Formulation and Evaluation of Floating Tablets of Ciprofloxacin Hydrochloride

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Abstract-The present study focuses on the formulation and evaluation of floating tablets containing Ciprofloxacin Hydrochloride, developed via direct compression technique. Various concentrations of Mimosa gum were employed as a natural polymeric matrix, while citric acid acted as a stabilizer and sodium bicarbonate served as the effervescent agent to facilitate buoyancy. Magnesium stearate and lactose were incorporated as lubricants and diluents, respectively. Each formulation underwent thorough assessment of both pre-compression and post-compression parameters to ensure optimal tablet characteristics. In vitro dissolution studies revealed that Formulation F4 demonstrated a drug release of 68.70% within 6 hours, indicating efficient and sustained drug delivery. Based on its performance, Formulation F4 holds strong potential for further advancement through bioavailability studies, pharmacokinetic profiling, and in vivo evaluations, positioning it as a promising candidate for novel gastro-retentive drug delivery systems.

Key-Word:- Ciprofloxacin Hydrochloride, floating tablet, mimosa gum, floating lag time, in vitro drug release.

INTRODUCTION

Oral formulations have earned a significant place among the various dosage forms due to the ease of administration, patient compliance, and flexibility in formulation. Gastro retentive floating drug delivery systems have emerged as efficient approaches for enhancing the bioavailability and controlled delivery of various therapeutic agents.

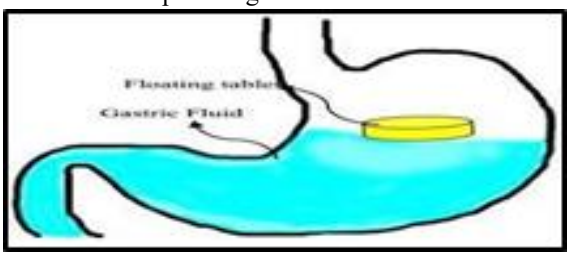


Fig-1.Tablet in Gastric Fluid

Different types of controlled drug delivery systems have been speculated for several routes of administration, as they require less frequent drug administration, provide more efficient therapeutic profile, reduce the incidence of adverse effects, etc. These systems achieve as well as maintain drug concentration within therapeutically effective range needed for treatment only when taken several times a day. Floating matrix systems appear to be a very attractive approach in controlled-release system. Floating matrix-type formulations are prepared from either swell able hydrophilic polymers and/or non swellable lipophilic excipients, like waxes and lipids, with carbonate or bicarbonate as the gas generating agent. Ciprofloxacin HCl is a broad-spectrum antibiotic active against both Gram-positive and Gram-negative bacteria. The biological half-life of ciprofloxacin HCl is 3–5 h. The drug should be administered twice a day. The dosage is equivalent of 250–750 mg of ciprofloxacin twice daily (116 mg of ciprofloxacin hydrochloride is approximately equivalent to 100 mg of ciprofloxacin). While the system is floating on gastric contents, drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This result is an increase in gastric residence time (GRT) and a better control of fluctuations in plasma drug concentrations. Floating systems can be classified into two types, non-effervescent system and effervescent systems. Longer residence time in the stomach could be advantageous for local action in the upper part of small intestine, for example, treatment of urinary Tract Infection (UTI) disease.

- Basic Gastrointestinal Tract Physiology

Anatomically the stomach is divided into 3 regions fundus, body, and antrum (pylorus). The proximal part

made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington.

1. Phase 1 (basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled toward the pylorus in a suspension form.

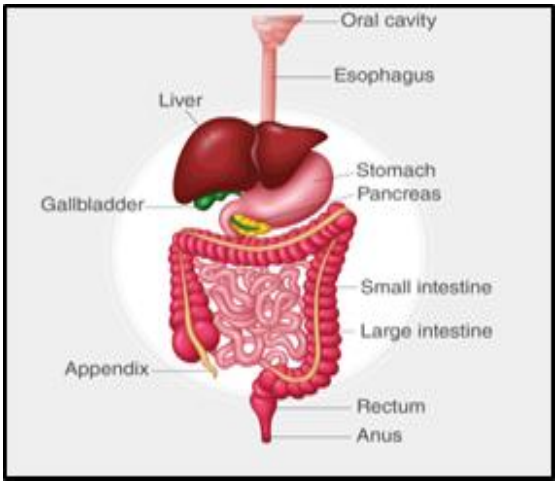


Fig-2. Gastrointestinal Tract

➢ Factors Affecting Gastric Retention

Gastric residence time of an oral dosage form is affected by several factors. To pass through the pyloric valve into the small intestine the particle size should be in the range of 1 to 2 mm. The pH of the stomach in fasting state is -1.5 to 2.0 and in fed state is 2.0 to 6.0. A large volume of water administered with an oral dosage form raises the pH of stomach contents to 6.0 to 9.0. Stomach doesn't get time to produce sufficient acid when the liquid empties the stomach; hence generally basic drugs have a better chance of dissolving in fed state than in a fasting state. It does not make any difference whether the meal has high protein, fat, or carbohydrate content as long as the caloric content is the same. However, increase in acidity and caloric value slows down gastric emptying time. Biological factors such as age, body mass index (BMI), gender, posture, and diseased states (diabetes. Charon's disease) influence gastric emptying. In the case of elderly persons, gastric emptying is slowed down. Generally females have slower gastric emptying rates than males. Stress increases gastric emptying rates while depression slows it down.

DRUG PROFILE

The following materials that were pharma grade or the best possible laboratory reagent were used as supplied by the manufacturer without further purification or investigation.

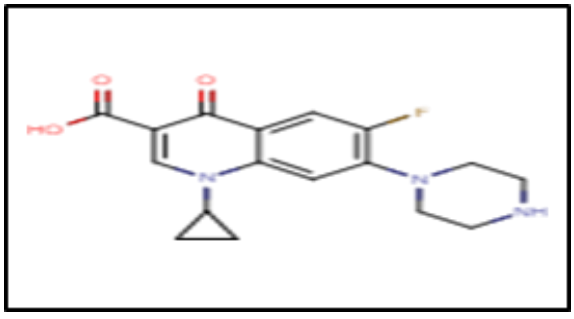
➢ Drug and Excipient Profile

- DRUG PROFILE

Name of Drug: - Ciprofloxacin HCL Molecular Formula: - $C_{17}H_{18}FN_3O_3$ Molecular Weight: - 331.34 g/mol. Category: - Antibacterial drugs.

IUPAC Name: - 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1, 4-dihydroquinoline-3- carboxylic acid

Structural Formula:-



Solubility: - The drug was mixed in ethanol, methanol, water and acetone. The drug was more soluble in water.
Melting point: - 310.10
Protein Binding: - 20% - 40%
Half Life: - 2.5 to 3.3
Mechanism of action:-
Ciprofloxacin acts on bacterial topoisomerase II (DNA gyrase) and topoisomerase
IV. Ciprofloxacin's targeting of the alpha subunits of DNA gyrase prevents it from supercoiling the bacterial DNA which prevents DNA replication.

Table no. 1: Drug Interaction

DRUG	INTERACTION
1,2-Benzodiazepine	The metabolism of 1, 2-Benzodiazepine can be decreased when combined with Ciprofloxacin.
Abacavir	Ciprofloxacin may decrease the excretion rate of Abacavir which could result in a higher serum level.
Abemaciclib	The metabolism of Abemaciclib can be decreased when combined with Ciprofloxacin.
Abiraterone	The metabolism of Abiraterone can be decreased when combined with Ciprofloxacin.
Acalabrutinib	The metabolism of Acalabrutinib can be decreased when combined with Ciprofloxacin.

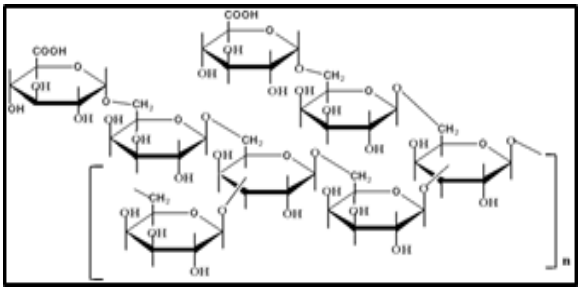
Metabolism:-
Ciprofloxacin is primarily metabolized by CYP1A2. The primary metabolites Oxo ciprofloxacin and sulociprofloxacin make up 3-8% of the total dose each. Ciprofloxacin is also converted to the minor metabolites desethylene ciprofloxacin and formyl ciprofloxacin. These 4 metabolites account for 15% of a total oral dose. There is a lack of available data on the enzymes and types of reactions involved in forming these metabolites.

Indication:-
Ciprofloxacin is only indicated in infections caused by susceptible bacteria. Ciprofloxacin immediate release tablets, oral suspensions, and intravenous injections are indicated for the treatment of skin and skin structure infections, bone and joint infections, complicated intra- abdominal infections, nosocomial pneumonia, febrile neutropenia, adults who have inhaled anthrax, plague, chronic bacterial prostatitis, lower respiratory tract infections including acute exacerbations of chronic bronchitis, urinary tract infections, complicated urinary tract infections in paediatrics, complicated pyelonephritis in paediatrics, and acute sinusitis.

Over dose
Patients experiencing an overdose may present with nausea, vomiting, abdominal pain, crystalluria, nephrotoxicity, and oliguria. Ciprofloxacin overdose typically leads to acute renal failure. An overdose may progress over the next 6 days with rising serum creatinine and BUN, as well as anuria.
Patients may require prednisone therapy, urgent haemodialysis, or supportive therapy. Depending on the degree of overdose, patients may recover normal kidney function or progress to chronic kidney failure. The oral LD50 in rats is >2000mg/kg.

Side Effect
- Nausea and vomiting
- Diarrhea
- Changes in liver function tests
- Skin rash
- Yeast infection (extended-release tablets)

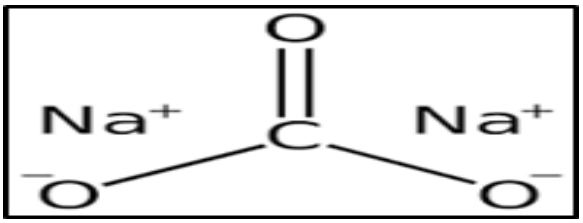
MIMOSA GUM:



a) Non-proprietary name Vachellia nilotica Acacia nilotica Babul
b) Synonyms – Babul, Thorn mimosa, Egyptian acacia, Thorny acacia, Senegalia Senegal, Acacia Senegal
c) Chemical name – Acacia, Senegal
d) Density - 1.35-1.49
e) Molecular weight/ Molar mass≈ 0.25×106
f) Boiling point- > 250ºC
g) Melting point- 0 – 100oC
h) Structural Formula-

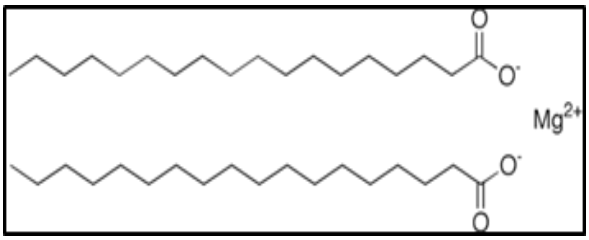
i) CAS number- 9000-01-5
j) Functional category –
Gum Arabic is used in the food industry as a stabiliser, emulsifying agent, and thickening agent in icing, fillings, soft candy, chewing gum, and other confectionery, and to bind the sweeteners and flavourings in soft drinks.

SODIUM BICARBONATE:



a) Non-proprietary Names BP: Sodium bicarbonate
JP: Sodium bicarbonate
PhEur: Natrii hydrogenocarbonas USP: Sodium Bicarbonate
b) Synonyms
Baking soda; E500; Effer-Soda; monosodium carbonate; Vichy, sodium acid carbonate; sodium hydrogen carbonate.
c) Chemical Name: Carbonic acid, monosodium salt
d) Empirical Formula and Molecular Weight:
NaHCO 84, 01
e) Structural Formula:
f) Functional Category Alkalizing agent, therapeutic agent.
g) Stability and Storage Conditions
Sodium bicarbonate is stable in dry air but slowly decomposes in post air and should therefore be stored in a well-closed container in a wool, dry place
h) Incompatibilities
In solution, sodium bicarbonate has been reported to be incompatible with many drug substances such as ciprofloxacin, amiodarone, nicardipine, and levofloxacin.

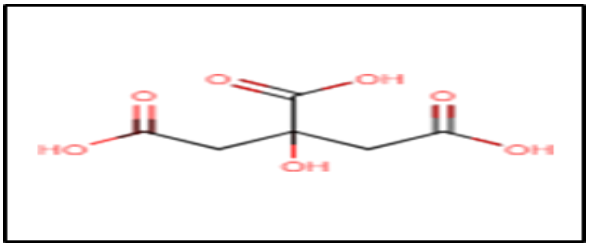
MAGNESIUM STEARATE:



a) Non-proprietary Names BP: Magnesium stearate
JP: Magnesium stearate PhEur Magnesil stearas
USPNF Magnesium stearate
b) Synonyms
Magnesium octadecanoate, octadecanoic acid, magnesium salt; stearic acid.
c) Chemical Name and CAS Registry Number: - Octadecanoic acid magnesium salt [557-04- 0]
d) Empirical Formula and Molecular Weight: - C36H70MgO4 591.34
e) Structural Formula
f) Functional Category: - Tablet lubricant
g) Description
Magnesium stearate is a very fine, light white, precipitated or led, impalpable powder of low bulk density, having a faint odour of citric acid and a characteristic taste. The powder is greasy to the touch and readily adheres to the skin.

CITRIC ACID

a) Non-proprietary Names – 2-Hydropropane-1, 2, 3-tricarboxylic acid
b) Synonym-
Acidum citricum, anhydrous citric acid, Acido citrico
c) Structural Formula



MATERIALS USED

Table no. 2: List of chemicals used with grade

Sr. No.	Materials Used	Grade	Provided By
1	Ciprofloxacin HCL	LR	STRAVA HEALTHCARE pvt. ltd
2	Mimosa gum	LR	Botanical Garden of SPCOP
3	Sodium bicarbonate	LR	Pallav chemicals & solvent pvt. ltd., Mumbai.
4	Citric acid	LR	Thomas baker(Chemicals) pvt. Ltd., Mumbai
5	Lactose	LR	Research-Lab Fine Chem Industries, Mumbai
6	Magnesium stearate	LR	Pallav chemicals & solvent pvt. ltd., Mumbai.

INSTRUMENTS USES:

Table no. 3: List of Instruments used

S.R. NO.	Instrument	Model	Manufacture
1	Double beam UV spectrometer	UV 1800	Shimadzu Corporation Japan
2	Dissolution Apparatus	TDT-08P	Electro lab
3	Electronic balance	2200	Anamed model
4	Hot air oven	-	Model Industrial LTD Mumbai
5	Tablet punching machine	-	6 Station tablet compression machine
6	Tablet hardness tester	-	Monento Hardness Tester (Secor India)
7	Friability apparatus	EF-1W	Electro lab Roche type Friabilator
8	Melting point apparatus	-	Super fit India LTD
9	Disintegration test apparatus	BIT-44 A	Bio-Technique INDIA

FORMULATION

Method:-

Accurately weighed quantities of Mimosa Gum & Sodium bicarbonate were taken in a mortar & mixed geometrically. To this mixture required quantity of drug was added & mixed slightly with pestle. This mixture was pass through 408 & later collected in plastic bag & blended for 5 min Later sufficient quantity of all excipient were added & the final blend was again through 40 thus obtained blend was mixed for 10 min. & directly compressed into tablet.

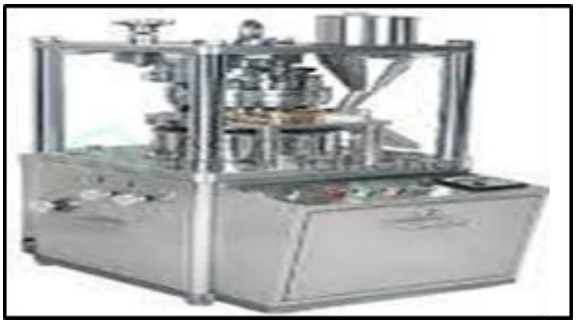


Fig-3. Direct Compression Machine

Table no. 4: Formulation Chart

Formulation code	F1	F2	F3	F4	F5	F6
Ciprofloxacin HCL	250	250	250	250	250	250
Mimosa gum	120	100	80	60	40	20
Sodium Bicarbonate	100	100	80	80	60	60
Citric acid	10	10	10	10	10	10
Lactose	10	30	70	90	130	150
Magnesium st.	10	10	10	10	10	10
TOTAL Wt.(mg)	500	500	500	500	500	500

Fig-4. Batches of Tablet Formulation

EVALUATION STUDY

Various parameters that need to be evaluated in gastro retentive formulations include floating duration, dissolution profiles, and content uniformity: hardness and friability bio adhesive test. In case of multiparticulate drug delivery systems, differential scanning calorimetry (DSC), particle size analysis, flow properties, surface morphology, and mechanical properties are also performed.

❖ Evaluation of tablets

a.) Appearance: The tablets were identified visually.
b.) Thickness: Thickness was measured using a calibrated dial calliper Five tablets of the formulation were picked randomly and thickness was measured individually.
c.) Hardness: Hardness was measured using Monsanto hardness tester.
d.) Friability: Twenty tablets were weighed and placed in the Roche Friabilator and apparatus was

rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using formula,

% F = {1-(Wt. /W)} ×100

Where,

%F-Friability in percentage, W-Initial weight of tablets,

Wt.-Weight of tablets after revolution

e) Weight variation:

Ten tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight.

f) Drug content uniformity:

Take ten tablet of each batch randomly triturate it. Weight accurately equivalent to 10 mg drug it transfer into 100ml volumetric flask 50ml of 0.1N HCL was added with the help of sonicator dissolve it make up volume up to 100ml & filter it pipette out 20ml form stock solution it transfer to 100ml volumetric flask make up volume 100ml with 0.1N HCL take the absorbance at 283 nm.

g) In vitro buoyancy studies:

The time interval between the introduction of the tablet into the dissolution medium and its buoyancy to the top of dissolution medium was taken as buoyancy lag time and the duration of buoyancy was observed visually.

The in vitro buoyancy was determined by floating lag time, per the method described by Rosa et al the tablets were placed in a 100- mL beaker containing 0.1N HCI. The time required for the tablet to rise to the surface and float was determined as floating lag time, and the total time duration till the tablet float on that 100ml 0,1N HCL was recorded as total floating time. Total floating time Department: pharmaceutics Evaluation Study SPCOP, Otur. more than 8 hr should be desired for achieving sustained release action.

i) In vitro drug release studies:-

The in vitro drug release was performed using USP 24 type II paddle apparatus using 900ml of 0.1N HCI at paddle rotation of 100rpm at 37±5° C the sample Department: pharmaceutics Evaluation Study SPCOP, Otur. were withdraw at predetermined time interval for period of 12Hr and analysed at 276 nm using double beam uv spectrophotometer the content of drug was calculated using equation generated from standard calibration curve.

J) Swelling Index Study: - Swelling of tablet excipients particles involves the absorption of a quid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecule. The liquid enters the particles through pores and bind to large molecule, breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of % weight gain by the tablet.

Method: One tablet was weighed and placed in a beaker containing 200 ml of 0.1n HCI. After each hour the tablet was removed from beaker and weighed again up to 10 hours. The weight gain by the tablet was) calculated by the formula.

Fig-5. Dissolution Apparatus

K.) Swelling Index Study: - Swelling of tablet excipients particles involves the absorption of a quid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecule. The liquid enters the particles through pores and bind to large molecule, breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of % weight gain by the tablet.

Method: One tablet was weighed and placed in a beaker containing 200 ml of 0.1n HCI. After each hour the tablet was removed from beaker and weighed again up to 10 hours. The weight gain by the tablet was) calculated by the formula.

RESULTS & DISCUSSION

The study focused on formulating floating tablets of Ciprofloxacin Hydrochloride using Mimosa gum and

other excipients through direct compression technique. A total of six batches (F1–F6) were evaluated for pre-compression and post-compression parameters, with emphasis on floating behavior, swelling index, drug release, and compatibility.

1. Calibration and Drug Release Profile

- Standard calibration curve showed excellent linearity ($R^2 = 0.999$) at 276 nm.
- Formulation F4 showed the most promising in-vitro drug release: 68.70% in 6 hours, ideal for extended-release applications.

2. FT-IR Compatibility Study

- FTIR analysis confirmed no major shift in characteristic peaks, indicating good compatibility between Ciprofloxacin HCL and excipients (Mimosa gum, citric acid, sodium bicarbonate).
- Functional groups (NH stretch, C=O, O-H) were preserved in both individual and combination spectra.

3. Pre-compression Parameters

Parameter	Range across batches
Angle of Repose	34.24°–37.84° (Good)
Bulk Density	0.360–0.719 g/cm³
Tapped Density	0.450–0.785 g/cm³
Carr's Index	8.33%–20% (Fair–Excellent)
Hausner's Ratio	1.09–1.25

Batch F4 showed excellent flow properties (Carr's index: 8.33%, Hausner's ratio: 1.09).

Post-compression Evaluation

Parameter	Observed Values
Weight variation	Within IP limits
Thickness	4.85–5.75 mm
Hardness	2.5–3.5 kg/cm²
Friability	0.01–0.12% (well below 1%)

All formulations passed the required physical tests for tablets.

5. Floating Behavior

- Floating Lag Time (FLT) ranged between 8–20 seconds.
- All tablets floated for more than 12 hours, indicating effective gastro-retention.
- F4 had the shortest FLT (8 sec) and sustained floating >12 hrs — desirable for prolonged action.

6. Swelling Index

- Swelling index increased over time, showing progressive hydration.
- Highest swelling observed in F5, while F4 also showed consistent and high swelling (up to 94.9%).
- Mimosa gum showed good gel-forming ability contributing to floating and release control.

7. In-vitro Drug Release

- F1 to F6 showed progressive and controlled drug release over time.
- F4 emerged as the best performing formulation:
  - Optimal drug release (68.7% in 6 hrs)
  - Balanced floating and swelling
  - Acceptable physical and flow properties

CONCLUSION

Ciprofloxacin HCL is an antibiotic drug that are used to manage and treat various infection (Urinary Tract Infection). Ciprofloxacin HCL is highly water-soluble drug (Class IV). After procurement of drug sample it was characterized for identification by FTIR. After identification check compatibility of drug with all excipient. It was found that it is compatible with all excipient there is no change in functional group. Flow property of Ciprofloxacin HCL tablet powder was found within range & or comply with official pharmacopeia. Physical property of Ciprofloxacin HCL tablet Hardness, friability Average weight also complies with standard reference. Floating lag time of all six formulations were within 1 min. Total floating time was more than 12 hrs. Hardness of tablet affect the floating lag time. The in vitro drug release profile indicated that Batch (F4) was the most promising formulation as the extent of drug release from this formulation was high as compare to other formulations, which are suitable for sustained release drug delivery system. The in vitro Drug release studies in Stomach pH conditions was carried out in 0.1 N HCL for 12 hrs. The Batch F4 shows 98.99% release in 12 hrs, so we concluded that rate of drug release increases in the Acidic environment of Stomach. Formulation F4 show desirable swelling index.

Mimosa Gum is water Sellable in nature it restricts movement of polymer and affect the swelling index.

REFERENCE

[1] C. Suzette et al. An innovative floating gastro retentive dosage system: formulation and in vitro evaluation Int. J. Pharm. (2009)

[2] Muthusamy K, Govindarajan G and Ravi T K, “Preparation and evaluation of Lansoprazole Floating Micropellets”, Ind. J. Pharm. Sci., 2005, 67(1):75-79.

[3] Remington: The Science and Practice of Pharmacy”, Mack Publishing Company, Pennsylvania 18042, 1995, Vol-II, 1080-1081.

[4] Y.I. Jeong et al. Preparation of ciprofloxacin-encapsulated poly(dl-lactide-co-glycolide) microspheres and its antibacterial activity J. Pharm. Sci. (2009)

[5] S. Baumgartner et al. Optimization of floating matrix tablets and evaluation of their gastric residence time Int. J. Pharm. (2000)

[6] Mudie DM, Amidon GL, Amidon GE. Physiological parameters for oral delivery and in vitro testing. J Mol Pharm. 2010; 7:1388–1405.

[7] Tadros M. Controlled-release effervescent floating matrix tablets of ciprofloxacin drochloride: development, optimization and in vitro-in vivo evaluation in health human volunteers. Eur J Pharm Bio pharm. 2010; 74:332–339.

[8] Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: a review. J AAPS Pharm Sci Tech. 2005; 6:372–390.

[9] Ibrahim H. A novel liquid effervescent floating delivery system for sustained drug delivery. Drug Discov Ther. 2009; 3(4):168–175.

[10] Pahwa R, Bhagwan S, Kumar V, et al. Role of natural polymers in the development of floating drug delivery system. J Pharm Res 2010;3(6):1312-18

[11] Garg S, Sharma S. Gastro retentive Drug Delivery Systems; 2003. Available from: http://www.bbriefings.

[12] Ali J, Khar RK, Ahuja A. Preformulation Studies, Dosage form Design. 1st Ed. New Delhi: Birla Publications Pt. Ltd.; 2004. p. 16-7.

[13] Garg R, das Gupta G. Preparation and evaluation of gastro retentive floating tablets of silymarin. Chem Pharm Bull 2009; 57:545-9.

[14] Manoj Goyal, S.C. Mehta. Floating Drug Delivery System", Journal Neha Narang," An Updated Review on Floating drug delivery system", International Journal of Applied