action against both Gram-positive and Gram-

negative pathogens. After being taken orally, esterases quickly hydrolyze CA, producing cefuroxime. Cefuroxime absorption is aided by the lipophilicity of CA due to the presence of the 1-acetoxyethylester group at position 4. Oral bioavailability is weak and inconsistent as a result of this modification's degradation of solubility. There are two types of CA: crystalline and amorphous. The amorphous form has higher solubility and is therefore more bioavailable. The oral bioavailability of CA ranges from 30% in the fasted state to 50% in the fed state in humans. A floating delivery system strategy was used in the work by Praveen Kumar Mandapalli et al. to create a dosage form of CA based on hydroxypropyl methyl cellulose (HPMC). The suitability of using several grades of HPMC (K4M, K15M, and K100M) in the formulation of gastroprotective floating drug delivery systems (GFDDS) of CA was assessed. In order to get a final tablet weight of 499.5 mg, nine formulations were developed by varying the drug-to-polymer ratio while keeping other constituents at required proportions. Tablets were manufactured utilizing the direct compression method. The primary ingredients were lactose monohydrate, sodium bicarbonate, magnesium stearate, talc, HPMC (K4M), HPMC (K15M), and HPMC (K100M). Out of all the formulations, F1 showed a 99.5% drug release percentage and a floating time of 2.03 minutes. As so, this formulation showed encouraging outcomes, demonstrating hogh gastric residence time.[23]

Cefpodoxime Proxetil :

Cefpodoximeproxetil undergoes conversion to its active form, cefpodoxime, within the body. Its mechanism of action involves inhibition of bacterial cell wall synthesis, thereby preventing bacterial proliferation. Moraxella catarrhalis, Escherichia coli, Klebsiella, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Haemophilusparainfluenzae, Neisseria gonorrhoeae, Hemophilusinfluenzae, and Streptococcus pneumoniae are just a few of the many bacteria that cefpodoxime effectively combats. This is because the essential cellular structure is crucial for the survival of bacteria. The development of a floating cefpodoximeproxetil drug delivery system made use of locust bean gum as a rate-retarding substance. Because of its neutral polymer composition, which consists of (1-6)-linked α-D-galactose side chains and a (1-4)-linked β-D-mannose backbone, locust bean gum—which is high in galactomannans—was chosen. Thirteen formulations were made and tested for their ability to float; formulations F10, F11, F12, and F13, which included sodium bicarbonate and locust bean gum in different proportions, showed sustained release over a 12-hour period. Among these formulations, F13, formulated with a locust bean gum to drug ratio of 0.3:1.0, exhibited optimal floating properties with a floating time of less than 14 minutes and achieved 95% drug release within 12 hours dissolution as per requirements. Consequently, F13 was identified as the final optimized formulation for the floating matrix tablet of cefpodoximeproxetil, aimed at prolonging gastric residence time and enhancing bioavailability. This study was conducted by L. Kukati et al., concluding the efficacy of F13 in achieving the desired objectives.[24]

Cephalexin

With pKa values between 5.2 and 7.3, the β-lactam antibiotic cephalexin (CPL) demonstrates lipophilic weak acid characteristics. It breaks down in intestinal settings (pH 6.5) but remains stable in gastric ones. With a brief biological half-life of around an hour, CPL is completely absorbed. However, because of sawtooth kinetics, its traditional dose forms require frequent administration (3–4 times daily), which leads to less-than-ideal therapy. Numerous sustained-release formulations have been created in order to overcome this restriction. However, the intestinal

instability of CPL and its limited absorption window in the upper gastrointestinal (GI) tract limit their effectiveness. CPL, HPMC K100M, HPMC K15M, stearyl alcohol, and NaHCO3 were used as the main ingredients in eleven formulations. The goal of adding HPMC's higher viscosity grades (K100M and K15M) was to modify release profiles. Increasing HPMC content, particularly HPMC K15M, significantly extended the floating lag time (FLT) from 15.8 to 126 s (formulations S8–S11). Notably, all formulations except S4 achieved sustained drug release over 8 hours. Formulation S4, lacking sustained-release material, exhibited complete drug release within 0.5 hours. The drug release rate inversely correlated with the amount and viscosity of HPMC in the formulations. Formulation S5, with the shortest FLT among S1–S11 formulations, was identified as the optimal gastro-floating tablet formulation. [25]

Clarithromycin

Clarithromycin, an advanced generation macrolide antibiotic, is utilized in the treatment of H. pylori infection and respiratory tract infections. Employing a controlled release formulation can mitigate drug resistance by maintaining antibiotic concentration above the minimum inhibitory concentration (MIC). Clarithromycin demonstrates concentration-dependent pharmacodynamics, with clinical success typically associated with a peak concentration to MIC ratio of approximately 10. Five formulations were developed utilizing Hydroxypropyl methylcellulose (HPMC) K4M, lactose, and sodium bicarbonate as ingredients. The third formulation exhibits reduced floating lag time and total floating time, leading Priyanka Shukla and Ajay Yadav to conclude that the H4 formulation possesses controlled release properties.[26]

Gemifloxacin Mesylate

The synthetic fluoroquinolone antibacterial agent gemifloxacin is effective against respiratory tract infections-causing bacteria such S. pneumoniae, H. influenzae, and M. catarrhalis. It has broad-spectrum activity against both gram-positive and gram-negative species. It is recommended mainly for acute sinusitis caused by bacteria (ABS). When administered orally to healthy people, gemifloxacin exhibits an average absolute bioavailability of 71%; absorption, not considerable first-pass metabolism, is the limiting factor. Gemifloxacinmesylate was formulated into ten preparations utilizing HPMCK4M, HPMCK15M, MCC, Gelucire50/13, Polyox WSR301, NaHCO3, and Talc as principal constituents. Among these, formulation F9 exhibited a floating lag time (FLT) of 30 seconds, with all formulations demonstrating a total floating time (TFT) of 12 hours. Bhikshapathi et al. concluded that formulation F9 possesses prolonged drug release properties.[27]

Levofloxacin

Levofloxacin, an antibiotic, is indicated for treating diverse bacterial infections like acute bacterial sinusitis, pneumonia, H. pylori infections, urinary tract infections, chronic prostatitis, and specific gastroenteritis types. It may also be employed with other antibiotics for tuberculosis, meningitis, or pelvic inflammatory disease when alternative therapies are limited. Levofloxacin is available in solid dosage forms, including oral, intravenous, and eye drop formulations. Nine formulations of Levofloxacin solid dosage forms were developed, incorporating Gelucire 43/01 (%), Methocel HPMC* K4M (%), and sodium bicarbonate (%). Among these, Formulation 1 exhibited a floating lag time (FLT) of 258 seconds and TFT (10hrs). V.T. Thakkar et al. concluded that Formulation 1 possesses extended drug release characteristics.[28]

Metronidiazole:

Metronidazole is a 5-nitroimidazole drug that has become the mainstay in the treatment of anaerobic infections worldwide Metronidazole, classified as

a nitroimidazole antimicrobial agent, is part of a drug class that shares similar mechanisms of action. These medications are commonly employed to treat analogous medical conditions, particularly infections. Antimicrobials, such as nitroimidazole agents, are utilized to combat infections caused by bacteria and protozoa. Metronidazole tablets function by eradicating the bacteria or protozoa responsible for the infection, thereby alleviating the infection symptoms. Six formulations of Metronidazole tablets were developed, incorporating main constituents such as HPMC-K4M, sodium alginate (medium viscosity), sodium alginate (low viscosity), locust gum, guar gum, carbopol 974P, NaHCO3, and Avicel.The floating lag time (FLT) for these formulations is as follows: M1 (2 seconds), M2-M5 (1 second each), and M6 (7200 seconds). Furthermore, all formulations exhibit a floating duration exceeding 24 hours. Consequently, M1 formulation demonstrates the longest gastric retention time among all formulations.[29]

Moxifloxacin

The fluoroquinolone antibiotic doxifloxacin is used to treat a variety of bacterial infections of the stomach, sinuses, skin, and lungs. This fourth-generation fluoroquinolone offers a chance for gastro-retentive drug delivery systems to increase bioavailability and lengthen gastric transit time because of its limited absorption window, which is mostly in the proximal gut. Additionally, moxifloxacin finds utility in plague prevention and treatment. In a study by Sadak Vali et al., nine formulations were developed using ingredients such as Mannitol, HPMC K 100 M, Tragacanth Gum, POLYOX, Lactose, Sodium Bicarbonate, Magnesium Stearate, and Aerosil. These formulations exhibited floating lag times ranging from 1.2 to 5.40 minutes and total floating times ranging from >10 to >14 hours. Notably, formulation F7 demonstrated the shortest floating lag time (1.20 min) and a total floating time exceeding 14 hours, indicating promising controlled release properties.[30]

Norflaxacin

Norfloxacin, a quinolone antibiotic, is utilized for treating various bacterial infections by inhibiting bacterial growth. It selectively targets bacterial infections and lacks efficacy against viral ailments like the common cold or flu. Prudent antibiotic usage is essential to maintain efficacy for future infections. The sustained release formulation aims to release the drug throughout the gastrointestinal tract. CHINTAN AUNDHIA et al. developed four formulations using HPMCK4M, PVPK30, NaHCO3, Citric acid, Mg stearate, and Talc as main ingredients. The floating lag times (in seconds) for the formulations are F1 (182), F2 (155), F3 (129), and F4 (170), with floating times ranging from 10 to 12 hours. Their analysis suggests that the third formulation exhibits favorable controlled release properties.[31]

Oflaxacin

One of the top five most prescribed antibiotics in Nepal is ofloxacin, a common fluoroquinolone antibiotic. It works against a variety of Gram-positive and Gram-negative pathogens with broad-spectrum activity. Because of its biological half-life, which is between five and six hours, frequent administration is required, which might result in problems including patient non-compliance and fluctuations in plasma levels. Controlled-release dose versions of ofloxacin are preferred to solve these issues. The bioavailability of ofloxacin is significantly influenced by gastrointestinal physiology. It demonstrates high solubility in the acidic environment of the stomach, facilitating preferential absorption in the upper gastrointestinal tract. However, precipitation occurs in the alkaline environment of the intestine, reducing absorption. Consequently, J. Padmavathy et al. developed a gastroretentive floating drug delivery system for ofloxacin.Their study involved formulating six formulations using polymers,

lactose, sodium bicarbonate, PVP K 90, isopropyl alcohol, talc, aerosol, and magnesium stearate as primary constituents. The floating lag times ranged from 4.5 to 6 seconds, with total floating times spanning 10 to 12 hours. Among these formulations, they identified the second formulation as possessing controlled-release properties suitable for a dosage form.[32]

Curcumin

A common coloring and flavoring ingredient in South Asian cuisines is curcumin, a pigment found in the Curcuma species. It has been used traditionally to treat a wide range of illnesses, including rheumatism, sinusitis, cough, diabetic sores, biliary diseases, and anorexia. Extensive research has revealed a wide range of biological and pharmacological activities of curcumin, including anti-inflammatory, antioxidant, antimutagenic, anticarcinogenic, anticoagulant, antiarthritic, antibacterial, antifungal, antiprotozoal, antiviral, anti-Alzheimer, anti-psoriatic, and neuroprotective properties. Curcumin's low gastrointestinal absorption and bioavailability, however, limit its medicinal usefulness. In addition to curcumin prodrugs, methods for improving solubility include complexation with macromolecules such as polysaccharides, cyclodextrins, and gelatin, as well as solid dispersions with polyvinyl pyrrolidone. The goal of Shishu et al. was to increase curcumin's water solubility in an acidic pH by combining it with β-cyclodextrin (β-CD). They created a sustained release floating drug delivery system (FDDS) to enhance absorption, target stomach cancers, and avoid alkaline breakdown in the intestine. Floating tablets of curcumin (CI) and curcumin β-cyclodextrin complex (CII) were created using HPMC K15M (200 mg), dicalcium phosphate (20 mg), sodium carbonate (40 mg), citric acid (20 mg), Carbopol 934P (25 mg), and magnesium stearate (10 mg). The two formulations showed similar total floating times (TFT) and floating lag times (FLT), ranging from 10 to 12 minutes and 16 to 17 hours, respectively. Therefore, both formulations appear promising for use as drug delivery systems with controlled release. [33]

Luteolin

Poly (ethyl acrylate), trimethylammonium-ethyl methacrylate chloride, and methyl methacrylate comprise the polycations referred to as Eudragit RS (EGT) polymers. These polymers, which are present in varying ratios, are produced from acrylic and methacrylic acids or their esters, such as butyl ester or dimethyl aminoethyl ester. Hydrophilicity is increased when quaternary ammonium groups are added to the polymer structure. Eudragit RS polymers are soluble in acidic digestive fluids due to their low percentage of hydrophilic quaternary ammonium groups (5%). Nonetheless, their capacity to create a matrix structure, swell without altering pH, and display permeability makes them perfect for drug delivery systems that use sustained release matrix technology. Common plant flavonoid luteolin (LUT), which possesses anti-inflammatory, antioxidant, anti-cancer, and anti-microbial properties, is involved in a number of biological processes. Microsponge systems are spherical structures that have channels that connect to one another to provide longer-lasting drug administration. These systems typically have a diameter of 5 to 300 µm with hole sizes of less than 0.25 µm. Microsponge systems are adaptable and come in a range of dose forms for topical (such as gel, emulsion) and systemic (such as tablets, capsules) administration. In comparison to other gastroprotective systems, microsponge systems have a number of benefits, such as low dose dumping, high entrapment efficiency (50–60%), improved drug stability, controlled and sustained release profiles, free-flowing characteristics, self-sterilization, and suitability for a variety of ingredients and vehicles. These advantages

translate into benefits for the pharmaceutical and financial industries.Five formulations containing distilled water, Tween 80, acetone, EGT, and EC as the main ingredients were created for the luteolin formulation. The total floating time (TFT) for each formulation was 8 hours..[34]

Artemisia Princeps Extract

For a very long time, Asian nations have utilized Artemisia princepsPampanini (Asteraceae), which is also referred to as "Sajabalssuk" in Korea, to treat a variety of ailments, including cancer, microbiological infections, colic pain, diarrhea, uterine metrorrhagia, metritis, vomiting, ulcers, and dysmenorrhea. It can be taken on its own for minor illnesses or in conjunction with other medicinal plants or conventional therapies for moderate to severe conditions. The main active ingredient found in Artemisia plants, euphemilin, has been shown to have a variety of biological properties, including cytoprotective, anti-oxidative, pro- and anti-apoptotic, and anti-inflammatory properties. Numerous biological actions, such as anti-inflammatory, antibacterial, anti-asthmatic, anti-cancerous, and neuroprotective properties, are exhibited by Artemisia species.When applied topically to experimentally produced gastrointestinal, hepatic, and pancreatic lesions, the ethanol extract of A. asiatica exhibits anti-oxidative and anti-inflammatory properties; nevertheless, dicoumarol may cause coagulopathy. Since dicoumarol cannot be extracted using isopropanol, an isopropanol extract was used in the current investigation to reduce this danger. Additionally, the isopropanol extract of A. princeps has higher quantities of eupatilin and jaceosidin than the ethanol extract does, which could result in pharmacological action that is more effective and less harmful or unpleasant side effects. Even though A. princeps has shown a range of biological activities, including anti-cancer, immunomodulatory, anti-oxidant, anti-diabetic, and antiatherosclerotic effects, the tablets' formulation contained IPAP, hydroxypropyl cellulose, MicroceLac® 100, lactose hydrate, microcrystalline cellulose, sodium bicarbonate, Eudragit® E100, croscarmellose sodium, calcium silicate, Aerosil® 200, carbomer, hypromellose, magnesium stearate, and talc.Out of all the formulations examined, Formulation 3 had the longest stomach retention time (FLT) at 10 minutes, F2 at 45 minutes, and F4 at 12 minutes..[35]

Tabulation shows the FLT and TFT of Anti-bacterial drugs :

S.NO.	Drug	FLT	TFT	Formulation
1	Berberine Hydrochloride	15.33 min	3 min	4
2	Cefadroxil	78 sec	6 hours	8
3	Cefiximetrihydrate	49 sec	>9 hours	7
4	Cefuroxime axetil	2.03 min	>12 hours	1
5	CefpodoximeProxetil	14 min	>12 hours	13
6	Cephalexin	4.9 sec	12 hours	5
7	Clarithromycin	74 sec	<12 hours	4
8	GemifloxacinMesylate	30 sec	12 hours	9
9	Levofloxacin	258 sec	10 hours	1
10	Metronidazole	2 sec	>24 hours	1
11	Moxifloxacin	1.2 min	>14 hours	7
12	Norflaxacin	2.9min	12 hours	3
13	Ofloxacin	4.5 sec	<12 hours	2
14	Curcumin	12 min	17 hours	1&2
15	luteolin	0 sec	>8 hours	ALL
16	Artemisia princeps	10 min	1 hour	3

CONCLUSION

The Gastro Retentive Drug Delivery Systems (GRDDS) offers increased bioavailability when compared to medications primarily active in the stomach. The floating lag time and total floating time in floating drug delivery systems is essential for drugs that require sustained release or targeted delivery to specific regions of the gastrointestinal tract. In this review we concluded that the Metronidazole drug has greater TFT(>24 hours) and less FLT(2 sec). So,among all the drugs in anti bacterial class Metronidazole is the best formulation for controlled and prolonged release action.

REFERENCES

1. Shinde Jitendra V, Malshikare Swapnali S and Chavan rajashree S. A Review on Floating Drug Delivery System. Published in International Journal of Trend in Scientific Research and Development (ijtsrd). 2020;4(3):427-433.
2. IyanSopyan, Sriwidodo, RetnoWahyuningrum and Norisca Aliza P. A review: Floating drug delivery system as a tool to improve dissolution rate in gatric. Int J App Pharm. 2020;12(4): 51-54.
3. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS Pharm Sci Tech. 2005;6(3):E372-E390.
4. Patil H, Tiwari RV, Repka MA. Recent advancements in mucoadhesive floating drug delivery systems: A mini-review. J Drug DelivSci Technol. 2016;31:65-71.
5. Singh BN, Kim KH. Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. J Control Release. 2000;63(3):235-259
6. Hancock BC, Christensen K, Clas SD; Microscale Measurement of the Mechanical properties of compressed Pharmaceutical powders, part 1: The Elasticity and Fracture Behavior of Microcrystalline Cellulose. Int. j. Pharm., 2000; 209: 27-35.
7. Introduction of Floating Tablet By: Pharma Tips | Views: 6868
8. Jaimini M. Formulation and Evaluation of Famotidine Floating Tablets. Articale, February 2007; with 585 reads DOI:10.2174/156720107779314730.
9. Khan F, Ibn Razzak SM, Khan ZR, Azad MA, Chowdhury JA, Reza S. Theophylline loaded gastroretentive floating tablets based on hydrophilic polymers: preparation and in vitro evaluation. Pak J Pharm Sci,2009;22(2): 155–161. [PubMed].
10. MahdeFormulation and Evaluation of Gastroretentive Floating Tablet of Bromocriptine Mesilate. Int J Pharm Sci, Vol 5; Sippl, 361-365.
11. Manimaran V.; Lecturer Department of Pharmaceutics SRM College of Pharmacy.
12. Mashadi AB, Newton JM; Assessment of the Mechanical properties of compacted sorbitol. Instant. J.Pharm. Pharmacol., 1987; 39: 67.
13. Ohwoavworhua F, Adelakun T; phosphoric acid- mediated depolymerisation and decrystallization of low crystallinity cellulose and some physicochemical properties. tropical journal of Pharmaceutical research, 2004; 4(2): 509- 516.
14. Patel Intragastric floating drug delivery system of cefuroxime axetil: In vitro
15. Maddiboyina B., Asthana A., Asthana G.S., Singh S., Ramya M., Sunnapu O., Kotla N. Formulation and characterization of polycarbophil coated mucoadhesive microspheres of repaglinide. J. Pharmaceut. Sci. Res. 2015
16. A. Kaushik, A. Tiwari, and A. Gaur, “Role of excipients and polymeric advancements in preparation of floating drug delivery systems,” Int. J. Pharm. Investig., vol. 5, no. 1, pp. 1–12, 2015, doi: 10.4103/2230- 973x.147219.

17. Goit LN, Yang S. Treatment of Hypertension: A Review. Yangtze Medicine. 2019;03(02):101–23.

18. Ramesh M. Review on Hypertension. International Journal of Current Trends in Pharmaceutical Research [Internet]. 2013;1(2):88 Available from: https://www.researchgate.net/publication/255964632

19. Anayantiarianto, hakim bangun*, adeyohana, jansensilalahi, "floating gastroretentive of amoxicillin using hard alginate capsules and its antibacterial activities " asian journal of pharmaceuticl and clinical research, vol 10, issue 5, 2017.

20. Jun Ji, Xin He, Xiao-Lin Yang, Wen-Juan Du, Cheng-Long Cui, Ling Wang, Xue Wang, Chun-Feng Zhang, and Chang-Run Guo, "The In vitro/vivo Evaluation of Prepared Gastric Floating Tablets of Berberine Hydrochloride " AAPS PharmSciTech. 2016.

21. Rajesh Kumar Jatav, Manish Bodana and Rakesh Kumar Jatav, "Formulation and Evaluation of Floating Tablet of Cefadroxil" Current Research in Pharmaceutical Sciences 2015; 05 (03): 95-105.

22. Pradip P Gade, Mohd. Majid Iqbal and K Sreenivasa Rao, "Development and In-Vitro Evaluation of Gastro-Retentive Floating Drug Delivery System of CefiximeTrihydrate" Research J. Pharm. and Tech.2 (3): July-Sept.

23. GovikariKoteshwar Rao a , Praveen Kumar Mandapalli b, *, RajendraprasadManthri c , VeerareddyPrabhakar Reddy, "Development and in vivo evaluation of gastroretentive delivery systems for cefuroxime axetil " Saudi Pharmaceutical Journal (2013) 21, 53–59.

24. L. Kukati , K. Chittimalli, and N. B. Shaik, " Formulation and Evaluation of Floating Tablets of CefpodoximeProxetil " J. Sci. Res. 6 (3), 563-579 (2014).

25. Lifang Yina, Chao Qin, Kaisheng Chen, Chunli Zhu, Hui Cao , Jianping Zhou, Wei He , Qiang Zhang, "Gastro-floating tablets of cephalexin: Preparation and in vitro/in vivo evaluation " International Journal of Pharmaceutics 452 (2013) 241–248.

26. Priyanka Shukla*, Ajay Yadav, "formulation and evaluation of floating drug delivery system of clarithromycin tablets " Indian Journal of Research in Pharmacy and Biotechnology,vol1(4), 2013.

27. D. V. R. N. Bhikshapathi1*, B. Haarika, S. Jyothi Sri and K. Abbulu, "Preparation and Evaluation of GemifloxacinMesylate Floating Matrix Tablets in Healthy Human Volunteers " International Journal of Pharmaceutical Sciences and Nanotechnology, Vol 10, 2017.

28. V.T. Thakkar,*, P.A. Shah , T.G. Soni , M.Y. Parmar , M.C. Gohel and T.R. "Gandhi , Fabrication and evaluation of levofloxacin hemihydrate floating tablet", Research in Pharmaceutical Sciences, October 2008; 3(2): 65-72.

29. laila h. emara1, aya r. abdou, ahmed a. el-ashmawy1, nadia m. mursi, "preparation and evaluation of metronidazole sustained release floating tablets", International Journal of Pharmacy and Pharmaceutical Sciences ISSN-0975-1491 ,Vol 6, Issue 9, 2014.

30. C. Sadak Vali, Abdullah Khan , M. PratibhaBharati , AsmaKhanam , M. Shaoukhatulla , M. Pradeep Kumar , B. NageswaraNaik and S. Siva Prasad, " fabrication, characterization and optimization of gastro retentive floating tablets of moxifloxacin using natural and semisynthetic polymers " ejpmr, 2020,7(10), 595-603.

31. Chintanaundhia* ,nirmal shah, snehalpatel, ashimkumarsen, priyankpatel, "Formulation and Evaluation of Floating Tablet of Norfloxacin " International Journal of Pharmaceutical Research | Jan - Mar 2020.

32. J. padmavathy , * d. saravanan , d. rajesh , " formulation and evaluation of ofloxacin floating tablets using hpmc " int j pharm pharmsci, vol 3, issue1, 170¬173.

33. Shishu, Neeta Gupta, and Nidhi Aggarwal, "Bioavailability Enhancement and Targeting of Stomach Tumors Using Gastro-Retentive Floating Drug Delivery System of Curcumin " AAPS PharmSciTech, Vol. 9, No. 3, September 2008 (2008).

34. Mohammed Jafar , , Mohammed Salahuddin , MohdSajjad Ahmad Khan , YasirAlshehry , NazarRadwanAlrwaili , Yazeed Ali Alzahrani , Syed Sarim Imam and Sultan Alshehri , "Preparation and In Vitro-In Vivo Evaluation of Luteolin Loaded GastroretentiveMicrosponge for the Eradication of Helicobacter pylori Infections", Pharmaceutics 2021, 13, 2094. https://doi.org/10.3390/pharmaceutics13122094 https://www.mdpi.com/journal/pharmaceutics

35. Joo -ilkim,sang -wookpark,jhong -jaelim, se-ilsohn,ji-sun shin,sangcheol par ,young pyojang,eunkyoungchung, hong -woo leekyung –taelee," Gastroprotective effects of the isopropanol extract of Artemisia princeps and its gastroretentive floating tablets on gastric mucosal injury", Acta Pharm. 67 (2017) 479–494 https://doi.org/10.1515/acph-2017-0037.

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