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Formulation and Evaluation of Gastroretentive Floating Tablet of Ciprofloxacin

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Abstract:
the present investigation aimed to develop and evaluate a gastro retentive effervescent floating tablet of ciprofloxin hydrochloride to enhance gastric residence time and sustain drug release in the upper gastrointestinal tract.ciprofloxacin exhibits site-specific absorption in the stomach and proximal small intestine.therefore prolongation of gastric retention is expected to improve its bioavailability and therapeutic efficacy.an effervescent floating drug delivery system(FDDS) was formulated using sodium bicarbonate as a gas- generating agent and hydrophilic matrix-forming polymer to ensure buoyancy and controlled drug release. Tablets were prepared by direct compression method and evaluated for precompression parameters including angle of repose, bulk density, tapped density. Hausner's ratio and carr's index to assess flow properties. Post compression evaluation involved hardness,friability,weight variation,thickness,drug content uniformity, floating lag time,total floating time,swelling index and in vitro dissolution studies in 0.1N HCl .the study concludes that the developed gastro retentive effervescent floating tablet of ciprofloxacin provides prolonged gastric retention with controlled drug release fllowing diffusion -controlled drug release,thereby offering a promising approach for improving bioavailability and patient compliance in antibacterial therapy.

Keywords: ciprofloxacin, hydrochloride, gstro retentive drug delivery system, floating tablet,HPMC,effervescent system.

1. Introduction[4]:

1.1 Gastroretentive Drug Delivery Syestem :

Gastro retentive Drug Delivery Systems (GRDDS) are advanced oral formulations designed to prolong gastric residence time (GRT) and improve the bioavailability of drugs with narrow absorption windows or those acting locally in the upper GI tract. By staying in the stomach for an extended period, these systems enhance therapeutic efficacy and patient compliance.

There Are 4 Types;

1. Floating Drug Delivery System
2. High Density Gastroretentive System
3. Swelling Gastroretentive System
4. Mucoadhesive Gastroretentive Drug Delivery System

1.2 Floating Drug Delivery System[6]:

Floating drug delivery systems are a type of gastro retentive technology designed to prolong the stay of a dosage form in the stomach. These systems float on the gastric contents, releasing the drug slowly, which improves bioavailability for drugs with narrow absorption windows in the upper GI tract. Various approaches include effervescent systems, non-effervescent systems, hollow microspheres, and matrix systems, each leveraging different mechanisms to achieve buoyancy and controlled release.

1.3 Swelling Gastroretentive Drug Delivey System: Swelling gastro retentive systems are designed to expand in the stomach, increasing their size and staying longer in the gastric environment. This prolongs drug release and improves bioavailability for drugs absorbed in the upper GI tract. These systems typically use swellable polymers like HPMC or alginates to achieve gastric retention and controlled.

Mucoadhesive Drug Delivery System: Mucoadhesive Drug Delivery Systems (DDS) use polymers that stick to the mucosal surface, enabling targeted delivery or sustained release. These systems can improve bioavailability and efficacy for drugs with upper GI absorption windows.

High Density Drug Delivery System: High-Density Drug Delivery Systems (DDS) are designed to be denser than gastric contents, causing them to sink and stay in stomach folds. This prolongs gastric retention and drug release, often using materials like barium sulphate or iron powder to achieve the desired density.

Floating drug delivery system Floating drug Delivery Systems (FDDS) are a type of gastro rete Page:01 delivery system (GRDDS) designed to prolong the residence time of dosage forms in the stomach. These systems remain buoyant on the gastric contents due to their low density compared to gastric fluids, allowing controlled and sustained drug release in the stomach or upper part of the small intestine.

Buoyancy: Once in the stomach, the body temperature causes the liquid to gas inflating the chamber and reducing the device's overall density to less than that of gastric fluids (1.004 gm/ml).

Controlled Release: While floating, the drug is released slowly from the system into the stomach, prolonging its residence time (GRT)

2. Mechanism of action:

1. The tablet comes in contact with gastric fluid (acidic pH).
2. Sodium bicarbonate reacts with hydrochloric acid (or organic acids like citric/tartaric acid).
3. CO_2 gas is released inside the tablet matrix.
4. The gas gets trapped in the swollen polymer (e.g., HPMC).
5. Tablet density becomes lower than gastric fluid, so the tablet floats.

Types:

2.1 Single-layer/Bilayer tablets: Often designed as floating matrices

2.2Floating capsules: Contain effervescent mixtures.

2.3Multiple-unit systems: Beads or pellets that provide consistent, uniform drug release.

1. Gas Generating System
2. Volatile Liquid System

Gas Generating System: Gas-generating systems in Gastro retentive Drug Delivery Systems (GRDDS) utilize effervescent reactions, typically between carbonates/bicarbonates and organic acids (citric/tartaric acid), to release carbon dioxide (CO2) upon contact with gastric fluids. The gas is trapped in a polymer matrix, decreasing the density and enabling the formulation to float, thus extending retention

Mechanism: The reaction produces (CO2) gas bubbles that get entrapped in the hydrocolloid layer (e.g.,

HPMC, chitosan) of the system, reducing its specific gravity to less than 1, allowing it to float on gastric contents

Effervescent Agents: Sodium bicarbonate, calcium carbonate, tartaric acid, and citric acid are commonly used to produce co2

Advantages:

1. Enhanced bioavailability, improved therapeutic efficacy, and prolonged residence time for drugs with narrow absorption windows.
2. Produces carbon dioxide (CO_2) in gastric fluid, enabling immediate tablet flotation.
3. Does not require complex manufacturing equipment.
4. Provides controlled and sustained drug release.

Volatile Liquid System: Volatile liquid-containing systems are a type of Effervescent Floating Drug Delivery System (FDDS) designed to improve gastro retention by incorporating volatile liquids (such as cyclopentane or ether) that evaporate at body temperature 37. These systems use the resulting gas pressure to inflate a chamber, ensuring the device remains buoyant on the stomach contents.

2.3.1Types Of Volatile Liquid System :

1.Inflatable Gastrointestinal Devices: These incorporate a deformable, hollow polymeric bag containing the volatile liquid

2.Intragastric-Osmotically Controlled Systems: These are more complex using a flexible module with pressure membrane to separate the drug

2.4 Non-Effervescent System: Non-effervescent floating drug delivery systems (FDDS) are gastro retentive dosage forms that stay buoyant in the stomach using swellable, gel-forming polymers (e.g., HPMC, CMC) or low-density materials rather than gas-generating agents. They are designed to increase gastric residence time for drugs with narrow absorption windows or those requiring local action in the upper gastrointestinal tract.

Mechanism: Upon contact with gastric fluid, the polymers hydrate, swell, and form a gelatinous, low-density layer that entraps air, allowing the system to float

3. EXPERIMENTAL Methodology:

3.1 Estimation of Ciprofloxacin: Ciprofloxacin is commonly estimated by the UV–visible spectrophotometric method. The method is based on the ability of ciprofloxacin to absorb ultraviolet light and obey Beer–Lambert's law within a suitable concentration range. A known quantity of the drug or tablet sample is dissolved in an appropriate solvent such as 0.1 N HCl or phosphate buffer, and the absorbance is measured at its maximum wavelength, usually around 276 nm. The concentration of ciprofloxacin in the sample is then calculated by comparing the absorbance with a standard calibration curve.

3.1.1 Preparation Of Ciprofloxin Floating Tablet:

Step 1: Weighing:Accurately weigh Ciprofloxacin and all excipients (HPMC, sodium bicarbonate, lactose monohydrate, sodium lauryl sulfate, and talc).

Step2:Drug–Polymer Mixing: Mix Ciprofloxacin with hydroxypropyl methylcellulose (HPMC) to form a uniform matrix.

Step 3:Addition of Gas-Generating Agent: Add sodium bicarbonate to the blend and mix gently to ensure uniform distribution.

Step 4:Addition of -Diluent and Surfactant: Add lactose monohydrate as diluent and sodium lauryl sul-

fate as wetting agent; mix thoroughly.

Step5: Lubrication: Finally, add talc as lubricant and blend lightly.

Step 6: Compression: Compress the final blend into tablets using a tablet compression machine.

3.2 Evolution Studies:

3.2.1Pre Evolution Test :

- **Angle of Repose:** Determines flowability of the powder blend. It is measured by the funnel method.
- **Bulk Density**: Indicates the packing ability of powder under gravity.
- **Tapped Density**: Represents the powder density after mechanical tapping.
- **Carr's Compressibility Index**: Evaluates compressibility and flow characteristics of powder blend.
- **Hausner's Ratio:** Indicates interparticle friction and flowability.

2.2.2Post Evolution Test:

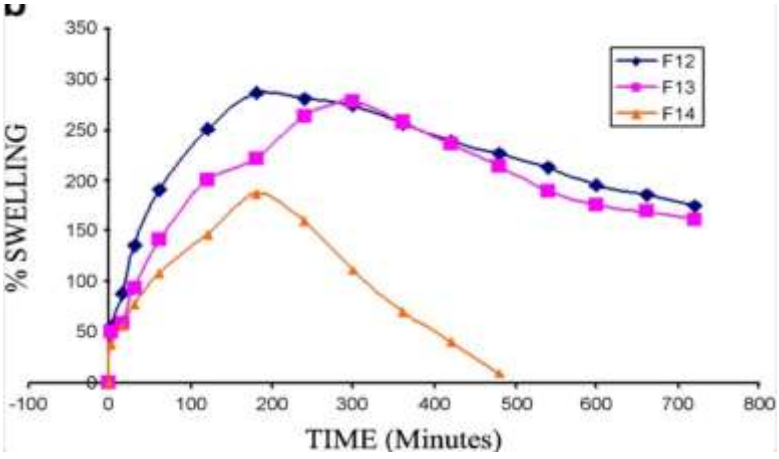
1. **Physical Appearance** Tablets were evaluated for color, shape, surface texture, and presence of defects.
2. **Weight Variation:** Test Ensures uniformity of tablet weight as per pharmacopeial limits.
3. **Thickness and Diameter:** Measured using Vernier calipers to maintain uniform tablet dimensions.
4. **Hardness Test Determines:** mechanical strength using Monsanto or Pfizer hardness tester.
5. **Friability Test:** Assesses tablet resistance to abrasion using Roche friability.
6. **Drug Content Uniformity:** Ensures uniform distribution of Ciprofloxacin in tablets.
7. **Floating Lag Time (FLT):** Time taken by tablet to rise to the surface of dissolution medium.

4. RESULTS AND DISCUSSION:

Sno:	Concentration	Absorbance
1	2	0.142Ab
2	4	0.286Ab
3	6	0.431Ab
4	8	0.588Ab
5	10	0.721Ab

Table 1: represents the standard calibrated data of ciprofloxacin tablet

Observation: The absorbance of Ciprofloxacin increases linearly with concentration and follows Beer–Lambert's law in the concentration range of 2–ug



Graph 1: Represents The Swelling Percentage with Time.

Sn0	Parameter	Formula	Range
1	Angle of response	Tan Teta=h/r	<30 degree
2	Bulk density	Db=M/V b	75
3	Tapped density	Dt=M/Vt	50
4	Cars index %	(Dt-Db)/Dt*100	5-15%
5	Hausner ratio	Dt/Db	<1.25

Table 2: represents the pre-evolution test for ciprofloxacin

Sno	Test	Specification
1	Weight Variation	Ip
2	Thickness	Uniform +/-5
3	Hardness	5-8kg
4	Friability	<1%
5	Drug Content	95-105
6	Floating Lag Time	60
7	Swelling Index	Progress Increase
8	In Vitro Drug Release	Sustaine Upto24hr

Table 3: represents the post evolutionary parameter of ciprofloxacin tablet.

Formulations with grades show poor swelling and sustained action due to the low viscosity. These polymer grades are unable to withhold swelling produced by a swelling agent in the tablets due to the poor gelling/viscosity. The showed good tablet integrity, swelling, and sustained release of ciprofloxacin HCl.Swelling agents used in this study are super disintegrating agents. The immediate tablet disintegration is due to the swelling nature of these agents. This character is utilized in the preparation of floating, swellable, and extended-release dosage form of ciprofloxacin HCl.

Sodium bicarbonate in the acidic environment reacts with the acid and produces carbon dioxide. The evolved gas will get entrapped in the matrix leading to floating of the tablet. The floating lag time decreased as the concentration of the sodium bicarbonate increased. The formulations containing different swelling agents with optimized concentration of polymer, swelling agent and sodium bicarbonate show different lag time. This may be due to variation in the mechanism of action of different swelling agents. produced its action by both swelling and wicking in the presence of water, whereas SSG shows only swelling. Wicking is caused due to the porosity and capillary action because of which the density of dosage form is reduced.

The regression coefficient (R2) values of release data of all formulations obtained by curve fitting method for zero-order, first-order, and Higuchi model are reported in Table. Most of the formulations follow the zero order and Higuchi model.The formulations that contain polymer concentration 25% w/w that of the drug show more retarded release, release in 12 h of the formulations F1, F2, F3, respectively. The polymer concentration is optimized to 15% w/w that of drug. Further, the change in swelling agent concentration changes the drug release in formulation. The decrease in swelling agent concentration retards the drug release.

The drug release is also dependent upon the type of swelling agent in the which releases. Increase in sodium bicarbonate concentration increases release rate. The formulations containing SSG (F2 and F3) show the good swelling nature, but the maximum swelling will occur at later hours, i.e., in formulation F2, swelling 233.36% is obtained in 24 h interval, and for the maximum swelling 178.73 is obtained in 5-h interval. The swelling at later hours may be due to gelling of SSG with water. shows poor swelling nature. The mechanism of drug release is predicted by using equation.

The n value of optimized formulation and that of all formulations is between 0-5 This indicates that the drug release depends on swelling, erosion, and diffusion. All formulations follow the non-/anomalous type of diffusion. in vivo nature of the tablet is observed in the radiographic pictures at different time intervals. Initially, the tablet appeared very clear, but later on, the tablet appeared dull, due to swelling of the tablet. The gastric retention is due to floating in the first few hours, and later, it is due to obstruction of the tablet at duodenum as seen in Fig..

5. CONCLUSION:

5.1 Conclusion of Ciprofloxacin Effervescent Tablet:

We conclude that Gastro retentive Floating tablet of Ciprofloxacin to be highly effective, superior of Immediate release dosage form. Gastro retentive system prolongs the gastric residence time & sustains the release of ciprofloxacin over 12-24 hrs. more stable in acidic media & absorbed and absorbed primarily in stomach and proximal small intestine. The prolonged release & proximal daily dosing, improved patient nature allows once compliance & reducing the frequency of administration. Finally, Ciprofloxacin is immediately releasing tablet & ensuring better efficacy by Maintaining therapeutic levels. in stomach for an Extended period.

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