FORMULATION AND IN VITRO CHARACTERIZATION OF CIPROFLOXACIN HCL FLOATING TABLETS

A Dissertation submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

CHENNAI-600 032

In partial fulfillment of the requirements for the degree of

MASTER OF PHARMACY

IN

PHARMACEUTICS

Submitted By

Reg No : 261311053

UNDER THE GUIDANCE OF

Mrs.S.Valarmathi, M.Pharm,

Associate Professor,

Department Of Pharmaceutics

ANNAI VEILANKANNI'S PHARMACY COLLEGE
SAIDAPET, CHENNAI -600015
OCTOBER -2015

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DECLARATION

I hereby declare that the dissertation work entitled **"FORMULATION AND IN VITRO CHARACTERIZATION OF CIPROFLOXACIN HCL FLOATING TABLETS"** is based on the original work carried out by me in Annai Veilankanni's Pharmacy College, Chennai and under the guidance of Mrs.S.Valarmathi,M.Pharm for submission to the Tamilnadu Dr. M.G.R. Medical University in the partial fulfilment of the requirement for the award of Degree of Master of Pharmacy in Pharmaceutics. The work is Original and has not been submitted in part or full for any other diploma or degree of this or any other university. The information furnished in this dissertation is genuine to the best of my knowledge and belief.

Chennai,

Date: 05-08-2015. 261311053

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TABLE OF CONTENTS

Affectionately Dedicated To

My Beloved Husband

& My Family

INTRODUCTION

LITERATURE REVIEW

AIM AND OBJECTIVE

PLAN OF WORK

DRUG PROFILE

POLYMERS & EXCIPIENTS PROFILE

MATERIALS & METHODS

RESULTS & DISCUSSIONS

SUMMARY & CONCLUSION

BIBLIOGRAPHY

LSIT OF ABBREVIATIONS

API	Active Pharmaceutical Ingredient
α	Alpha
BP	British Pharmacopoeia
β	Beta
BD	Bulk Density
Conc.	Concentration
cm	Centimeter
CMC	Carboxy methyl cellulose
EC	Ethyl Cellulose
ER	Extended Release
et al.	and others
Fig.	Figure
FTIR	Fourier Transformed Infrared Spectroscopy
KG	Kilogram
GI	Gastrointestinal
GIT	Gastrointestinal Tract
GRT	Gastric retention time
FDDS	Floating drug delivery system
HRS	Hours
HR	Hausner's ratio
HCL	Hydrochloric Acid
HPMC	Hydroxy Propy Methyl Cellulose
HPLC	High Performance liquid chromatography

IP	Indian Pharmacopoeia
IR	Infrared
KBr	Potassium bromide
M	Molar
mg	Milligram
mm	Millimeter
ml	Milliliter
min	Minutes
μg	Microgram
NC	No Change
pH	Negative logarithm of hydrogen ion concentration
Ph.Eur	European Pharmacopocia
PVP	Poly vinyl pyrolidone
rpm	revolutions per minute
R^2	Correlation factor
RT	Real Time
RH	Relative Humidity
Sec.	Second
SR	Sustained
TD	Tapped Density
Temp.	Temperature
USP	United States Pharmacopocia
V	Volume
W	Wait

LIST OF TABLES

LIST OF FIGURES

1 .INTRODUCTION

Gastro retentive Drug Delivery System

Since the last three decades many drug molecules formulated as Gastro Retentive Drug Delivery System (GRDDS) have been patented keeping in view its commercial success. The bioavailability of drugs with an absorption window in the upper part of the GIT (gastro intestinal tract) is generally limited with conventional pharmaceutical dosage forms. These drugs can be delivered ideally by slow release from the stomach to give a localized effect at the site of action. Improved efficacy is expected for drugs that are used in the treatment of gastric disorders like ulcers and bacterial infections (H.pylori that resides in the antral region of stomach behind the mucosal layer). Many drugs categorized as once-a-day delivery have been demonstrated to have suboptimal absorption due to dependence on the transit time of the dosage form, making traditional extended release development challenging. Therefore, a system designed for longer gastric retention will extend the time within which drug absorption can occur[1].

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing sustained release systems for better absorption and enhanced bioavailability.

The residence time of conventional sustained release dosage forms and, thus, of their drug release into the stomach and upper intestine is often short. To overcome this restriction and to increase the bioavailability of these drugs, sustained drug delivery systems, with a prolonged residence time in the stomach, can be used.

Gastro-retentive dosage forms (GRDFs) are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug to the upper part of the gastrointestinal (GI) tract. This technology has generated enormous attention over the last few decades owing to its potential application to improve the oral delivery of some important drugs, for which prolonged retention in the upper GI tract can greatly improve their oral bioavailability and/or their therapeutic outcome

Suitable Drug Candidates for Gastro retention[2]

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency

- Drugs with narrow absorption window in GI tract, e.g., riboflavin and levodopa
- Drugs which are primarily absorbed from stomach and upper part of GIT e.g., calcium supplements, chlordiazepoxide and cinnarazine
- Drugs that act locally in the stomach, e.g., antacids and misoprostol
- Drugs that degrade in the colon, e.g., ranitidine HCl and metronidazole
- Drugs that disturb normal colonic bacteria, or degrade in the colon e.g: Amoxicillin trihydrate
- Poorly soluble at an alkaline pH
- Particularly useful for the treatment of peptic ulcers caused by H. Pylori Infections

FLOATING DRUG DELIVERYSYSTEM

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process[1]

Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as[2, 3]:

- Drugs with short half-life require frequent administration, which increase the chances of missing dose of drug leading to poor patient compliance
- A typical peak-valley plasma concentration-time profile is obtained which makes it difficult to attainment of steady state condition
- The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{SS} values fall or rise beyond the therapeutic range
- The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs

In order to overcome the drawbacks of conventional drug deliver systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits[4].

Controlled Drug Delivery Systems:

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue[5].

Controlled drug delivery or modified drug delivery systems are conveniently divided into four categories.

i. Delayed release
ii. Sustained release
iii. Site-specific targeting
iv. Receptor targeting

More precisely, Controlled delivery can be defined as: -

1) Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects.
2) Localized drug action by spatial placement of a controlled release system adjacent to or in the diseased tissue.
3) Targeted drug action by using carriers or chemical derivatives to deliver drug to a particular target cell type.
4) Provide a physiologically/therapeutically based drug release system. In other words, the amount and the rate of drug release are determined by the physiological/ therapeutic needs of the body.

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug. Controlled drug delivery usually results in substantially constant blood levels of the active ingredient as compared to the uncontrolled fluctuations observed when multiple doses of quick releasing conventional dosage forms are administered to a patient.

Advantages of Controlled Drug Delivery System:

1. Avoid patient compliance problems.
2. Dosage frequency were reduced
   a) Minimize or eliminate local side effects
   b) Minimize or eliminate systemic side effects
   c) Obtain less potentiation or reduction in drug activity with chronic use.
   d) Minimize drug accumulation with chronic dosing.
3. Improve efficiency in treatment
   a) Cures or controls condition more promptly.
   b) Improves control of condition i.e., reduced fluctuation in drug level.
   c) Improves bioavailability of some drugs.

d) Make use of special effects, eg. Sustained-release aspirin for morning relief of arthritis by dosing before bedtime.

4. Economy i.e. reduction in health care costs. The average cost of treatment over an extended time period may be less, with less frequency of dosing, enhanced therapeutic benefits and reduced side effects. The time required for health care personnel to dispense and administer the drug and monitor patient is also reduced

Disadvantages:

1) Decreased systemic availability in comparison to conventional dosage forms, which may be due to incomplete release, increased first-pass metabolism, increased instability, insufficient residence time for complete release, site specific absorption, pH dependent stability etc.
2) Poor in vitro – in vivo correlation.
3) Possibility of dose dumping due to food, physiologic or formulation variables or chewing or grinding of oral formulations by the patient and thus, increased risk of toxicity.
4) Retrievals of drug are difficult in case of toxicity, poisoning or hypersensitivity reactions.
5) Reduced potential for dosage adjustment of drugs normally administered in varying strengths.

Oral Controlled Drug Delivery Systems[6,7]

Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either local or systemic action.

All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage form (solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology. Therefore the scientific framework required for the successful development of oral drug delivery systems consists of basic understanding of (i) Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug (ii) the anatomic and physiologic characteristics of the gastrointestinal tract and (iii)

physicochemical characteristics and the drug delivery mode of the dosage form to be designed.

The main areas of potential challenge in the development of oral controlled drug delivery systems are

- ✓ Development of a drug delivery system: To develop a viable oral controlled release drug delivery system capable of delivering a drug at a therapeutically effective rate to a desirable site for duration required for optimal treatment
- ✓ Modulation of gastrointestinal transit time: To modulate the GI transit time so that the drug delivery system developed can be transported to a target site or to the vicinity of an absorption site and reside there for a prolonged period of time to maximize the delivery of a drug dose
- ✓ Minimization of hepatic first pass elimination: If the drug to be delivered is subjected to extensive hepatic first-pass elimination, preventive measures should be devised to either bypass or minimize the extent of hepatic metabolic effect

Conventional oral controlled dosage forms suffer from mainly two adversities[8]. The short gastric retention time (GRT) and unpredictable gastric emptying time (GET). A relatively brief GI transit time of most drug products impedes the formulation of single daily dosage forms.

Altering the gastric emptying can overwhelm these problems. Therefore it is desirable, to formulate a controlled release dosage form that gives an extended GI residence time.

Extended release dosage form with prolonged residence time in stomach are highly desirable for drugs.

i. That are locally active in stomach,
ii. That have an absorption window in the stomach or in the upper small intestine,
iii. That are unstable in the intestinal or colonic environment,
iv. Have low solubility at high pH values.

Gastro retentive Dosage Form (GRDF):[9,10]

It is evident from the recent scientific and patient literature that an increased interest in novel dosage forms that are retained in stomach for a prolonged and predictable period of time exists today in academic and industrial research groups. One of the most feasibleapproaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time (GRT), i.e. gastro retentive dosage form (GRDFs or GRDS).

GRDFs extend significantly the period of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form.

Dosage form with prolonged GRT, i.e. gastro retentive dosage form (GRDF), willbring about new and important therapeutic options such as:

1) This application is especially effective in sparingly soluble and insoluble drugs. It is known that, as the solubility of a drug decreases, the time available for drug dissolution becomes less adequate and thus the transit time becomes a significant factor affecting drug absorption. To override this problem, erodible, gastro retentive dosage forms have been developed that provide continuous, controlled administration of sparingly soluble drugs at the absorption site[11].

2) GRDFs greatly improve the pharmacotherapy of the stomach through local drug release, leading to high drug concentration at the gastric mucosa. (For e.g. Eradicating Helicobacter pylori from the sub mucosal tissue of stomach) making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis, reduce the risk of gastric carcinoma and administer non-systemic controlled release antacid formulations (calcium carbonate).

3) GRDFs can be used as carriers for drugs with so-called absorption windows. These substances for e.g. antiviral, antifungal and antibiotic agents (Sulphonamides, Quinolones, Penicillin's, Cephalosporin's, amino glycosides, Tetracycline's etc.) are taken up only from very specific sites of the GI mucosa.

BIOLOGICAL ASPECTS OF GRDFs:[12]

Role of GI tract:

Stomach

The stomach is J-shaped organ located in the upper left hand portion of the abdomen, just below the diaphragm. It occupies a portion of the epigastric and left hydrochondriac region. The main function of the stomach is to store the food temporarily, grind it and then release it slowly into the duodenum. Due to its small surface area very little absorption takes place from the stomach. It provides barrier to the delivery of drugs to small intestine.

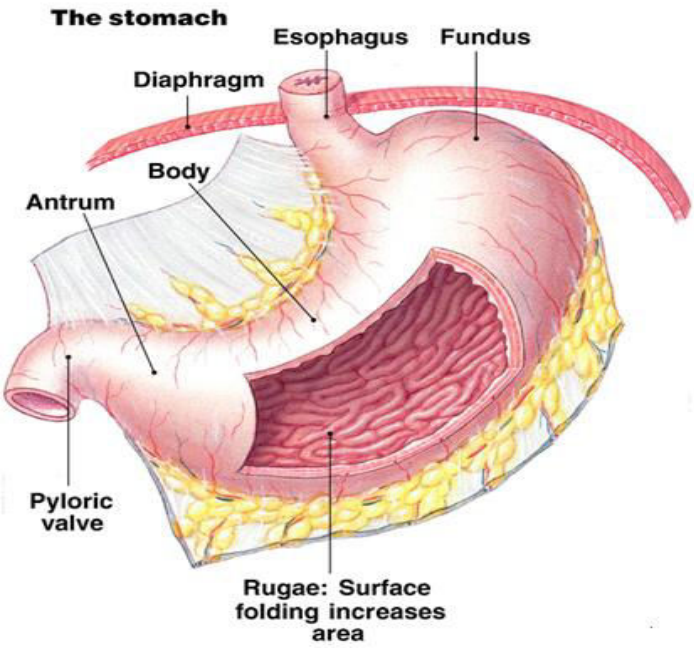


Fig1: Anatomy of Stomach

Physiology of stomach:

The stomach is divided into three anatomical regions. I) Fundus ii) Body and iii) Pylorus (or antrum). The proximal stomach consisted of fundus and body, which serves as a reservoir for ingested materials, whereas the distal region (pylorus) is the major site of mixing motions, acting as a pump to propel gastric contents for gastric emptying. Gastric emptying occurs both in fasting as well as fed states[13].

The GI tract is always in a state of continuous motility. There are two modes of motility pattern. The digestive mode and interdigestive mode. In case of fasted state an interdigestive series of electrical events occurs in cyclic manner both through stomach and small intestine every 2-3 hr. This electrical activity is termed as interdigestive my electric cycle.

Phase I	:	Period of no contraction.
Phase II	:	Period of intermittent contraction.
Phase III	:	Period of regular contractions at the maximal frequency that migrate distally.
Phase IV	:	Period of transition between phase III and phase I.

PHASE I:

The quiescent period, lasts from 30 to 60 minutes and is characterized by a lack of secretary, electrical and contractile activity.

PHASE II:

Exhibits intermittent activity for 20-40 min, during which the contractile motions increase in frequency and size. Bile enters the duodenum during this phase, whereas gastric mucus discharge occurs during the latter part of phase II and throughout phase III.

Phase III:

Has a housekeeping role and serves to clear all indigestible materials from the stomach and small intestine. Consequently, a controlled-release gastrointestinal drug delivery system must be capable of resisting the house keeping action of phase III. Studies revealed that in the fed state, the gastric emptying rate is slowed since the onset of MMC is delayed. It can be concluded that feeding results in a lag time before onset of gastric emptying cycle[14, 15].

PHASE IV:

Is the transition period of 0-5 minutes between Phase III &I.

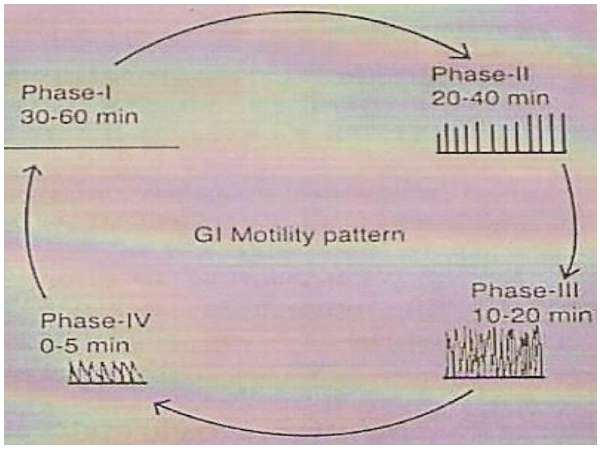


Fig 2-: Interdigestivemyloelectriccycle

REQUIREMENTS FOR GASTRO RETENTION [16]

From the discussion of the physiological factors in stomach, to achieve gastro retention, the dosage form must satisfy some requirements. One of the key issues is that the dosage form must be able to withstand the forces caused by peristaltic waves in the stomach and constant grinding and churning mechanisms. It must resist premature gastric emptying and once the purpose has been served, it should be removed from the stomach with ease.

APPROACHES TO GASTRIC RETENTION [17,18]

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach. These systems include: Floating systems,Bio adhesive systems, swelling and expanding systems, High density systems, Modified systems

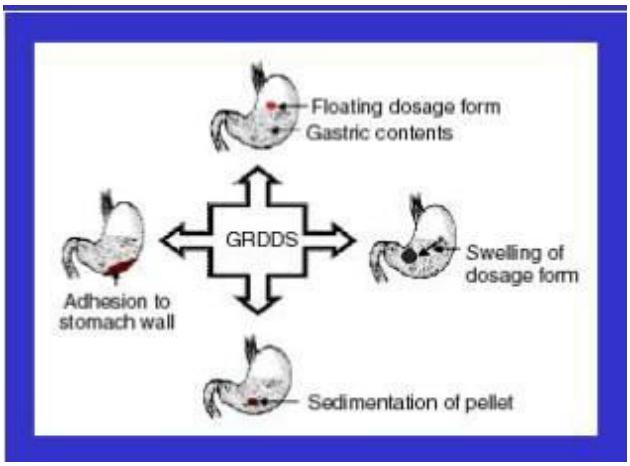


Fig 3 Classification of gastro retentive drug delivery system

Buoyant/ Floating Systems:

Floating Drug Delivery Systems [19] (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations. Floating systems can be classified into two distinct categories, non-effervescent and effervescent systems.

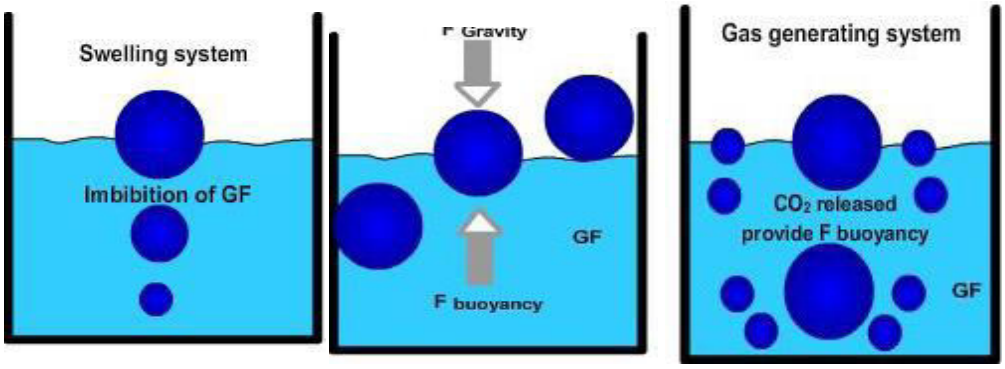


Fig 4: Mechanism of floating system

Bio/Muco-adhesive Systems:[17]

Bio/muco-adhesive systems are those which bind to the gastric epithelial cell surface or mucin and serve as a potential means of extending the GRT of drug delivery system in the stomach, by increasing the intimacy and duration of contact of drug with the biological membrane.

The surface epithelial adhesive properties of mucin have been well recognized and applied to the development of GRDDS based on bio/muco-adhesive polymers. The ability to provide adhesion of a drug (or a delivery system) to the GI wall provides a longer residence time in a particular organ site, thereby producing an improved effect in terms of local action

or systemic effect. Binding of polymers to the mucin/epithelial surface can be divided into three broad categories: –

1. Hydration-mediated adhesion.
2. Bonding-mediated adhesion.
3. Receptor-mediated adhesion.

Swelling and Expanding Systems:[18]

These are the dosage forms, which after swallowing; swell to an extent that prevents their exit from the pylorus. As a result, the dosage form is retained in the stomach for a long period of time. These systems may be named as "*plug type system*", since they exhibit the tendency to remain logged at the pyloric sphincter if that exceed a diameter of approximately 12-18 mm in their expanded state. The formulation is designed for gastric retention and controlled delivery of the drug into the gastric cavity. Such polymeric matrices remain in thegastric cavity for several hours even in the fed state.A balance between the extent and duration of swelling is maintained by the degree of cross-linking between the polymeric chains. A high degree of cross-linking retards the swelling ability of the system maintaining its physical integrity for prolonged period.

High Density Systems:[20]

These systems with a density of about 3 g/cm^3 are retained in the rugae of the stomach and are capable of withstanding its peristaltic movements. A density of 2.6-2.8 g/cm^3 acts as a threshold value after which such systems can be retained in the lower part of the stomach. High-density formulations include coated pellets. Coating is done by heavy inert material such as barium sulphate, zinc oxide, titanium dioxide, iron powder etc. They are retained in the antrum of stomach.

Incorporation of Passage Delaying Food Agents:

Food excipients like fatty acids e.g. salts of myristic acid change and modify the pattern of the stomach to a fed state, thereby decreasing gastric emptying rate and permitting considerable prolongation of release. The delay in the gastric emptying after meals rich in fats is largely caused by saturated fatty acids with chain length of C_{10}-C_{14}.

Ion Exchange Resins[21]:

A coated ion exchange resin bead formulation has been shown to have gastric retentive properties, which was loaded with bicarbonates. Ion exchange resins are loaded with bicarbonate and a negatively charged drug is bound to the resin. The resultant beads were then encapsulated in a semi-permeable membrane to overcome the rapid loss of carbon dioxide. Upon arrival in the acidic environment of the stomach, an exchange of chloride and bicarbonate ions take place. As a result of this reaction carbon dioxide was released and trapped in the membrane thereby carrying beads towards the top of gastric content and producing a floating layer of resin beads in contrast to the uncoated beads, which will sink quickly.

Osmotic Regulated Systems[22]:

It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating support in a bio erodible capsule. In the stomach the capsule quickly disintegrates to release the intragastricosmotically controlled drug delivery device. The inflatable support inside forms a deformable hollow polymeric bag that contains a liquid that gasifies at body temperature to inflate the bag. The osmotic controlled drug delivery device consists of two components – drug reservoir compartment and osmotically active compartment.

TYPES OF FLOATING DRUG DELIVERY SYSTEMS (FDDS)[23-25]

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are:

A. Effervescent System, and
B. Non- Effervescent System.

EFFERVESCENT SYSTEM:-

Effervescent systems include use of gas generating agents, carbonates (ex. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO_2) gas, thus reducing the density of the system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporates at body temperature[26].

These effervescent systems further classified into two types.

I. Gas Generating systems

II. Volatile Liquid/Vacuum Containing Systems.

Gas – Generating Systems:

Intra Gastric Single Layer Floating Tablets or Hydro dynamically Balanced System (HBS):

These are formulated by intimately mixing the CO_2 generating agents and the drug within the matrix tablet. These have a bulk density lower than gastric fluids and therefore remain floating in the stomach unflattering the gastric emptying rate for a prolonged period. The drug is slowly released at a desired rate from the floating system and after the complete release the residual system is expelled from the stomach. This leads to an increase in the GRT and a better control over fluctuations in plasma drug concentration.

These are also compressed tablets containing two layers i.e.,

i. Immediate release layer and
ii. Sustained release layer.

Multiple Unit type floating pills:

These systems consist of sustained release pills as 'seeds' surrounded by double layers. The inner layers consist of effervescent agents while the outer layer is of swellable membrane layer. When the system is immersed in dissolution medium at body temperature, it sinks at once and then forms swollen pills like balloons, which float as they have lower density. This lower density is due to generation and entrapment of CO_2 within the system.

Volatile Liquid / Vacuum Containing Systems:

Intragastric Floating Gastrointestinal Drug Delivery System: These systems can be made to float in the stomach because of floatation chamber, which may be a vacuum or filled with air or a harmless gas, while drug reservoir is encapsulated inside a micro porous compartment.

Inflatable Gastrointestinal Delivery Systems:

In these systems an inflatable chamber is incorporated, which contains liquid ether that gasifies at body temperature to cause the chamber to inflate in the stomach. These systems are fabricated by loading the inflatable chamber with a drug reservoir, which can be a drug, impregnated polymeric matrix, then encapsulated in a gelatin capsule.

After oral administration, the capsule dissolves to release the drug reservoir together with the inflatable chamber. The inflatable chamber automatically inflates and retains the drug reservoir compartment in the stomach. The drug continuously released from the reservoir into the gastric fluid[27].

IntragastricOsmotically Controlled Drug Delivery System:

It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating support in a biodegradable capsule. In the stomach, the capsule quickly disintegrates to release the intragastircosmotically controlled drug delivery device. The inflatable support inside forms a deformable hollow polymeric bag that contains a liquid that gasifies at body temperature to inflate the bag. The osmotic pressure controlled drug delivery device consists of two components; drug reservoir compartment and an osmotically active compartment[28].

The drug reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid and has a drug delivery orifice. The osmotically active compartment contains an osmotically active salt and is enclosed within a semi permeable housing. In the stomach, the water in the GI fluid is continuously absorbed through the semi permeable membrane into osmotically active compartment to dissolve the osmotically active salt. An osmotic pressure is thus created which acts on the collapsible bag and in turn forces the drug reservoir compartment to reduce its volume and activate the drug reservoir compartment to reduce its volume and activate the drug release of a drug solution formulation through the delivery orifice. The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflate the support. The deflated drug delivery system is then emptied from the stomach.[10]

NON-EFFERVESCENT SYSTEMS:[7]

The Non-effervescent FDDS based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as Polycarbonate, Polyacrylate, Polymethacrylate, polystyrene as well as bioadhesive polymer such as Chitosan and Carbopol. The various types of this system are as:

Single Layer Floating Tablets:

They are formulated by intimate mixing of drug with a gel-forming hydrocolloid, which swells in contact with gastric fluid and maintain bulk density of less than unity. The air trapped by the swollen polymer confers buoyancy to these dosage forms.

Bilayer Floating Tablets:

A bilayer tablet contain two layer one immediate release layer which release initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach.

Alginate Beads:

Multi unit floating dosage forms were developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm diameter can be prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, which can maintain a floating force for over 12 hours.

Hollow Microspheres:

Hollow microspheres (micro balloons), loaded with drug in their outer polymer shells were prepared by a novel emulsion-solvent diffusion method. The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 40^0C. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in microsphere

of polymer with drug. The micro balloons floated continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours *in vitro*.[29]

Factors Controlling Gastric Retention Time of Dosage Form: [10,13]

The gastric retention time (GRT) of dosage form is controlled by several factors that affect their efficacy as a gastroretentive system.

- **Density of dosage form**: – the density of gastric fluid is reported to be 1.004g/cm^3.the density of the dosage from should be less than this for buoyancy, so that it is retained in stomach for longer period of time. The dosage from may be having a high density in the beginning, but due to reduction in density by swelling it will float in stomach
- **Size of the dosage from**: –studies on the effect of particle size on gastric retention have been inconclusive. In general it is know that indigestive solids larger than 1-2mm are retained in stomach throughout the post-prandial period, after which they are emptied in stomach throughout the post-prandial period, after which they are emptied by cyclically recurring burst of interdigestive gastric contractions. However studies have suggested that this observation cannot be generalized. Many recent studies have shown that non-disintegrating tablets as large as 7mm can be emptied from human stomach during the post-prandial period, while 13mm tablets are retained until arrival of subsequent sweeping "housekeeper wave". This emphasizes the need for size enlargement of DF in stomach in order to prolong GRT[30]
- **Shape of dosage form** – Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KPSI) are reported to have better GRT. 90% to 100% retention at 24 hours compared with other shapes
- **Single or multiple unit formulation** – Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms
- **Fed or unfed state** – Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the

MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.[31]

- **Nature of meal** – Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release
- **Caloric content** – GRT can be increased by four to 10 hours with a meal that is high in proteins and fats
- **Frequency of feed** – The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC
- **Gender** – Mean ambulatory GRT in males (3.4±0.6 hours) is less compared with their age and race-matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface[32]
- **Age** – Elderly people, especially those over 70, have a significantly longer GRT
- **Posture** – GRT can vary between supine and upright ambulatory states of the patient. Concomitant drug administration – Anticholinergics like Atropine and Propantheline, opiates like Codeine and prokinetic agents like Metoclopramide and Cisapride[33]

Advantages of FDDS:[34,35]

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

- ✓ Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site
- ✓ Controlled delivery of drugs
- ✓ Delivery of drugs for local action in the stomach
- ✓ Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate
- ✓ Treatment of gastrointestinal disorders such as gastro-esophageal reflux
- ✓ Simple and conventional equipment for manufacture
- ✓ Ease of administration and better patient compliance
- ✓ Site-specific drug delivery

Disadvantages of FDDS:[36]

- ✓ Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted
- ✓ Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems
- ✓ High variability in gastric emptying time due to its all or non-emptying process
- ✓ Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diametral size. Therefore patients should not be dosed with floating forms just before going to bed

List of Drugs - Floatable Drug Delivery Systems:[37]

S. No.	DOSAGE FORM	DRUGS
1	Microspheres	Aspirin, Grisiofulvin, p-nitroanilline, Ibuprofen, Terfinadine, Tranilast.
2	Granules	Diclofenac sodium, Indomethacin, Predmisolone
3	Films	Cinnarizine
4	Powders	Several basic drugs
5	Capsules	ChlordiazepoxideHCl, Diazepam, Furosemide, L-Dopa, benserazide, Misoprostol, Propranolol HCl, Ursodeoxycholic acid
6	Tablets/pills	Acetaminophen, Acetylsalicylic acid, Amoxicillin trihydrate, Ampicillin, Atenolol, Chlorpheniramine, Cinnazirine, Diltiazem, Fluorouracil, Isosorbidemononitrate, Isosorbidedinitrate, p-aminobenzoic acid, Piretanide, Prednisolone, Quinidine gluconate, Riboflavin-5-phosphate, Sotalol, Theophylline, Verapamil HCl

Marketed Products of FDDS: [10\]

S. NO.	BRAND NAME	DRUG (DOSE)	COMPANY, COUNTRY	REMARKS
1.	Modapar®	Levodopa (100 mg), Benserazide (25 mg)	RocheProducts, USA	Floating CR capsule
2.	Valrelease®	Diazepam (15 mg)	Hoffmann-LaRoche, USA	Floating capsule
3.	Liquid Gavison®	Al hydroxide (95 mg), Mg carbonate (358 mg)	GlaxoSmith Kline, India	Effervescent floating liquid alginate preparation
4.	Topalkan®	Al-Mg antacid	Pierre Fabre Drug, France	Floating liquid alginate preparation
5.	Conviron	Ferrous sulphate	Ranbaxy, India	Colloidalgel forming FDDS
6.	Cifran OD®	Ciprofloxacin (1 gm)	Ranbaxy, India	Gas-generating floating tablet

2. LITERATURE REVIEW

Mohammad Shahidul Islam *et al.,* [38]The purpose of this work is to determine the in-vitro release kinetic of Ciprofloxacin Hcl sustained release dosage form using HPMC K15M, HPMC K4M and HPMC K4M premium polymers. From this studies they concluded that at least 6% HPMC K15M CR showed desired sustained release and at least15% HPMC K4M and 6.7%HPMC K4M premium met the desire sustained action. It proved that HPMC K15M was better than HPMC K4M CR and HPMC K4M premium for Ciprofloxacin Hcl sustained release matrix tablets by direct compression.

A.Badoni *et al.,* [39]Stated that GRDDS offers various potential advantages for a drug with poor bioavailability. Drug absorption in gastro intestinal tract is highly variable process and prolong gastric retention time of dosage form extends the time for drug absorption. Different approaches of GRDDS are studied each having their own advantages and disadvantages .In future it can early assumed that GRDDS will become more popular in terms of developing drugs to systemic circulation with improving efficiency of various types of pharmacotherapy.

KrishnarajanDevarajan *et al.,* [40] Assessed that hydro dynamicaly balanced tablets of Ciprofloxacin Hcl can be formulated with an approach to increase gastric residence and thereby increase the drug bioavailability. An attempt to develope floating tablets of ciprofloxacin Hcl using Sodium bicarbonate as gas generating agent and HPMC (K100M, K4M,E50M) as hydrophilic polymer by direct compression. The formulated tablets showed compliance for physical and chemical parameters and the result of stability studies indicates that the most suitable storage condition and temperature for Ciprofloxacin floating tablets was 2-8 C for a period of 60days.

Ajay Bagherwal *et al.,* [41]Concluded that increase in the proportion of polymer (HPMC K4M andCarbopol 934 was associated with decrease in overall cumulative drug release rate. Release of formulation batch with carbopol 12% was found to maximum release at the end of6hours.Therelease from the system was found to concentration independent and matrix diffusion mediated. The tablets was found t have excellent physical characters.

K.Ravishankar *et al.,*[42] Prepare Ciprofloxacin bioadhesive and floating tablets to increase the gastric residence time and as well as bioavailability thereby it increases patient compliance. These floating tablets prepared by using polymers like HPMC K4M and carbopol .Sodium bicarbonate with combination of citric acid are used as gas generating agents.

Upendarrao.Galla *et al.,*[43]Stated that the principle of hydro dynamically balanced controlled drug delivery system offers a suitable and practical approach to obtained controlled release of Ciprofloxacin with enhance bioavailability and reduce the dosing frequency. The Ciprofloxacin floating tablets were prepared by using polymers like HPMC K4M, HPMC K15M.From the result concluded that the floating lag time increases with increase hardness. HPMC K15M shows better control release than other formulation and marketed product.

Balachandra M. Habade *et al.,*[44] In this present work attempt to prepare floating drug delivery with prolong gastric residence time. The release of Ciprofloxacin from formulation is proportional to the concentration of polymer. As concentration of polymer increases the drug release decreases. This study floating tablets were prepared by using sodium bicarbonate as a gas generating agent in methocel polymer of different grades.

Ravindra J. Salunke *et al.,*[45] The purpose of current study is to develope and optimize a Hydro dynamically balanced system of ciprofloxacin Hcl as a single unit capsules using Response surface methodology.The formulation were prepared by using HPMC K4M, carbopol 934 and the amount of drug Release after 12hours was noted. The formulation were evaluated for in-vitro buoyancy and in-vitro release studies.

E.Sathishreddy *et al*[46] Sustained release floating tablets of Ciprofloxacin were successfully prepared with hydrophilic polymer like HPMC K15M.From the pre formulation studies of drug excipient compatibility was observed and it found that there is no such type of incompatibilities was existed. The formulation batches were evaluated for physical parameters, floating properties and dissolution profile. The drug content of all tablets was in the range of 98-102%.

N.H Foda *et al.,*[24]The purpose of this work is to study the various antibiotic drugs thatformulated in gastro retentive drug delivery system. The present study was showed the development of gastro retentive drug delivery system for various antibiotic which used to

increase the bioavailability of drug and also increases the gastric residence time that leads to release of drug for long period of time in controlled manner.

Rajinikanth PS ***et al.,***[25] Developed gastro retentive floating tablets of amoxicillin for use in treatment of gastric infections that caused in stomach by microorganisms. The developed floating tablets are evaluated for physical parameters and in-vitro drug release characteristics. Sodium bicarbonate with combination of citric acid used as gas generating agent. This formulation is highly effected to cure H.pylori infection that occurred in stomach.

Kunal P Nayak ***et al.,***[27]Assessted the various approaches in gastro retentive drug delivery system and list out their advantages and disadvantages in delivering various types of drugs to stomach. They list out the various approaches like low density, high density, bioadhesive drug delivery systems ,magneticswellable and expandable drug delivery system that used to prolong the gastric retension time there by increase bioavailabiity of various drugs.

Whithead L. ***et al.,***[26]Formulated and evaluated amoxicillin floating tablets using various hydrophilic polymers. Sodium alginate used as floating agent and the formulated tablets are evaluated for in-vitro drug release. The floating tablets of amoxicillin showed desired release of drug and also increases buoyancy help to increase gastric residence time thereby enhances the bioavailability of drug.

Nayak A.K ***et al.,***[29]The purpose of this work is to study detail about gastro retentive drug delivery system and various approaches of gastro retentive system. These drug delivery increase the gastro retentive time and bioavailability of various drugs. It also known as site specific drug delivey system that delivers drug to stomach to treat various diseases like peptic, gastric ulcers and infections that caused by various microorganisms.

Ali J. ***et al.,***[47] Developed bioadhesive tablets of ofloxacin to deliver drug to stomach to treat gastric infections. The tablets are developed by using various mucoadhesive polymers like chitosan,sodium alginate, methocel polymers. These mucoadhesive tablets are used to enhance the bioavailability of ofloxacin by increasing the gastric residence time.Theseshowscontrolled release of drug for a prolong period of time.

DebjitBhowmik *et al.,*[48] A novel floating controlled-release drug delivery system was formulated in an effort increase the gastric retention time of the dosage form and to control drug release. One of the most feasible approaches for achieving a prolonged and predictable dug delivery profiles in the gastrointestinal tract is to control the gastric residence time, using

gastroretentive dosage forms that will provide us with new and important therapeutic options. Floating matrix tablets are designed to prolong the gastric residence time after oraladministration, at a particular site and controlling the release of drug especially useful for achieving controlled plasma level as well as improving bioavailability.

Raju D. B ***et al.,***[49] Sustained release gastroretentive dosage forms enable prolonged and continuous input of the drug to the upper parts of gastrointestinal tract and improve the bioavailability of medication that is characterized by narrow absorption window. Gastroretentive floating drug delivery systems (GFDDS) of Metformin hydrochloride, an antidiabetic drug with an oral bioavailability of only 50 %(because of its poor absorption from lower gastrointestinal tract) have been designed and evaluated. Hydroxy propyl methyl cellulose (HPMC K4M) and carbopol 934P were used as polymers and sodium bicarbonate as gas generating agent to reduce floating lag time. Tablets were prepared by wet granulation method. Floating tablets were evaluated for hardness, friability, weight variation, drug content, floating properties and in vitro release pattern. The in vitro drug release followed first order kinetics and drug release was found to be diffusion controlled.

Kshirsagar R.V *et al.,*[50]The objective of the present study was to develop a hydro dynamically balanced system of Metformin as a single unit floating tablet. Various grades of low-density polymers were used for the formulation of this system. They were prepared by physical blending of Metformin and the polymers in varying ratios. The formulation was optimized on the basis of in vitro buoyancy and in vitro release in simulated gastric fluid pH 1.2. Effect of Carbopol as a release modifier was studied to ensure the delivery of drug from the floating tables over a prolonged time period. Tablets prepared with HPMC K15M and Carbopol gave the best in vitro percentage release and were taken as the optimized formulation. By fitting the data into zero order, first order, Korsmeyer and peppas, and Higuchi model it was concluded that the release followed Korsmeyer and peppas release, as the correlation coefficient (R2 value) was higher for Korsmeyer and Peppas release. All the six formulations produced robust tablets with optimum hardness, consistent weight uniformity and low tablet friability. In vitro drug release tests of these tablets indicated controlled sustained release of Metformin HCl and 96-99% released at the end of 8hr in formulation containing high viscosity polymers.

PoonamSalunke *et al.,* [51] Ionotropic gelation technique can successfully used for preparation of Metformin hydrochloride microcarriers using different permeability polymer and gas forming agent. Various formulation variables such as concentration of gas forming agent combination of polymer, calcium chloride concentration, cross linking time were used, which are influenced to the drug entrapment efficiency, particle size and shape, floating behavior, and *in-vitro* drug release. The FTIR and DSC studies did not reveal any significant drug interactions. From above all results we conclude that CaCO3 is more suitable for sustained drug delivery system as compared to NaHCO3. The formulation M5 shows the satisfactory results of evaluation parameters, it remains floated up to 24 hrs. Shows 94% drug release within 24 hrs. It means this formulation is suitable for floating sustained drug delivery system.

Brijesh S.Dave *et al.,* [52] developed a gastroretentive drug delivery system of Ranitidine hydrochloride .Guar gum, Xanthan gum, and Hydroxy propyl methyl cellulose used as a gel forming agents. Sodium bicarbonate was incorporated as a gas- forming agent. The effect of citric acid and stearic acid on drug release profile and floating properties were investigated. He concluded HPMC K4M and $NaHCO_3$ were essential to achieve in vitro buoyancy. By selecting suitable composition of citric acid (release rate enhancer) and stearic acid (release rate retardant) the dissolution profile can be achieved.

Ichikawa *et al.,* [53] developed a new multiple type of floating dosage system composed of effervescent layers and swellable membrane layers coated on sustained release pills. The inner layer of effervescent agents containing sodium bicarbonate and tartaric acid was divided into 2 sublayers to avoid direct contact between the 2 agents. These sublayers were surrounded by a swellable polymer membrane containing polyvinyl acetate and purified shellac. When this system was immersed in the buffer at 37°C, it settled down and the solution permeated into the effervescent layer through the outer swellable membrane. CO_2 was generated by the neutralization reaction between the 2 effervescent agents, producing swollen pills (like balloons) with a density less than 1.0 g/mL. It was found that the system had good floating ability independent of pH and viscosity and the drug (para-amino benzoic acid) released in a sustained manner.

Li *et al.,* [54] evaluated the contribution of formulation variables on the floating properties of a gastro floating drug delivery system using a continuous floating monitoring device and

statistical experimental design. The formulation was conceived using taguchi design. HPMC was used as a low-density polymer and citric acid was incorporated for gas generation. Analysis of variance (ANOVA) test on the results from these experimental designs demonstrated that the hydrophobic agent magnesium stearate could significantly improve the floating capacity of the delivery system. High-viscosity polymers had good effect on floating properties. The residual floating force values of the different grades of HPMC were in the order K4 M > E4 M > K100 LV > E5 LV but different polymers with same viscosity, i.e., HPMC K4M, HPMC E4M did not show any significant effect on floating property. Better floating was achieved at a higher HPMC/carbopol ratio and this result demonstrated that carbopol has a negative effect on the floating behavior.

Nur and Zhang ***et al.,***[55] developed floating tablets of captopril using HPMC (4000 and 15 000 cps) and carbopol 934P. Invitro buoyancy studies revealed that tablets of 2 kg/cm^2 hardness after immersion into the floating media floated immediately andtablets with hardness 4 kg/cm^2 sank for 3 to 4 minutes and then came to the surface. Tablets in both cases remained floating for 24 hours. The tablet with 8kg/cm^2 hardness showed no floating capability. It was concluded that the buoyancy of the tablet is governed by both the swelling of the hydrocolloid particles on the tablet surface when it contacts the gastric fluids and the presence of internal voids in the center of the tablet (porosity). A prolonged release from these floating tablets was observed as compared with the conventional tablets and a 24-hour controlled release from the dosage form of captopril was achieved.

Talwar ***et al.,***[56] developed a once-daily formulation for oral administration of ciprofloxacin. The formulation was composed of 69.9% ciprofloxacin base, 0.34% sodium alginate, 1.03% xanthum gum, 13.7% sodium bicarbonate, and 12.1% cross-linked poly vinyl pyrrolidine. The viscolysing agent initially and the gel-forming polymer later formed a hydrated gel matrix that entrapped the gas, causing the tablet to float and be retained in the stomach or upper part of the small intestine (spatial control). The hydrated gel matrix created a tortuous diffusion path for the drug, resulting in sustained release of the drug (temporal delivery).

Praveen Nasa ***et al.,***[57]From the present study, it was concluded that the formulation F5 (containing 160 mg of Methocel K100M and 40 mg of Methocel E50) was the optimum formulation amongst all the test batches. It exhibited satisfactory pre-compression properties, as well as, showed satisfactory dissolution profile as a sustained release formulation. Not

only this, the formulation was also found to possess appropriate floating characteristics, as revealed in the *in vitro* buoyancy studies. Moreover, the dissolution profile of the optimized formulation showed similarity to the marketed formulation. Therefore, it may be concluded from the investigation that a combination of Methocel K100M and Methocel E50 in the ratio of 4:1 may be satisfactorily used in the formulation of floating drug delivery system for a freely soluble drug such as Metformin.

3. AIM AND OBJECTIVE

Ciprofloxacin Hcl is commonly known as broad spectrum antibiotic medicine which is used to treat infections caused by gram positive and gram negative microorganism. These also prescribed in treatment of respiratory and urinary tract infections. Ciprofloxacin conventional tablets have been used from long period of time for the treatment of bacterial infections.CiprofloxacinHcl is an acidic drug which is primarily absorbed in stomach. The bioavailability of Ciprofloxacin is 69% and its half life is 4 hours.

The present investigation of work is to prepare Ciprofloxacin floating tablets by using polymers like HPMC K4M, Eudragit 100S, guar gum, and the prepared tablets are characterized by using different evaluation parameters like buoyancy lag time, floating time, in-vitro drug release, uniformity of drug content, hardness, friability etc.And the best suited formulation of Ciprofloxacin Hcl is compared with marketed product.

- To improve half life which shows prolong action of drug in controlled manner for long period in stomach.
- To increase bioavailability of drug by increasing gastric residue time.
- Ciprofloxacin floating tablets are used to decrease dose frequency of drug also avoid fluctuations that cost by conventional tablets and also it helps to reduce the adverse effects caused by ciprofloxacin at higher doses.

4. PLAN OF WORK

It was planned to carry out the following

PART-1

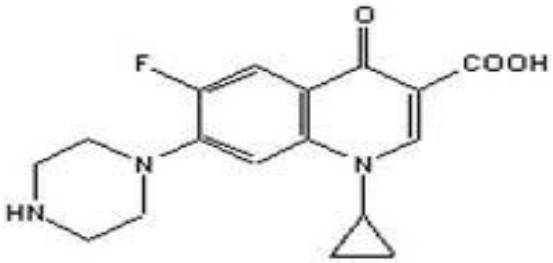
1. Estimation of Ciprofloxacin Hcl drug
2. Drug-Polymer compatibility studies by FTIR
3. Preparation of granules for Ciprofloxacin Hcl floating tablets
4. Preformulation studies of granules by
    - Angle of repose
    - Bulk density
    - Tapped density
    - Compressibility index
    - Hausner's ratio

PART-2

1. Compression of granules in tablets
2. Characterization of Ciprofloxacin Hcl floating tablets by
    - Hardness test
    - Friability test
    - Weight variation
    - Diameter
    - Thickness
    - Drug content uniformity
    - Buoyancy lag time
    - Floating time
3. In-vitro dissolution studies
4. Stability studies
5. Kinetic analysis of dissolution data

5. DRUG PROFILE

CIPROFLOXACIN[58,59]



Description of Ciprofloxacin

Ciprofloxacin is faintly yellowish to light yellow crystalline powder

Chemical Data

Chemical name	**:**	1-Cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-Quinoline-3-carboxylic acid
Formula	**:**	C_{17} H_{18} F N_3 0_3
Molecular mass	**:**	331.346 g/mol

Physical Data

Solubility	**:**	Freely soluble in distilled water, Phosphate buffer PH 6.8 & 7.5
Melting point	**:**	255-257ºC
Drug Category	**:**	Fluoroquinolones

Pharmacokinetic Data

Absorption	:	Rapidly and well absorbed from GIT with peak plasmaConcentration after 2hours
Bioavailability	:	69%
Half life	:	4 hours
Distribution	:	Bile (high concentration) , CSF(10%) ,crosses placentalbarrier
Protein binding	:	20-40%
Metabolism	:	Hepatic including CYP A2
Excretion	:	Renal (major), non renal routes like hepatic, biliyarytransluminal Secretion

Analytical Data

Absorption maxima	:	277nm
pKa value	:	6.09

Mechanism of Action

Ciprofloxacin Hcl drug has invitro activity against a wide range of gram negative and gram positive organism. Ciprofloxacin inhibits bacterial DNA gyrase, an enzyme Responsible for countering excessive supercoiling of DNA during replication of transcription .But the mechanism action of Ciprofloxacin is different from other antimicrobial agents such as Beta lactum,tetracyclins, aminoglycosides therefore organism resistant to these drug may susceptible to Ciprofloxacin Hcl drug.

Uses[60]

Ciprofloxacin is used for treatment of a number of infections including infection of Joints and bones, gastroenteritis, malignant otitis externa, respiratory tract infections,

cellulities, urinary tract infections, anthrax, skin structural infections, typhoid fever. Ciprofloxacin Hcl also used in treatment of community acquired pneumonia, chronic bacterial prostastitis, nosocomial pneumonia etc..

Brand Names	:	Cipro, Cipro XR, Proquin XR, Ciloxan.
Available Dosages	:	Tablets, Intravenous solutions, eye and ear drops
Dosing	:	Adult dose is 250-750mg (immediate release tablets) for Every 12hours or 500-1000mg (extended release tablets), 200-400mg (i.v),Child dose is 200-400mg/kg bid

Contraindications

Ciprofloxacin administration may become contra indicated to some drugs thatmay metabolize by enzyme CYP A2 and some drugs like Tizanidine. Ciprofloxacin Contraindicated in persons with a history of hypersensitivity to this drug and other quinoline drugs.

Pregnancy

Ciprofloxacin comes under pregnancy category C where there is no evidence studies of Ciprofloxacin in pregnant women so it should not used during pregnancy.

Nursing Mothers

Ciprofloxacin should avoid in nursing women.

Pedriatic population

Ciprofloxacin should not used in infants as they have not developed sufficient enzymes to metabolise drug and it should not used to children via intravenous route.

Adverse reactions

Ciprofloxacin may cause mild adverse reactions like nausea, vomiting, diarrhoea, rashes, abnormal liver functions and it may cause some rare but serious adverse effects like Myasthenia gravis including muscle weakness, breathing problem, neuropathy, photosensitivity reactions etc.

Drug Interaction

Ciprofloxacin may interact with some drugs like amoxicillin, trimethoprim, azithromycin, cephalexin and some herbal and natural supplements. This drug can interact with NSAIDS causes Black box warning which leads to Achiles tendon rupture.

Storage

Oral products should be stored at 5±25ºC, Ophthalmic products should be stored At 2±25ºC intravenous solutions should be stored at 25ºC

6. POLYMER AND EXCIPIENTS PROFILE

EUDRAGIT[61,62,63]

Nonproprietary Names	**:**	Ph.Eur:Ammonio methacrylate copolymer USP/NF: Ammonio methacrylate copolymer NF
Synonyms	**:**	Acrylates, ammonium methacrylate copolymer
Chemical Name	**:**	Poly(ethyl acrylate copolymer co-trimethyl Ammonioethyl methacrylate chloride)

Description

Eudragit 100S polymer is a white crystalline powder with faint amine like odour.

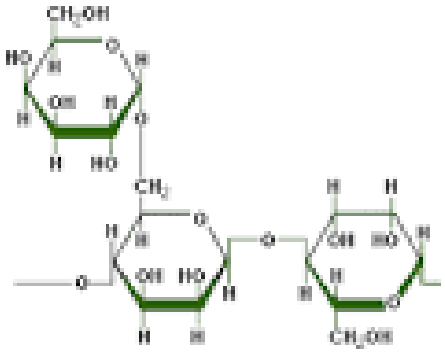
Pharmaceutical Applications

Eudrgit is an advance polymer which is widely used nowadays. Eudragit is used infilm coating and enteric coating for tablets. It also used in sustain release formulations. Eudragitused in ophthalmic drug delivery system to prepare ocular drug delivery system. Eudragit also used in vaginal drug delivery to prepare intra vaginal tablet and it used in preparation of buccal sublingual formulations. Eudragit polymer also widely used in gastro retentive drug delivery system in preparation of pH dependent and floating tablets. It is also used in gene delivery and vaccine delivery in the form of microspheres and nano particles etc.

Stability and Storage Conditions

Eudragit powder is a stable material at room temperature. It should stored in well closed container and should be protected direct contact with sunlight and stored at room temperature.

GUAR GUM



Nonproprietary Names	:	BP: Guar galactomannan, phEur: guar USPNF: gar gum galactomannan.
Synonyms	**:**	Galactosal: guar flour: jaguar gum; meyprofin
Chemical name	:	Galactomannan polysaccharide
Empirical formula	:	$C_6 H_{12} O_6$
Molecular weight	:	220.00 g/mol
Description	**:**	Guar gum is aodourless, white to yellowish powder with bland taste.

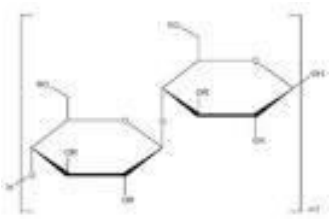
Applications in pharmaceutical technology,[61-63]

Guar gum commonly used in cosmetics, food products and pharmaceutical formulations. It also used in preparation of sustain release matrix tablets in place of cellulose derivatives. It also used solid dosage form as binder and disintegrant. Guar gum also used in some oral and topical products as a suspending agent, thickening agent and stabilizing agent. Guar gum used in gastro retentive drug delivery like floating drug delivery system etc. These polymer also used in preparation of creams and ointments as stabilizing agent. Guar gum is a natural polymer which also used as binding agents in formulation of oral dosage form

Stability and storage condition

Guar gum is stable at PH 4.0-10.5 and the powder should be stored in a well closed container in a cool, dry place and should be avoid direct contact with sunlight.

HYDROXY PROPYL METHYL CELLULOSE



Nonproprietary name	**:**	BP:Hypermellose , IP:Hydroxy propyl methyl cellulose, phEur: Hypermellosum, USP:Hypermellose
Synonyms	**:**	HPMC, Methocel, methyl cellulose propylene glycolether, Metalose, tylopur
Chemicalnames	:	Cellulose hydroxyl propyl methyl ether
Empirical formula	:	(O CH_2 CH (OH) CH_3)
Molecular weight	:	10000-500000 g/mol
Description	**:**	HPMC is an odourless and tasteless white or creamywhite fibrous or granular powder

Applications in pharmaceutical technology,[61-63]

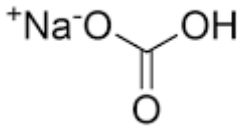
HPMC widely used in oral, ophthalmic and topical pharmaceutical forrmulations. In oral products it is mainly used as tablet binder, film coating agent and also matrix used in extended release tablet formulation. HPMC also used as suspending and thickening agent in topical formulations. It also used as stabilizing and emulsifying agent in topical gels and ointments. In additional it used in manufacturing of capsules, as an adhesion in plastic

bandages and as a wetting agent for hard contact lenses. HPMC also used in cosmetic and food products.HPMC polymer also used in preparation of gastro retentive dosage form.

Stability and storage condition

HPMC K_4M is a stable material but it is hygroscopic after drying. It stable.at pH 3-11 and it should be stored in well closed container in a cool and dry place.

SODIUM BICARBONATE



Nonproprietary name[64]	:	Backing soda, bread soda, cooking soda, bicarbonate of soda
Synonyms	**:**	Sodium bicarb, bicarb sodium, bicarb
Chemical name	:	Sodium hydrogen carbonate
Molecular formula	:	$NAHCO_3$
Molecular mass	:	84.007g/mol
Description	:	It is aodourless white crystal or powder which is soluble in Water

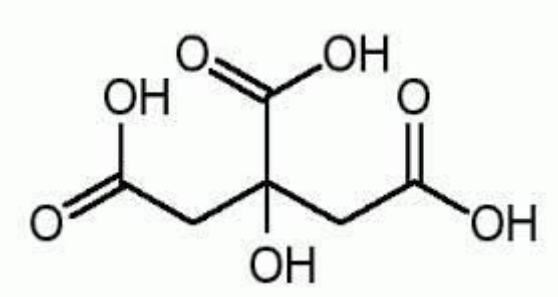
Applications in pharmaceutical technology

Sodium bicarbonate used as preservative and antiseptic agents. It also used as effervescent agent in floating tablets. It also used in personal hygiene as product preparation of toothpaste. It also used as a cleansing agent and scrubbing agent. It mainly used in treatment of acidosis as a antacids and it can used to treat digestive disorders and urinary alkalinisation.

Stability and storage conditions

Sodium bicarbonate is a stable in dry air at room temperature. In moist air it decompose by generating carbon dioxide. It should be stored in tight well closed container in a cool and dry place should be avoid direct sunlight.

CITRIC ACID



Nonproprietary name[64]	:	3-carboxy-3-hydroxypentanedioic acid,2- hydroxy - 1,2,3- Pro Panetri carboxylic acid
Chemical name	:	2-hydroxy propane -1, 2, 3- tri carboxylic acid
Molecular formula	:	$C_6 H_8 O_7$
Molecular mass	:	92.1235 g/mol
Description	:	Citric acid is aodourless, crystalline white solid granular to Fine powder with strong acidic taste

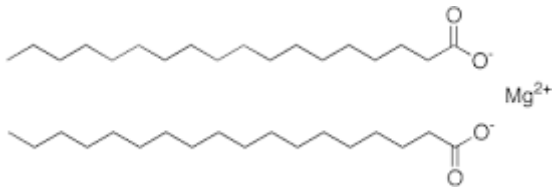
Applications in pharmaceutical technology

Citric acid can used as flavouring agent and preservative in food and especially in soft drinks and in ice creams. It also used as emulsifying agent in ice creams and also used as cleaning and chelating agent in hard water. In combination with sodium bicarbonate it used as gas generating agent. It also used in cosmetic preparation and pharmaceutical agent. Citric acid also used as a ingredient of antiviral tissue. It can also usedas colouring agent and adult ant in food industries.

Stability and storage conditions

Citric acid monohydrate may stored for 36months from date of manufacturing. It should be stored at relative humidity of 50% and a temperature range of 10±30ºC. It should be stored in well closed container and avoid direct contact with sunlight.

MAGNESIUM STEARATE



Nonproprietary name[64]	:	Magnesium salt
Synonym	:	Octadecanoic acid, magnesium salt
Chemical name	**:**	Magnesium octadecanoate
Molecular formula	:	Mg $(C_{18}\ H_{35}\ O_2)_2$
Molecular mass	:	591.27g/mol
Description	:	Magnesium stearate is a very fine, light white powder milled powder with characteristic taste with slight odour which is greasy to touch.

Applications in pharmaceutical technology

Magnesium stearate mainly used as a diluents in manufacturing of medical tablets, capsules and powder. It also used as lubricating agent that prevent sticking of the tablet to equipments. It can also used as food additives and also manufacturing of animal and vegetable oils.

Stability and storage conditions

Magnesium stearate is a stable product which should be stored tightly in well closed container in cool and dry place and should be stored at room temperature.

STARCH

Nonproprietary Name[64]	:	BP: Maize starch, Potato starch, Rice Starch Tapioca Starch, Wheat starchJP: Corn Starch, Potato Starch, Rice Starch, PhEur: Maize Starch, Pea Starch USP-NF: Corn Starch, Tapioca Starch, Potato
Synonyms	**:**	Amido; amidon; amilo; amylum; Pharmgel; amylum; triticiamylum; fecule; maydisamylum
Chemical Name	:	Starch
Empirical Formula	:	$(C_6H_{10}O_5)$ n
Molecular Weight	:	300–1000 g/mol

Description

Starch occurs as an odorless and tasteless, fine, white to off-white powder. It consists of very small spherical or ovoid granules or grains whose size and shape are characteristic for each botanical variety.

Functional Category:

Tablet and capsule diluent; tablet and capsule disintegrant; tablet binder; thickening agent.

Applications in Pharmaceutical Formulation or Technology:

Starch is a versatile excipient used primarily in oral solid-dosage formulations where it is utilized as a binder, diluent, and disintegrant. In tablet formulations, freshly prepared starch paste is used at a concentration of 3–20% w/w (usually 5–10%, depending on the starch type) as a binder for wet granulation. The required binder ratio should be determined by optimization studies, using parameters such as tablet friability and hardness, disintegration

time, and drug dissolution rate. Starch is one of the most commonly used tablet disintegrants at concentrations of 3–25% w/w; a typical concentration is 15%. Starch paste is used in ointment formulations, usually in the presence of higher ratios of glycerin. Starch has been investigated as an excipient in novel drug delivery systems for nasal and other site-specific delivery systems. Starches are useful carriers for amorphous drug preparations, such as pellets with immediate or delayed drug release obtained, for example, by melt extrusion and they can improve the bioavailability of poorly soluble drugs. Starch, particularly rice starch, has also been used in the treatment of children's diarrheal diseases

Stability and Storage Conditions

Dry starch is stable if protected from high humidity. Starch is considered to be chemically and microbiologically inert undernormal storage conditions. Starch solutions or pastes are physically unstable and are readily metabolized by microorganisms; they should therefore be freshly prepared when used for wet granulation. Starch should be stored in an airtight container in a cool, dry place.

7 . MATERIALS AND METHODS

THE FOLLOWING MATERIALS USED IN THE PRESENT STUDY

TABLE NO-1

S.No	*MATERIALS USED*	*SUPPLIER / MANUFACTURERS*
1	***CIPROFLOXACIN HCL***	***MNS laboratory, Hyderabad***
2	***HPMC K4M***	***Reddy's lab, Hyderabad***
3	*EUDRAGIT 100S*	***Reddy's lab, Hyderabad***
4	*GUAR GUM*	***Yucca enterprises, Mumbai***
5	***SODIUM BICARBONATE***	***Rankem lab, Gujarat***
6	***CITRIC ACID***	***Rankem lab, Gujarat***
7	***MAGNESIUM STEARATE***	***Himedia laboratories, Mumbai***
8	***STARCH***	***Finar chemicals, Ahmadabad***

THE FOLLOWING EQUIPMENTS ARE USED IN PRESENT STUDY

TABLE NO-2

S.No	*EQUIPMENTS USED*	*COMPANY/ SUPPLIER*
1	***U.V.SPECTROPHOTOMETER***	***Analytical spetro 2060 plus***
2	***ELECTRONIC BALANCE***	***Eagle instrument pvt.***
3	*FOURIER TRANSFORM INFRA REDSPECTROSCOPY (FTIR)*	***Perkin Elmer ND Spectrum RX1***
4	*TABLET PUNCHING MACHINE*	***Cadmach punching machine***
5	***HARDNESS TESTER***	***SSN tablet hardness tester***
6	***FRIABILATOR***	***Electro laboratories***
7	***DISSOLUTION APPARATUS***	***Electronic India microprocessor dissolution apparatus***
8	***BESTO VERNIER CALIPERS***	***Electro laboratories***

EXPERIMENTAL STUDIES

CALIBRATION CURVE OF CIPROFLOXACIN HYDROCHLORIDE

ANALYTICAL METHODS:

CALIBRATION OF CIPROFLOXACIN HYDROCHLORIDE:

A spectrophotometric method based on the measurement of absorbance 277 nm in a 0.1 HCl was used in the present study for the estimation of Ciprofloxacin HCl.

REAGENTS:

Preparation of 0.1N HCl[65,66]:

8.5ml of Concentrated HCl was taken in a volumetric flask and it was made up to 1000ml with distilled water.

STANDARD SOLUTION:

100mg of Ciprofloxacin HCl pure drug was dissolved in 100ml of 0.1N Hcl(stock solution) 10ml of solution was taken and make up with100ml of 0.1N Hcl(100µg/ml).

.

PROCEDURE:

From the standard solution aliquots of 2ml, 4ml, 6ml, 8ml,10ml were pipette out to 100 ml standard measuring flask and made up to 100 ml with 0.1 N HCl. The absorbance of the above solutions was measured in UV-spectrophotometer at 277 nm using0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line which indicates the drug is pure.

Table -3: calibration curve of Ciprofloxacin

S.No	*Concentrations(µg/ml)*	*Absorbance (nm)*
1	***0***	***0.000***
2	***2***	***0.107***
3	*4*	***0.219***
4	*6*	***0.342***
5	***8***	***0.441***
6	***10***	***0.542***

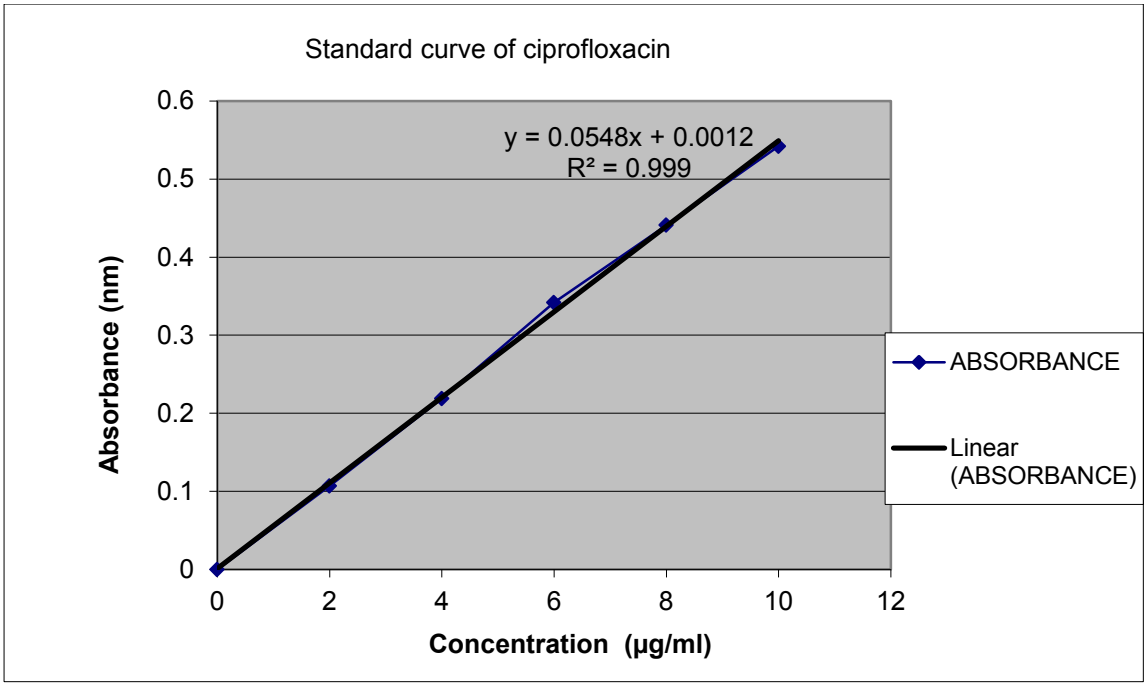


Fig 5: Standard curve of Ciprofloxacin Hcl

COMPATABILITY STUDIES BY FTIR STUDIES

Drug-polymer compatibility studies:[65]

FTIR analysis:

Infrared spectroscopy was conducted using an Perkin Elmer FTIR combined to PC (with spectrum 2000 analysis software) was recorded in region of 4000 to 400 cm. The procedure consisted of dispersing a sample as shown in table in KBr and compressing into discs by applying a pressure of 5 tons for 5min in a hydraulic press. The pellet was placed in light path and the spectrum was obtained.

Table 4: Composition of drug and polymers samples for IR studies

S. No	*SAMPLES FOR FTIR STUDIES*
1	*Ciprofloxacin Hcl*
2	*HPMC K4M*
3	*Eudragit 100S*
4	*Guar gum*
5	*Ciprofloxacin Hcl + HPMC K4M*
6	*Ciprofloxacin Hcl + Eudragit 100S*
7	*Ciprofloxacin Hcl+ Guar gum*
8	*Ciprofloxacin Hcl+ HPMC K4M+ Eudragit 100S+ Guar gum+ Sodium bicarbonate+ Citric acid*

3. PREPARATION OF CIPROFLOXACIN HYDROCHLORIDE FLOATING TABLETS [66]

Floating tablets of Ciprofloxacin Hcl were prepared by wet granulation technique using various polymers like HPMC K4M, Eudragit100S, Guar gum with combination of sodium bicarbonate and citric acid as gas generating agent. The composition of each formulation is given in formulation table no - 5. Totally seven batches of granules were prescribed by using different single and combination of polymers.F1 contains 150mg of HPMC K4M, F2 contains150mg of Eudragit 100S, F3 contains 150mg of guar gum, F4 contains 75mg of HPMC K4M and 75mg Eudragit 100S, F5 contain 75mg of Eudragit 100Sand 75mg of guar gum, F6 contain 75mg of HPMC K4M and 75mg guar gum, F7 contains 50mg of HPMC K4M, 50mg Eudragit 100S and 50mg guar gum. Magnesium stearate used as a lubricant.

Ciprofloxacin Hcl is passed through sieve no.20, HPMC K4M,Eudragit 100S,Guar gum, sodium bicarbonate, citric acid passed through sieve no.40. Magnesiunstearate is passed through sieve no 60. The shifted materials of Ciprofloxacin Hcl was geometrically mixed with polymer and sodium bicarbonate and citric acid and blended for 10minutes.Then add starch mucilage slowly drop wise manner to form a coherent mass.The formed coherent mass was sieved manually through sieve no.16 to form granules. Then the granules are collected and dried in hot air oven at 40^0C ± 2^0C for 2 hours. The dried granules were passed through

sieve no.20. Magnesium stearate is added to the dried granules then subjected to pre formulation studies. After the completion of preformulation studies, the granules of all formulations were compressed into tablets by using tablets punching machine

Table-5: Formulation of Ciprofloxacin Hcl floating tablets

Formulation Batches	*Ciprofloxacin Hcl (mg)*	*HPMC K4M (mg)*	*Eudragit 100S (mg)*	*Guar gum (mg)*	*Sodium bicarbonate (mg)*	*Citric acid (mg)*	*Starch mucilage (mg)*	*Magnesium stearate (mg)*
F1	*250*	*150*	*-*	*-*	*50*	*15*	*25*	*10*
F2	*250*	*-*	*150*	*-*	*50*	*15*	*25*	*10*
F3	*250*	*-*	*-*	*150*	*50*	*15*	*25*	*10*
F4	*250*	*75*	*75*	*-*	*50*	*15*	*25*	*10*
F5	*250*	*-*	*75*	*75*	*50*	*15*	*25*	*10*
F6	*250*	*75*	*-*	*75*	*50*	*15*	*25*	*10*
F7	*250*	*50*	*50*	*50*	*50*	*15*	*25*	*10*

Weight of each tablet – 500 mg

PREFORMULATION STUDIES

Bulk Density:[67]

It refers to a measurement to describe packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in mg/ml

Procedure:

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder in to a measuring cylinder and the initial volume was noted. This initial volume is called bulk volume. The powder was tapped 3 times till a constant volume called bulk density was obtained. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$P_b = m/v_b$$

Where,

m = mass of the granules

v_b = bulk volume

Tapped Density:[67]

After determining the poured bulk density,Weighed quantity of API was taken into a graduated cylinder. Volume occupied by DRUG was noted down. Then the cylinder was subjected to 500, 750 & 1250 taps in tap density tester (Electro Lab USP II). According to USP, the blend was subjected for 500 taps. % Volume variation was calculated and subjected for additional 750 taps. % Variation is calculated.

$$\mathbf{P_t = m/v_t}$$

Tapped bulk density=Mass of powder/Tapped volume of the powder.

Compressibility Index:

Weighed API was transferred to 100ml-graduated cylinder and subjected to 500,750&1250 taps in tap density tester (Electro lab). The difference between two taps should be less than 2%. The %of compressibility index calculated using formula

$$CI = v_b - v_t / v_b \times 100$$

Limits :

S.No	Compressibility index	Flow
1	5-12	Free flow
2	12-16	Good flow
3	18-21	Fair
4	23-25	Poor
5	33-38	Very Poor
6	>40	Extremelypoor

Hausner's Ratio:

It is measurement of frictional resistance of the drug. The ideal range should be 1.2 –1.5. It is the determined by the ratio of tapped density and bulk density.

$$\text{Hausner's ratio} = v_i / v_b$$

Where

v_t = Tapped volume

v_i = Bulk volume

Limits:

S. No	Hausner' ratio	Flow
1	1.0-1.11	Excellent
2	1.1-1.18	Good
3	1.19-1.25	Fair
4	1.26-1.34	Possible
5	1.35-1.45	Very poor
6	>1.60	Very very poor

Angle of repose:[69]

Angle that can be obtained between the free surface of a powder heap and horizontal plane. The angle of repose was measured by allowing the powders to fall over a graph sheet placed on horizontal surface through a funnel kept at a certain convenient height (about 2 cm).

The height of the heap was measured and then circumference of the base of heap was drawn on a graph sheet with the help of a pencil. The radius of the circle obtained was measured. The angle of repose is given as,

$$\theta = \tan^{-1}(h/r)$$

Where

Θ = angle of repose

H = height of the heap

R = radius of the base of the heap

Limits:

Angle of Repose (Degrees)	*Type of Flow*
<20	***Excellent***
20-30	***Good***
30-34	***Passable***
>40	***Very Poor***

CHARACTERIZATION OF CIPROFLOXACIN HCL FLOATING TABLETS

The formulated tablets were evaluated for the following physicochemical characteristics:

Various standards have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. These include thickness, size, diameter, shape, weight, hardness, disintegration and dissolution characters. The diameter and shape depends on the die and punches selected for the compression of tablets. The remaining specifications assure that tablets do not vary from one production lot to another. The following standards or quality control tests were carried out on Ciprofloxacin floating tablets .

General appearance:[70-71]

The general appearance of tablets, its visual identity and overall "Elegance" is essential for consumer acceptance, control of lot-to-lot uniformity and general tablet-to-tablet uniformity and for monitoring the production process. The control of general appearance involves measurement of attributes such as a tablets size, shape, colour, presence or absence of odour, taste, surface textures, physical flows and consistency.

The formulated tablets were assessed for its general appearance and observations were made for shape, color, texture and odour.

Hardness test:[65]

Hardness of the tablet was determined by using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

Weight Variation:[72]

20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 5% for 500 mg tablets and none by more than double that percentage.

The percentage deviation was calculated by using following formula

% Deviation = (Individual weight – Average weight) / Average weight x 100

Limits:

Average weight of a tablet	*%deviation*
130 mg or less	***±10***
>130 mg and < 324 mg	***±7.5***
324 mg or more	***±5.0***

Friability test:[69]

Friability is the loss of weight of tablet in the container/package due to removal of fine particles from the surface. This test is applicable to compressed tablets and is intended to determine the physical strength of tablets.

It is usually measured by the use of Roche friabilator. The drum is attached to the horizontal axis of a device that rotates at 25 ± 1 rpm. It should be ensured that with every turn of the drum the tablets roll or slide and fall on to the drum wall or onto each other.

Ten tablets are weighed (w_1) and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After 4 minutes of this treatment or 100 revolutions, the tablets are weighed (w_2) and this weight was compared with the initial weight of tablet. The loss of weight may be due to abrasion is a measure of the tablet friability. The value is expressed in percentage. A maximum loss of weight not greater than 1% is acceptable for most tablets.

if the tablets are cracked, chipped or broken after tumbling, the sample fails the test. The friability was determined using the following formula:

$$\text{friability} = \frac{(w_1 - w_2)}{w_1} \times 100$$

Where,

w_1 = weight of ten tablets before test

w_2 = weight of ten tablets after test.

Estimation of Drug Content:[66]

20 tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of Ciprofloxacin Hydrochloride was transferred in to a 100 ml volumetric flask and volume made up with0.1N HCl. Further 1ml of the above solution was diluted to 10 ml with 0.1N HCl and absorbance of the resulting solution was observed at 277 nm.

Floating test:[70]

The tablets were placed in a 100ml beaker containing 0.1N Hcl. The time between introducing of dosage form and its buoyancy on 0.1N Hcl and the time during at whichthe dosage form remain buoyant were measured.

Buoyancy lag time:[37]

The time taken for the dosage form to emerge on surface of medium is Called Floating lag time (FLT). Total duration of time during which the dosage form remains buoyant is called Total floating time (TFT).

IN VITRO DISSOLUTION STUDIES OF TABLETS:[66]

Dissolution parameters:

Apparatus	--	USP-II, Paddle Method
Dissolution Medium	--	0.1 N HCl
RPM	--	50
Sampling intervals (hrs)	--	1,2, 3,4,5, 6,7, 8,9,10,11 and 12hour
Temperature	--	37°c $\pm$ 0.5°c

Dissolution Study:

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.]

Procedure:

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –11 (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 277 nm using UV-spectrophotometer.

Stability studies

The concentration of an active ingredient of any formulation may decrease with increase in temperature and time. This will lead to decrease the potency of the product. Stability study in different temperatures should be carried out to predict the stability of the formulations

Stability studies were aimed at determining the result of aging and storage under various conditions on the formulated floating tablets. Stability studies are used to find out whether any chemical degradation of ciprofloxacin formulations take place or not. The formulated tablets were stored at $4^{o}\pm 2^{o}C$ (in refrigerator), $27^{o}\pm 2^{o}C$ (in room temperature) and $45^{o}C \pm 2^{o}C$ (in accelerated stability chamber) for 45 days. Three tablets were taken from all the stored samples at the intervals of 15^{th}, 30^{th} and 45^{th} days and analysed for drug content and in vitro release studies were carried out to determine the percentage of ciprofloxacin released[71]

KINETIC ANALYSIS OF DISSOLUTION DATA:[72-76]

The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of matrix systems. As a model-dependent approach, the dissolution data was fitted to five popular release models such as zero-order, first-order, diffusion and exponential equations, which have been described in the literature. The order of drug release from matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from matrix systems was studied by using Higuchi equation, erosion equation and Peppa's-Korsemeyerequation. The results are given in Table no 26 and the graphical representation are presented in fig no 24.

Zero Order Release Kinetics

It defines a linear relationship between the fraction of drug released versus time.

$Q = k_o t$

Where, Q is the fraction of drug released at time t and $k_o$is the zero order release rate constant.

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First Order Release Kinetics:

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics. The equation that describes first order kinetics is

$$In\ (1-Q) = -\ K_1 t$$

Where, Q is the fraction of drug released at time t and k_1 is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

Higuchi equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$$Q=K_2 t^{½}$$

Where, K2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusionprocess based on the Fick's law, square root time dependant.

Power Law:

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppa's and Korsemeyer equation (Power Law).

$$M_t/M_\alpha = K.t^n$$

Where, M_t is the amount of drug released at time t and M_α is the amount released at time α, thus the $M_t/M_\alpha$is the fraction of drug released at time t,k is the kinetic constant and n is the diffusional exponent. To characterize the mechanism for both solvent penetration and drug release n can be used as abstracted in Table. A plot between log of M_t/M_α against log of time will be linear if the release obeys Peppa's and Korsemeyer equation and the slope of this plot represents "n" value.

Diffusion exponent and solute release mechanism for cylindrical shape

Diffusion Exponent	Overall solute diffusion mechanism
0.45	Fickian diffusion
0.45<n<0.89	Anomalous (non-fickian) diffusion
0.89	Case II transport
n>0.89	Super Case II transport

8. RESULTS AND DISCUSSION

The present study was undertaken to formulate ciprofloxacin floating tablets using three polymers and with three different ratios and prepared by wet granulation method. Before compression of the powder, evaluation studies such as bulk density, tapped density, angle of repose, compressibility index and Hausner ratio were determined and tabulated in Table No 14 After compression, evaluation tests of tablets such as general appearance, hardness, weight variation, friability, and content uniformity and other parameters such as in vitro drug release, IR analysis studies and stability studies were also preformed and the results are presented.

Drug-Polymer compatibility studies:

The physical and chemical state of polymers like HPMC K4M, Eudragit 100S, Guar gum and their admixture of polymer and drug used in Ciprofloxacin floating tablets prepared were studied by FTIR.

FTIR studies:

The samples for FTIR Spectral analysis were shown in table no.5 and peaks were shown in figure 5 to 12 and the interpretation of FTIR spectrum of Ciprofloxacin Hcl intable 8 .The physical mixture of drug and polymer was characterized by FTIR spectralanalysis for any physical as well as chemical alterations of drug characteristics. From theresult it was concluded that there was no interface of functional groups as principle peak ofCiprofloxacin Hydrochloride were found to be unaltered in the drug polymer physicalmixture. The physical parameters of drug as well as excipients concluded that there was nochange in peaks of admixture compared with drug whichindicates that the drug and excipients are compatible.

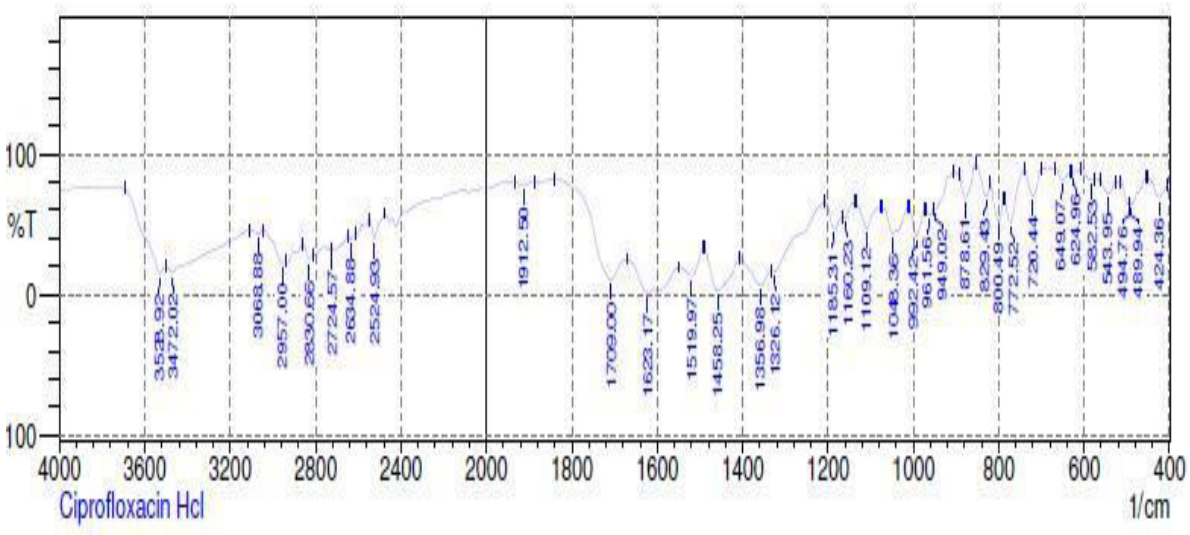


Fig 6: FTIR Spectrum of Ciprofloxacin Hcl

Table -6: FTIR Spectrum of Ciprofloxacin Hydrochloride

S.NO	*WAVE NUMBER (CM-)*	*ASSIGNMENT (Functional groups)*
1	*1623.17*	*C=O carbonyl group*
2	*1458.25*	*C-N Stretch*
3	*3528.92*	*O-H Stretch*
4	*3472.02*	*N-H Stretch*
5	*2957.00*	*Aliphatic C-H Stretch*
6	*2830.66*	*N-C Stretch*
7	*1519.97*	*C=O Stretch of quinoline*

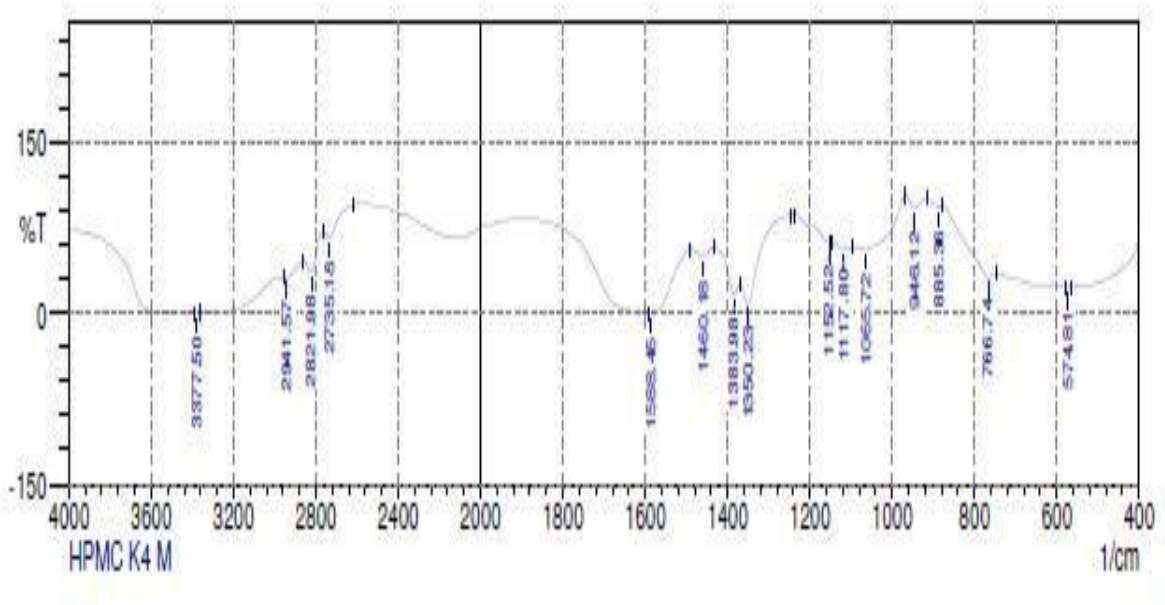


Fig7: FTIR Spectrum of HPMC K4M

Table-7: FTIR Spectrum HPMC K4M

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional groups)*
1	*3377.50*	*O-H Stretching*
2	*2941.57*	*CH2 Stretching*
3	*1588.45*	*C=C Stretching*
4	*1460.18*	*Ar C-C Stretching*
5	*1383.98*	*C-O Stretching*
6	*946.12*	*O-H Bending*

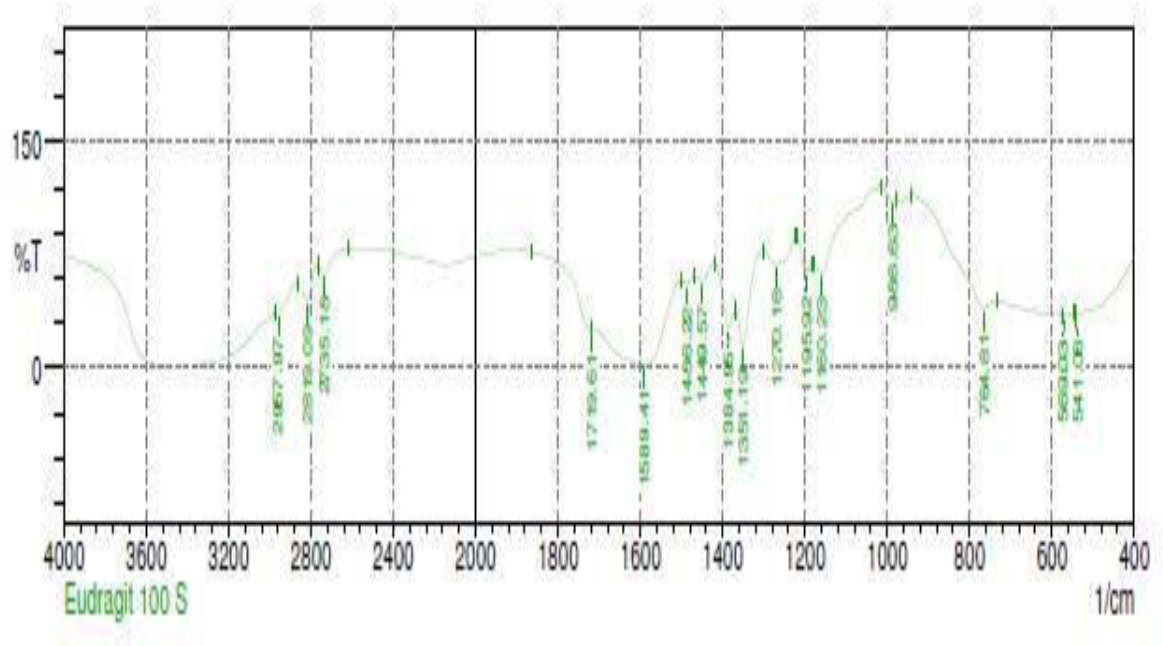


Fig 8: FTIR Spectrum of Eudragit 100S

Table-8: FTIR Spectrum of Eudragit 100S

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional groups)*
1	*2957.97*	*C-H Stretching*
2	*1719.61*	*C=O Stretching*
3	*1449.57*	*C=C Stretching*
4	*986.63*	*C-O Stretching*
5	*764.81*	*C-H Bending*

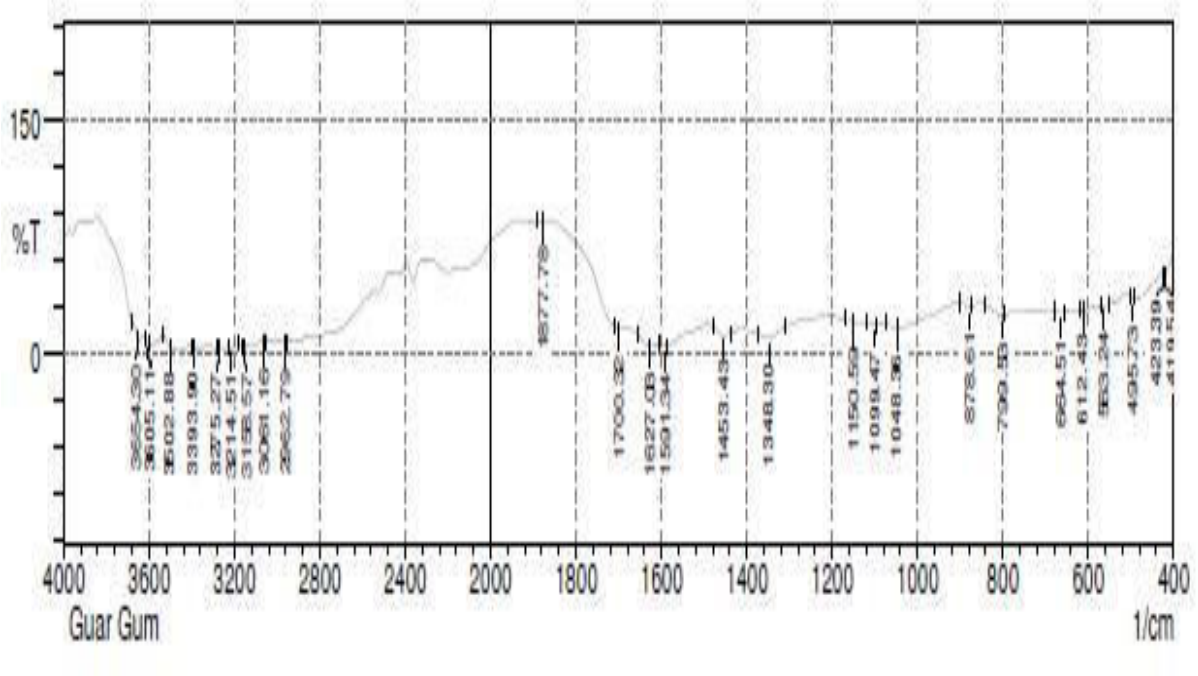


Fig 9: FTIR Spectrum of Guar gum

Table-9: FTIR Spectrum Guar gum

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional groups)*
1	*3393.90*	*O-H Stretching vibration*
2	*2962.79*	*C-H Stretching of CH2 group*
4	*1348.30, 1453.43*	*Symmetrical deformation of CH2 group*
5	*1150.59, 1099.47*	*C-OH & primary alcohol; -CH2OH Stretching mode*
6	*1048.36*	*-CH2 twisting vibration*
7	*878.61*	*Galactose& Mannose*
8	*799.53*	*(1-4), (1-6) linkage of Galactose& Mannose respectively*

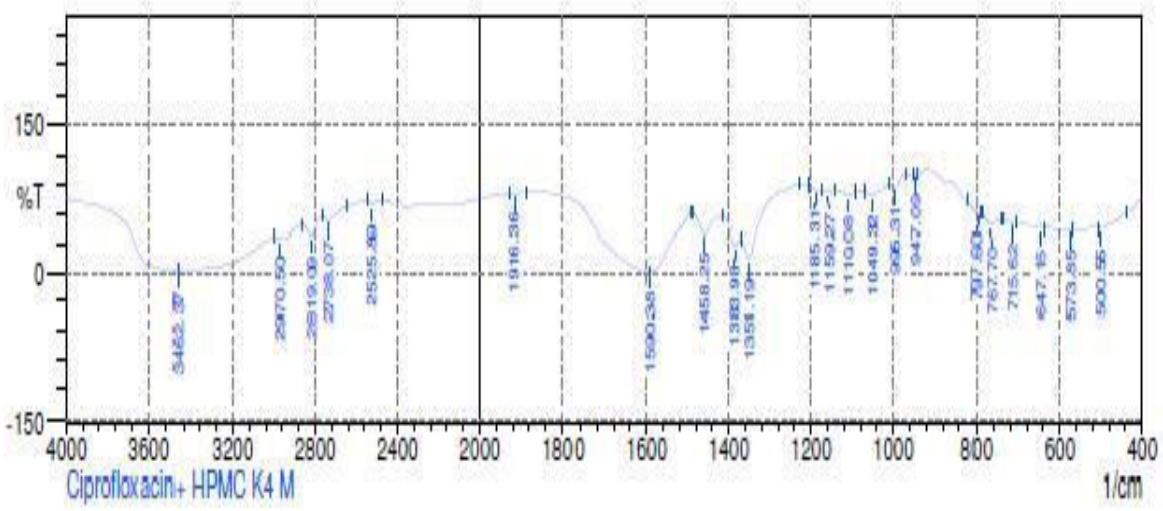


Fig 10: FTIR Spectrum of Ciprofloxacin Hcl& HPMC K4M

Table-10: FTIR Spectrum Ciprofloxacin Hcl& HPMC K4M

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional group)*
1	*1590.38-1623.17*	*C=O Stretching*
2	*1458.25*	*C-N Stretch*
3	*3462.37-3528.92*	*O-H Stretch*
4	*3462.37*	*N-H Stretch*
5	*2819.09-2830.66*	*Aliphatic C-H Stretch*
6	*1590.38*	*N-C Stretch*
7	*1383.98*	*C-O Stretching*
8	*947.09*	*O-H Bending*

Discussion:

Ciprofloxacin Hcl contains functional groups like C=O (Carbonyl group), C-N (Cyanide group), O-H (Hydroxyl group), N-H (Amino group), Aliphatic C-H group, N-C (Isocyanide group) etc., which are not disturbed when combined Ciprofloxacin Hcl with HPMC K4M. It states that combination of Ciprofloxacin Hcl with HPMC K4M doesnot shows any interactions with functional groups present in Ciprofloxacin Hcl as well as HPMC K4M. So we can conclude that Ciprofloxacin Hcl and HPMC K4M are compatible with each other.

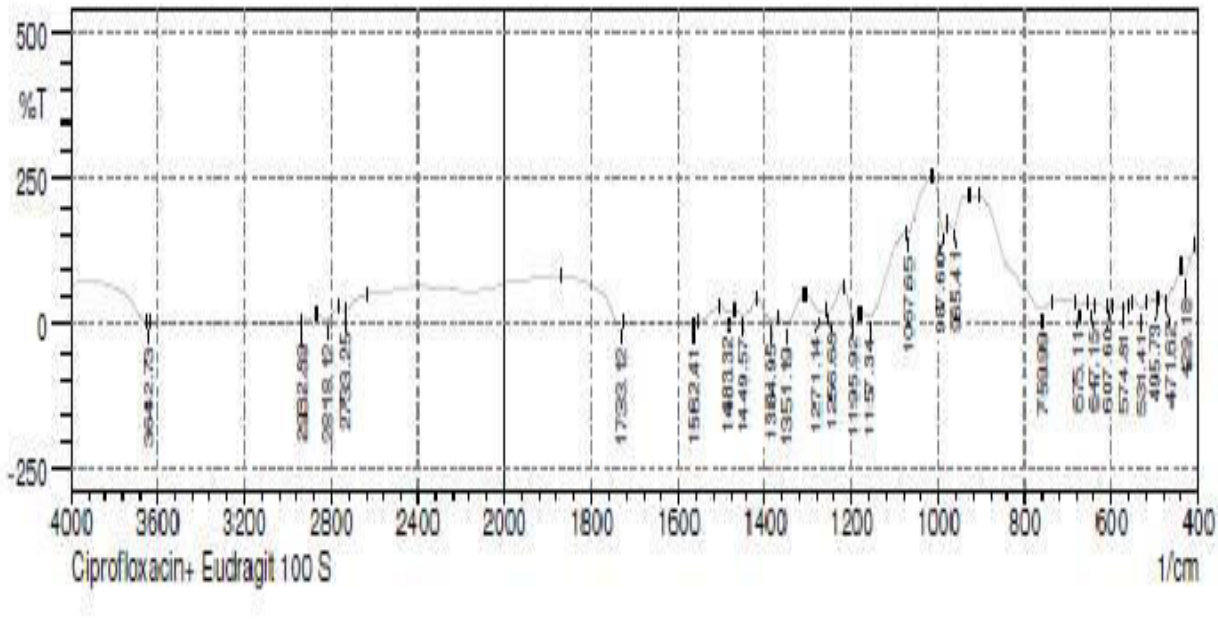


Fig 11: FTIR Spectrum of Ciprofloxacin Hcl&Eudragit 100S

Table-11: FTIR Spectrum Ciprofloxacin Hcl&Eudragit 100S

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional group)*
1	*1733.12*	*C=O Stretching*
2	*1449.57-1458.25*	*C-N Stretch*
3	*3528.92-3642.73*	*O-H Stretch*
4	*3472.02-3642.73*	*N-H Stretch*
5	*2932.89-2957.00*	*Aliphatic C-H Stretch*
6	*2818.12-2830.66*	*N-C Stretch*
7	*1483.32-1519.97*	*C=O Stretch of quinoline*

Discussion:

Ciprofloxacin Hcl contains functional groups like C=O (Carbonyl group), C-N(Cyanide group), O-H (Hydroxyl group), N-H (Amino group), Aliphatic C-H group, N-C(Isocyanide group), C=O of quinolineetc., which are not disturbed when combinedCiprofloxacin Hcl with Eudragit 100S. It states that combination of CiprofloxacinHclwith Eudragit 100Sdoesnot shows any interactions with functional groups present inCiprofloxacin Hcl as well as Eudragit 100S. So we can conclude that Ciprofloxacin Hcland Eudragit 100S are compatible with each other.

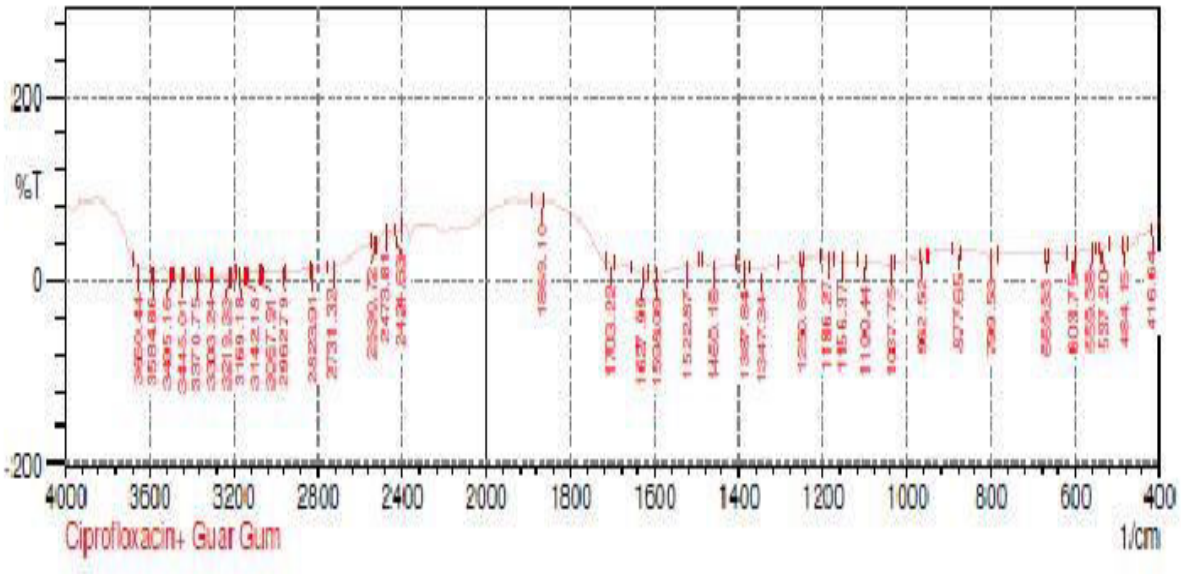


Fig 12: FTIR Spectrum of Ciprofloxacin Hcl& Guar gum

Table-12: FTIR Spectrum Ciprofloxacin Hcl& Guar gum

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional group)*
1	*1627.99*	*C=O Stretching*
2	*1460.18*	*C-N Stretch*
3	*3370.75-3584.86*	*O-H Stretch*
4	*3495.16*	*N-H Stretch*
5	*2962.79*	*Aliphatic C-H Stretch*
6	*2823.91*	*N-C Stretch*
7	*1522.87*	*C=O Stretch of quinoline*

Discussion:

Ciprofloxacin Hcl contains functional groups like C=O (Carbonyl group), C-N(Cyanide group), O-H (Hydroxyl group), N-H (Amino group), Aliphatic C-H group, N-C(Isocyanide group), C=O of quinoline etc., which are not disturbed when combinedCiprofloxacin Hcl with Guar gum. It states that combination of CiprofloxacinHclwith Guar gum doesnot shows any interactions with functional groups present in CiprofloxacinHcl as well as Guar gum. So we can conclude that Ciprofloxacin Hcl and Guar gumarecompatible with each other.

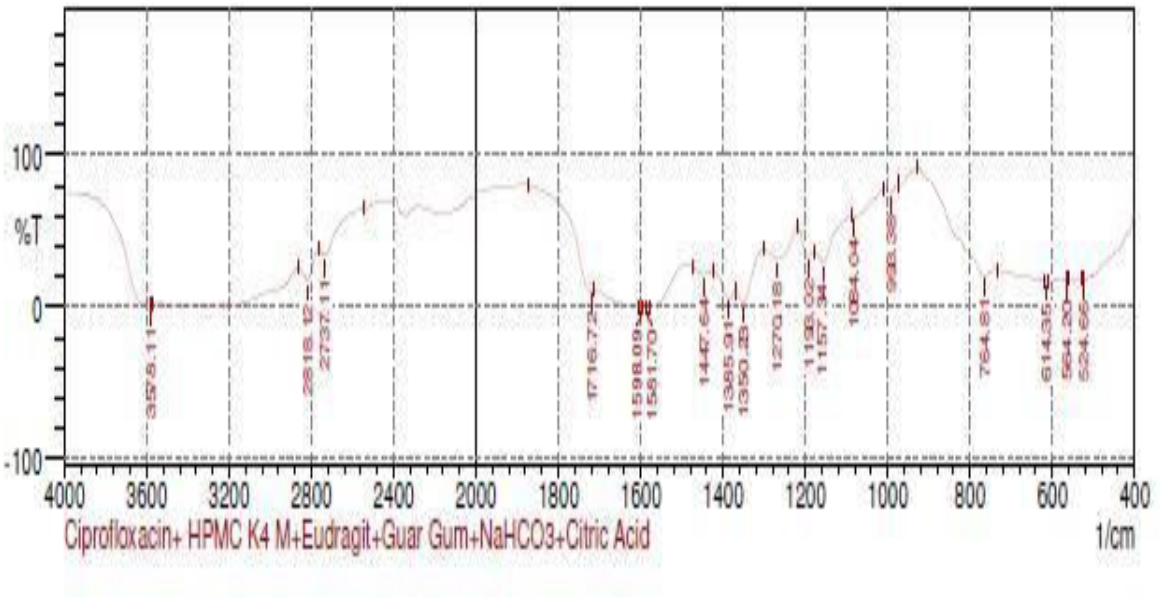


Fig 13: FTIR Spectrum of Ciprofloxacin Hcl, HPMC K4M, Eudragit 100S, Guar gum, $NAHCO_3$ & Citric acid

Table-13: FTIR Spectrum Ciprofloxacin Hcl, HPMCK4M, Eudragit 100S, Guar gum, NaHCO3 & Citric acid

S.No	*WAVE NUMBER (cm)*	*ASSIGNMENT (Functional group)*
1	*1598.09*	*C=O Stretching*
2	*1447.64*	*C-N Stretch*
3	*3578.11*	*O-H Stretch*
4	*2818.12*	*Aliphatic C-H Stretch*
5	*1581.70*	*C=C Stretching*
6	*1385.91*	*C-O Stretching*
7	*993.38*	*O-H Stretch*
8	*1385.91-1447.64*	*Symmetrical deformation of CH2 group*
9	*1084.04-1157*	*C-OH & primary alcohol; -CH2OH Stretching mode*
10	*764.81*	*(1-4), (1-6) linkage of Galactose& Mannose respectively*

Discussion:

Ciprofloxacin Hcl contains functional groups like C=O (Carbonyl group), C-N(Cyanide group), O-H (Hydroxyl group), Aliphatic C-H group, N-C (Isocyanide group) etc which are not disturbed when combined Ciprofloxacin Hcl with HPMC K4M, Eudragit 100S and Guar gum. It states that combination of Ciprofloxacin Hcl with HPMC K4M,Eudragit100S and Guar gum doesnot shows any interactions with functional groups present inCiprofloxacin Hcl as well as HPMC K4M, Eudragit 100S and guar gum. So we can conclude that Ciprofloxacin Hcl, HPMC K4M, Eudragit100S and Guar gum are compatible with each other.

Preformulation studies of granules of Ciprofloxacin Hcl floating tablets

The granules of CiprofloxainHcl floating tablets were prepared by wet granulation technique. The prepared granules are subjected to preformulation studies by following methods.

Angle of repose:

The granules of all seven formulations are subjected to angle of repose by funnel method. The value of angle of repose was found in the range of **22º71′-26º15′**. The result proved that the granules of all formulations showed excellent flow properties.

Bulk density*:*

Bulk density of all the granules was measured by using measuring cylindermethod and the resultant values was found in the range of **0.37-0.85 g/cm**. It showed that the bulkiness is within the acceptable limits.

Tapped density:

The tapped density of all granules was determined by tapping the Measuring cylinder for required times and the values are were noted in tableand the tapped density values was found in the range of 0.42-0.49 g/cm. The result proven that the tapped density values are within the acceptable limits.

Compressibility index:

The compressibility of granules are done by tapped density minus bulk density and divided with tapped density values. And the resultant values is in the range of **9-15**. It indicates that the granules showed good flow properties.

***Hausner's ratio*:**It is the ratio of tapped density value to bulk density value and the resultant values of Hausner's ratio of all the formulations is between **1.10-1.18** which indicate that the granules shows good flow.

Table No-14: Evaluation of granules of Ciprofloxacin Hcl floating tablets

S. No	*Formulation code*	*Angle of response*	*Bulk density (gm/ml)*	*Tapped density (gm/ml)*	*Compressibility index (%)*	*Hausner's ratio*
1	*F1*	*22º71'*	*0.42*	*0.49*	*11.22*	*1.166*
2	*F2*	*22º91´*	*0.386*	*0.435*	*11.34*	*1.126*
3	*F3*	*24º52´*	*0.393*	*0.436*	*9.86*	*1.1*
4	*F4*	*24º01'*	*0.375*	*0.429*	*12.59*	*1.14*
5	*F5*	*25º17´*	*0.3707*	*0.417*	*11.16*	*1.13*
6	*F6*	*26º15´*	*0.40*	*0.448*	*10.714*	*1.1*
7	*F7*	*24º92´*	*0.85*	*0.455*	*15.39*	*1.18*

Characterization of Ciprofloxacin Hcl floating tablets

General appearance:

The formulated tablets were evaluated for organoleptic charactes. The tablets are circular in shape, yellowish in colour, with no characteristic odour. All tablets showed elegance in appearance.

Hardness test:

The hardness of Ciprofloxacin Hcl floating tablets were measured by Pfizer hardness tester and the values were tabulated in table. The hardness of all tablets in all formulations was within the range of **4.5-5.1 kg/cm².** So all formulated tablets passes the test.

Friability test:

The friability of Ciprofloxacin Hcl floating tablets were performed by using Roche friabilator and thethe friability of all formulated tablets was within 1%. It proedthat all formulations are within the acceptable limits.

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Diameter:

The diameter of Ciprofloxacin Hcl floating tablets were measured by using BestoVernier calipers and there is no deviation in the diameter values of all formulated tablets indicates uniform diameter.

Thickness:

The thickness of Ciprofloxacin Hcl floating tablets were measured by using Vernier calipers. Thickness must be controlled to facilitate packaging. The result showed that the tablets of all the formulations shows uniform thickness.

Table 15: Evaluation of Ciprofloxacin Hcl floating tablets

S. No.	*Formulation code*	*Hardness(kg)*	*Friability (%)*	*Thickness (mm)*	*Diameter (mm)*
1	*F1*	*4.85*	*0.631*	*4.17*	*10.19*
2	*F2*	*4.8*	*0.413*	*5.14*	*10.8*
3	*F3*	*5.1*	*0.462*	*5.16*	*11.0*
4	*F4*	*4.75*	*0.381*	*4.4*	*10.7*
5	*F5*	*4.5*	*0.54*	*4.16*	*10.9*
6	*F6*	*5.0*	*0.761*	*4.5*	*11.0*
7	*F7*	*4.8*	*0.62*	*4.2*	*10.8*

Weight variation test:

The weight variation of tablets were done by weighing the individual tablet weight and the average weight of 20 tablets which were selected randomly from each formulation batches. No more than two tablets should go more than the preferred deviation. The percentage deviation is 7.5% for more than 130 mg tablets and here actual weight of tablet is 500 mg. So the acceptable deviation was 7.5%, thus all formulation passes the test.

Drug content (%):

The percentage of drug content were done by dissolving individual tablet in 0.1N Hcl and transferred to a 100ml volumetric flask. The absorbance of the resulting solution is measured by Ultraviolet Spectroscopy at 278nm. As per IP, the content uniformity should be in the range of 90-110%. The result showed that the percentage of Ciprofloxacin Hcl in all formulations was ranging from **96-99%.** It released that the drug is uniformly dispersed in the formulation and confirms the homogeneous mixing of the drug and the polymer. So all the formulated tablets passes the test.

Table 16: Weigh variation and Estimation of Drug content of floating tablets

S. No	*Formulation code*	*Weight variation*	*Drug content (%)*
1	*F1*	*498±2.5*	*98.12*
2	*F2*	*496±3.2*	*97.23*
3	*F3*	*497±2.7*	*98.63*
4	*F4*	*499±1.13*	*99.54*
5	*F5*	*498±3.5*	*97.83*
6	*F6*	*495±4.3*	*97.38*
7	*F7*	*497±4.2*	*99.17*

Buoyancy lag time:

It is the time taken during which of dosage form remains buoyant on 0.1N Hcl were measured and the values were listed in table. The buoyancy lag time values were found in the range of **134-166 sec.**

Total floating time:

It is the total duration of time during which the dosage form remains buoyant is measured and the values were ranges between **356-485 min** which was noted in table.

Table 17: Floating Lag time and floating time of formulations

S.No	*Formulation code*	*Floating Lag Time (Sec)*	*Floating Time (hours)*
1	*F1*	*150*	*10.0*
2	*F2*	*144*	*10.5*
3	*F3*	*151*	*8.0*
4	*F4*	*134*	*12.5*
5	*F5*	*154*	*9.0*
6	*F6*	*166*	*9.5*
7	*F7*	*140*	*11.0*

At Initial Time: o sec **At Floating Time: 2 mins 46 secs**

Fig 14: Floating Studies for Optimized formulation (F4): (Ciprofloxacin Hcl + HPMC K4M+ Eudragit 100S)

In-vitro dissolution studies*:*

The in-vitro dissolution studies of all seven formulation of Ciprofloxacin floating tablets were shown in following tables no 18-25and figure 15-22

The percentage drug release of all formulations after 12 hours using HPMC K4M, Eudragit 100Sand guar gum was found to be 88.12% (F1), 90.68% (F2) and 73.45% (F3) repectively. And the percentage drug release of combination of HPMC K4M with Eudragit 100S is 98.87% (F4), Eudragit 100S with guar gum is 85.67% (F5),HPMC K4M with guar gum is 79.93% (F6) and HPMC K4M with Eudragit 100S and guar gum is 95.45% (F7).

From the in-vitro drug release, it was observes that the maximum drug release was found in formulation F4 is **98.87%.** It shows that F4 formulation exhibits optimized drug release when compared with other formulation. The dissolution profile of all formulations of Ciprofloxacin Hcl floating tablets were shown in following table no 18-25

Table-18: Dissolution profile of Formulation (F1):

(Ciprofloxacin Hcl + HPMC K4M)

S.No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.094*	*1.740*	*0.224*	*11.22*
2	*2*	*0.117*	*2.166*	*0.279*	*14.3*
3	*3*	*0.162*	*3.00*	*0.387*	*19.8*
4	*4*	*0.221*	*4.092*	*0.527*	*27.01*
5	*5*	*0.276*	*5.111*	*0.659*	*33.73*
6	*6*	*0.326*	*6.037*	*0.778*	*39.84*
7	*7*	*0.387*	*7.166*	*0.924*	*47.3*
8	*8*	*0.434*	*8.037*	*1.036*	*53.04*
9	*9*	*0.523*	*9.685*	*1.249*	*63.92*
10	*10*	*0.589*	*10.907*	*1.407*	*71.98*
11	*11*	*0.653*	*12.092*	*1.559*	*79.81*
12	*12*	*0.721*	*13.351*	*1.722*	*88.12*

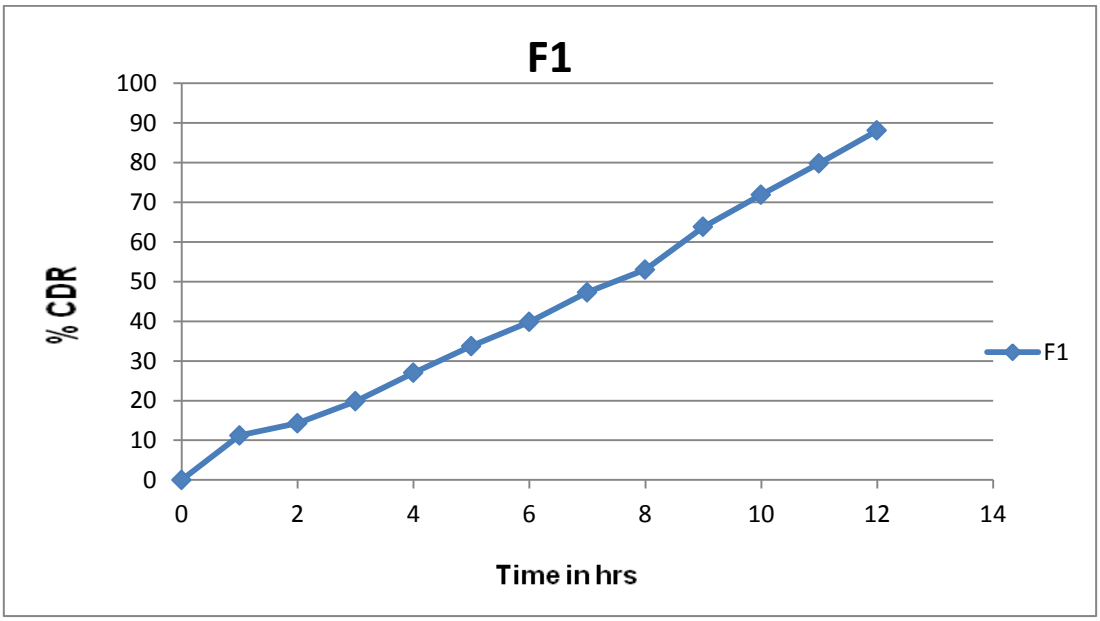


Fig 15: Dissolution profile of Formulation (F1):

Table no-19:Dissolution profile of Formulation (F2):

(Ciprofloxacin Hcl + Eudragit 100S)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.079*	*1.462*	*0.188*	*9.43*
2	*2*	*0.132*	*2.444*	*0.315*	*16.13*
3	*3*	*0.176*	*3.259*	*0.42*	*21.51*
4	*4*	*0.245*	*4.537*	*0.585*	*29.94*
5	*5*	*0.294*	*5.444*	*0.702*	*35.93*
6	*6*	*0.342*	*6.330*	*0.817*	*41.8*
7	*7*	*0.411*	*7.611*	*0.981*	*50.23*
8	*8*	*0.476*	*8.814*	*0.137*	*58.17*
9	*9*	*0.562*	*10.407*	*0.342*	*68.68*
10	*10*	*0.616*	*11.400*	*0.471*	*75.28*
11	*11*	*0.672*	*12.440*	*0.605*	*82.13*
12	*12*	*0.742*	*13.74*	*0.772*	*90.68*

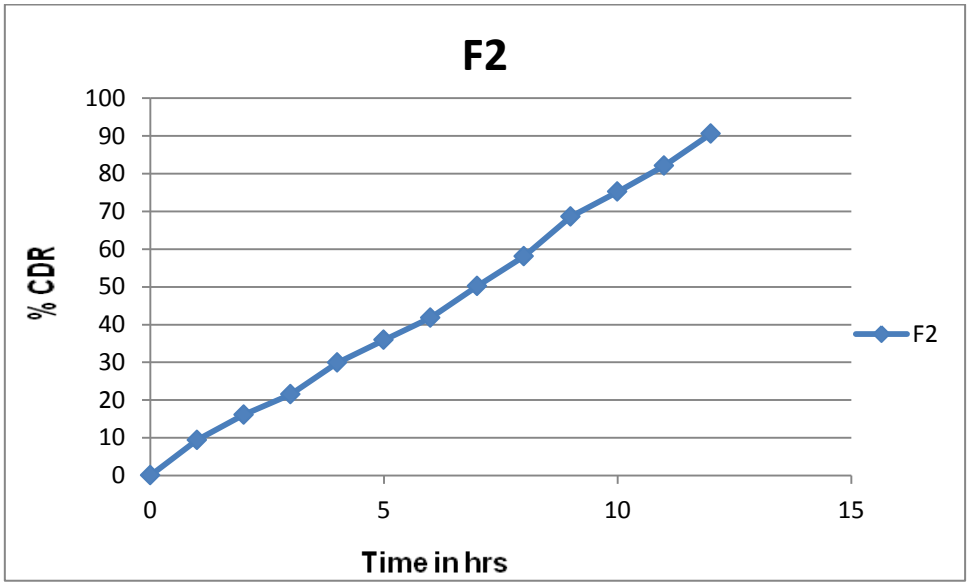


Fig 16: Dissolution profile of Formulation (F2):

Table-20: Dissolution profile of Formulation (F3):

(Ciprofloxacin Hcl + Guar gum)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.069*	*1.277*	*0.164*	*8.24*
2	*2*	*0.085*	*1.574*	*0.203*	*10.38*
3	*3*	*0.112*	*2.074*	*0.267*	*13.68*
4	*4*	*0.153*	*2.833*	*0.365*	*18.7*
5	*5*	*0.21*	*3.88*	*0.501*	*25.66*
6	*6*	*0.247*	*4.574*	*0.590*	*30.18*
7	*7*	*0.297*	*5.500*	*0.709*	*36.3*
8	*8*	*0.344*	*6.37*	*0.821*	*42.04*
9	*9*	*0.421*	*7.796*	*1.005*	*51.45*
10	*10*	*0.473*	*8.759*	*1.129*	*57.81*
11	*11*	*0.572*	*10.592*	*1.366*	*69.91*
12	*12*	*0.601*	*11.129*	*1.435*	*73.45*

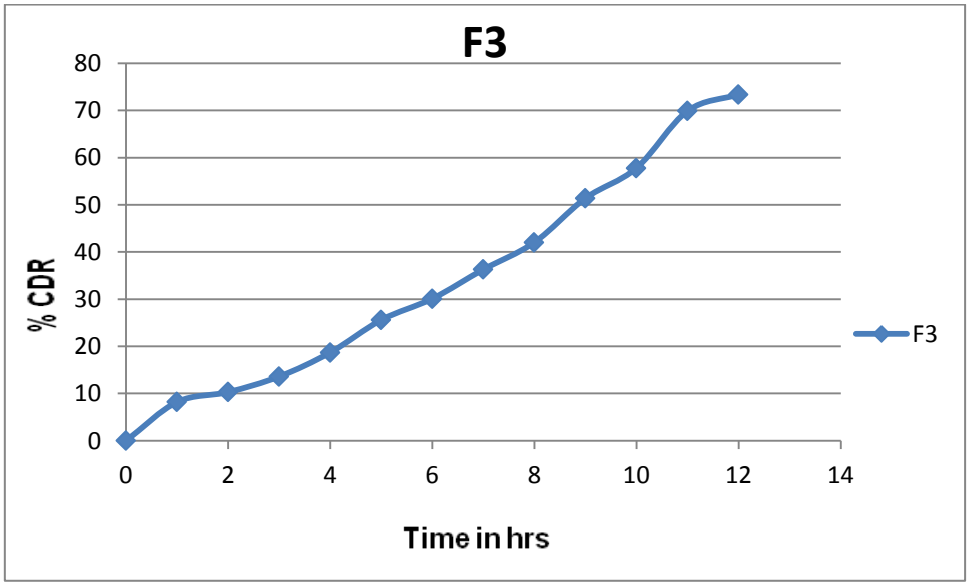


Fig 17: Dissolution profile of Formulation (F3):

Table-21: Dissolution profile of Formulation (F4):

(Ciprofloxacin Hcl + Eudragit 100S+ HPMC K4M)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.102*	*1.88*	*0.243*	*12.18*
2	*2*	*0.171*	*1.166*	*0.408*	*20.9*
3	*3*	*0.222*	*4.111*	*0.53*	*27.13*
4	*4*	*0.301*	*5.574*	*0.719*	*36.78*
5	*5*	*0.36*	*6.667*	*0.86*	*44*
6	*6*	*0.429*	*7.944*	*1.024*	*52.43*
7	*7*	*0.497*	*9.203*	*1.187*	*60.74*
8	*8*	*0.565*	*10.463*	*1.349*	*69.05*
9	*9*	*0.632*	*11.703*	*1.509*	*77.24*
10	*10*	*0.699*	*12.944*	*1.66*	*85.43*
11	*11*	*0.752*	*13.925*	*1.79*	*91.91*
12	*12*	*0.809*	*14.98*	*1.93*	*98.87*

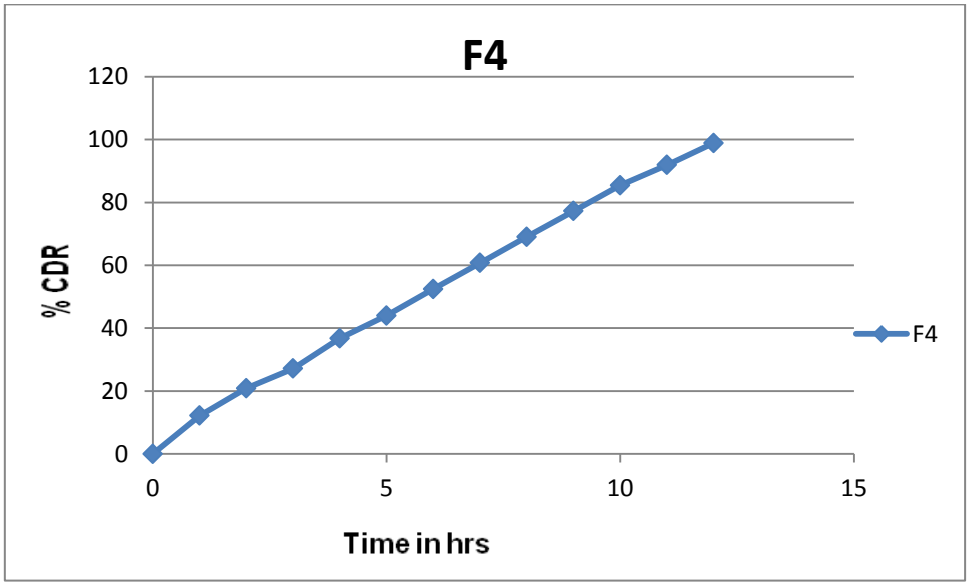


Fig 18: Dissolution profile of Formulation 4 (F4):

Table-22: Dissolution profile of Formulation (F5):

(Ciprofloxacin Hcl +Eudragit 100S+ Guar gum)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.083*	*1.537*	*0.198*	*9.91*
2	*2*	*0.105*	*1.944*	*0.25*	*12.83*
3	*3*	*0.138*	*2.55*	*0.329*	*16.86*
4	*4*	*0.198*	*3.66*	*0.473*	*24.2*
5	*5*	*0.255*	*4.722*	*0.609*	*31.16*
6	*6*	*0.306*	*5.67*	*0.731*	*37.4*
7	*7*	*0.342*	*6.33*	*0.817*	*41.8*
8	*8*	*0.411*	*7.611*	*0.98*	*50.23*
9	*9*	*0.482*	*8.925*	*1.51*	*58.91*
10	*10*	*0.557*	*10.314*	*1.33*	*68.07*
11	*11*	*0.623*	*11.537*	*1.488*	*76.14*
12	*12*	*0.701*	*12.98*	*1.674*	*85.67*

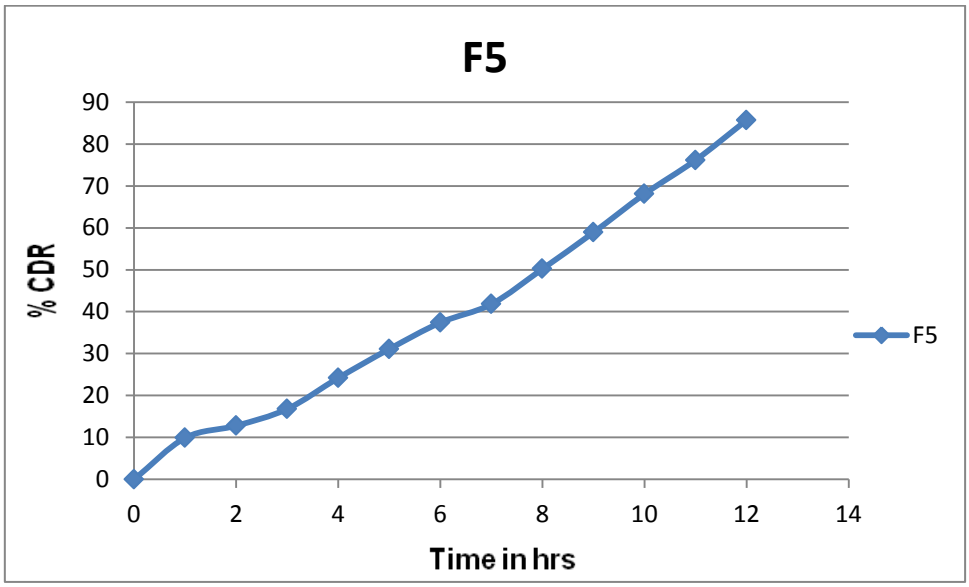


Fig 19: Dissolution profile of Formulation (F5):

Table-23: Dissolution profile of Formulation (F6):

(Ciprofloxacin Hcl+ HPMC K4M+ Guar gum)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.088*	*1.629*	*0.210*	*10.51*
2	*2*	*0.100*	*1.851*	*0.238*	*12.22*
3	*3*	*0.125*	*2.314*	*0.298*	*15.27*
4	*4*	*0.175*	*3.24*	*0.418*	*21.38*
5	*5*	*0.244*	*4.518*	*0.582*	*29.82*
6	*6*	*0.296*	*5.48*	*0.707*	*36.17*
7	*7*	*0.335*	*6.203*	*0.80*	*40.94*
8	*8*	*0.394*	*7.296*	*0.941*	*48.15*
9	*9*	*0.442*	*8.19*	*1.055*	*54.02*
10	*10*	*0.512*	*9.481*	*1.223*	*62.57*
11	*11*	*0.593*	*10.981*	*1.416*	*72.47*
12	*12*	*0.654*	*12.11*	*1.562*	*79.93*

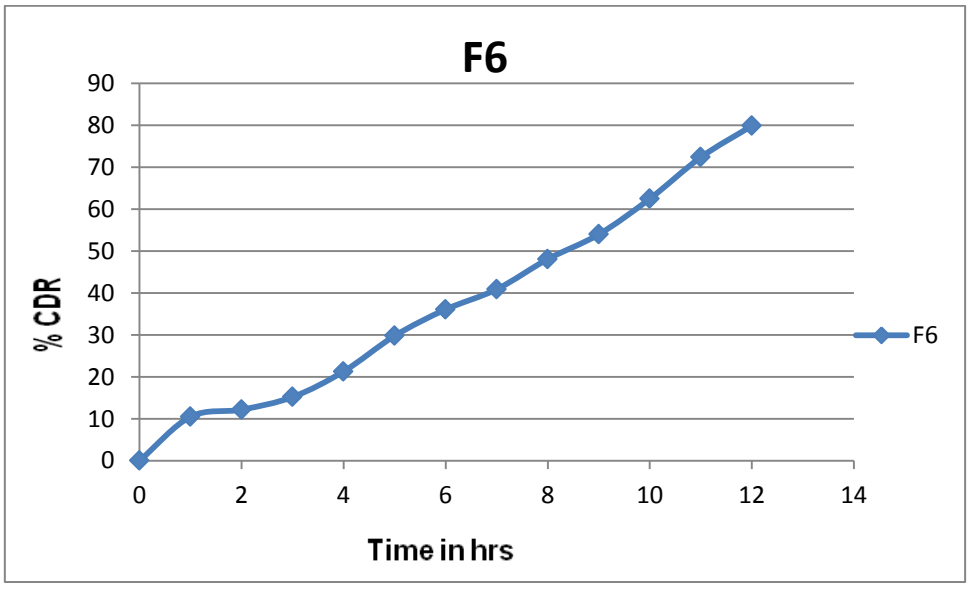


Fig 20: Dissolution profile of Formulation (F6):

Table -24: Dissolution profile of Formulation (F7):

(Ciprofloxacin Hcl+HPMC K4M+ Eudragit 100S+ Guar gum)

S,No	*Time (hrs)*	*Absorbance (278nm)*	*Concentration (µg/ml)*	*Amount of drug release*	*Percentage of drug release (%)*
1	*1*	*0.092*	*1.703*	*0.219*	*10.98*
2	*2*	*0.156*	*2.889*	*0.372*	*19.06*
3	*3*	*0.203*	*3.759*	*0.484*	*24.81*
4	*4*	*0.254*	*4.703*	*0.606*	*31.04*
5	*5*	*0.321*	*5.944*	*0.766*	*39.23*
6	*6*	*0.373*	*6.907*	*0.891*	*45.58*
7	*7*	*0.418*	*7.740*	*0.998*	*51.08*
8	*8*	*0.503*	*9.314*	*1.201*	*61.47*
9	*9*	*0.577*	*10.685*	*1.378*	*70.52*
10	*10*	*0.668*	*12.370*	*1.595*	*81.64*
11	*11*	*0.712*	*13.185*	*1.70*	*87.02*
12	*12*	*0.781*	*14.463*	*1.865*	*95.45*

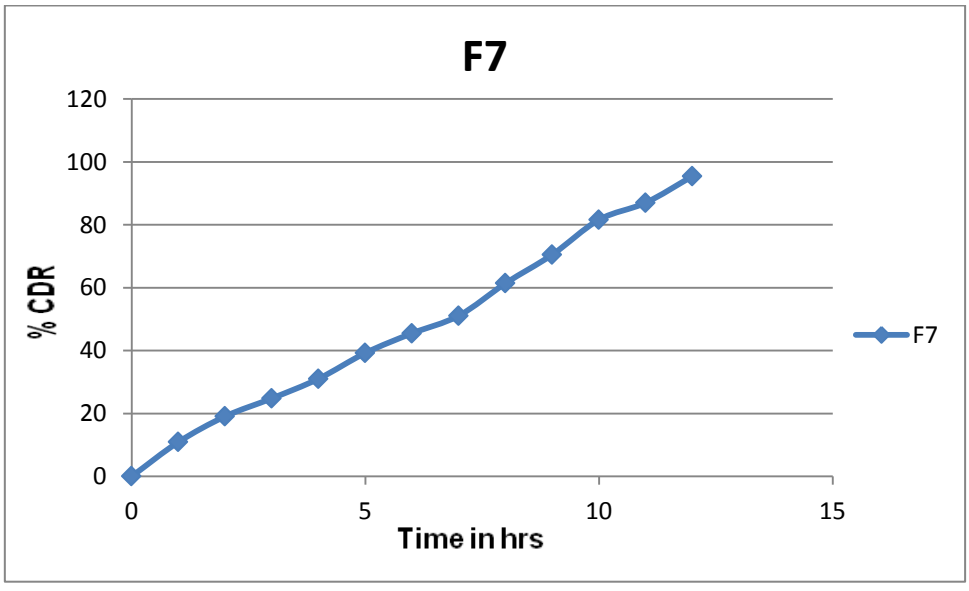


Fig 21: Dissolution profile of Formulation (F7):

Table-25:Comparitive In-vitro Dissolution study of Ciprofloxacin Hcl floating tablets (F1-F7)

Time (hrs)	*Cumulative % Drug Release*						
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*
1	*11.22*	*9.43*	*8.24*	*12.18*	*9.91*	*10.51*	*10.98*
2	*14.3*	*16.13*	*10.38*	*20.9*	*12.83*	*12.22*	*19.06*
3	*19.8*	*21.51*	*13.68*	*27.13*	*16.86*	*15.27*	*24.81*
4	*27.01*	*29.94*	*18.7*	*36.78*	*24.2*	*21.38*	*31.04*
5	*33.73*	*35.93*	*25.66*	*44*	*31.16*	*29.82*	*39.23*
6	*39.84*	*41.8*	*30.18*	*52.43*	*37.4*	*36.17*	*45.58*
7	*47.3*	*50.23*	*36.3*	*60.74*	*41.8*	*40.94*	*51.08*
8	*53.04*	*58.17*	*42.04*	*69.05*	*50.23*	*48.15*	*61.47*
9	*63.92*	*68.68*	*51.45*	*77.24*	*58.91*	*54.02*	*70.52*
10	*71.98*	*75.28*	*57.81*	*85.43*	*68.07*	*62.57*	*81.64*
11	*79.81*	*82.13*	*69.91*	*91.91*	*76.14*	*72.47*	*87.02*
12	*88.12*	*90.68*	*73.45*	*98.87*	*85.67*	*79.93*	*95.45*

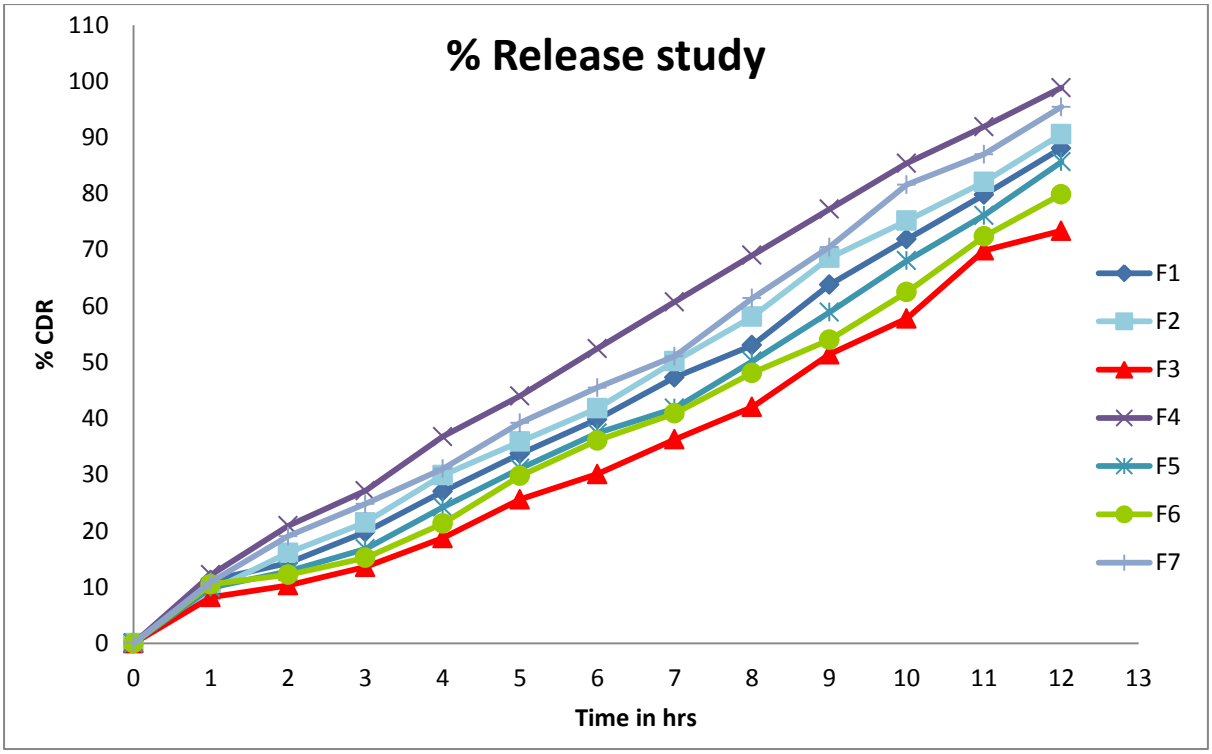


Fig 22: Comparitive In-vitro Dissolution study of Ciprofloxacin Hcl floating tablets (F1-F7)

Kinetic Analysis of dissolution data:

To know the mechanism of drug release from these formulations, the data were treated according to zero order[72],first order[73], Higuchi's model[75]and Korsmeyermodel[76] The release rate kinetic data for all the formulations are shown in table. When data were plottedaccording to zero order, the formulation showed high linearity with regression co-efficient values (R^2) between**0.993 – 0.998.**

Diffusion is related to transport of drug from the dosage matrix into the invitrostudy fluid depending on the concentrations. This is explained by Higuchi's equations, as the plot showed high linearity with regression co-efficient values (R^2) between **0.878- 0.938**.

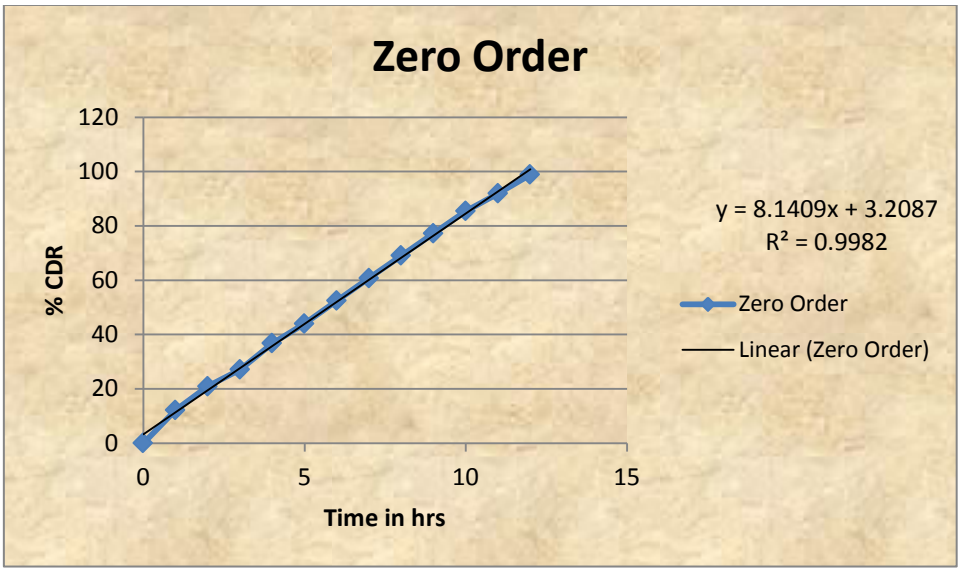
By using Korsmeyer model, if n= 0.45, it is Fickiandiffusion , if n= 0.45-0.89 it is non-Fickian transport. Here all the formulations showed 'n' values between**0.806-0.929**. So all the formulations follows non- Fickian diffusion transport mechanism. Finally all the formulations follows the mechanism of both diffusion and erosion.

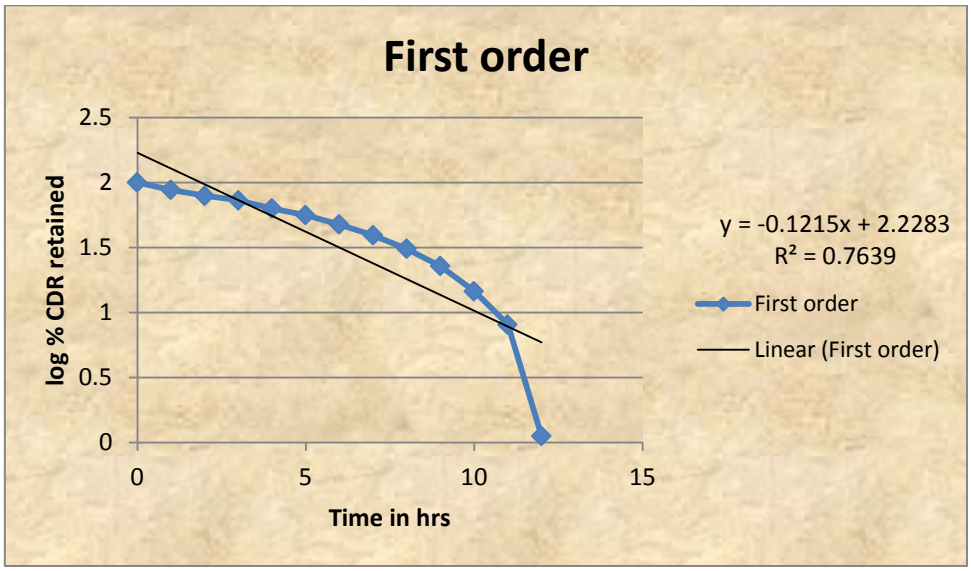
Table 26-: Kinetic Analysis of dissolution data:

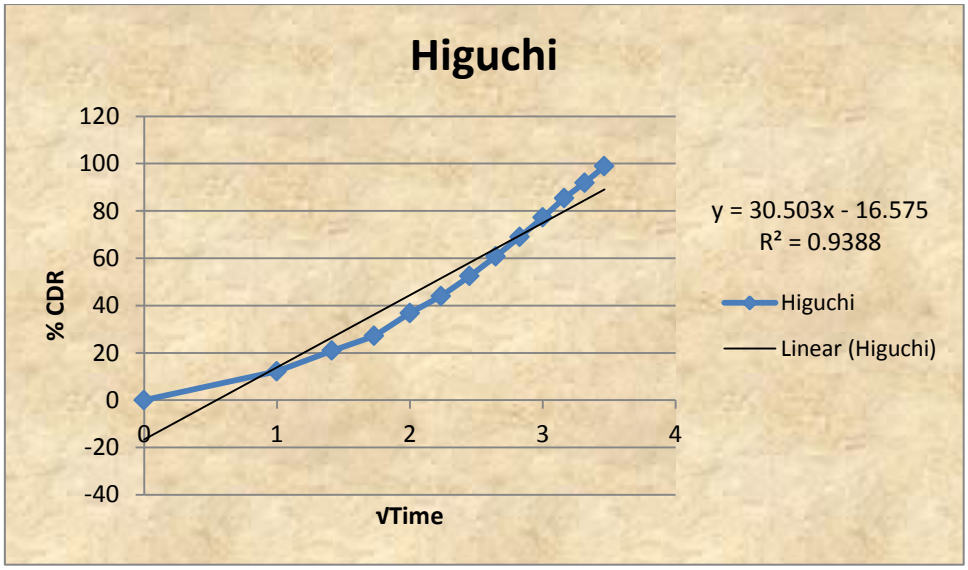
S.No	*Formulation code*	*Regression co-efficient ($R^{2)}$*			*Korsmeyer' plot*	
		Zero order plot	*First order plot*	*Higuchi's plot*	*R^2*	*Slope (n)*
1	*F1*	*0.993*	*0.886*	*0.896*	*0.970*	*0.887*
2	*F2*	*0.997*	*0.889*	*0.910*	*0.993*	*0.929*
3	*F3*	*0.988*	*0.880*	*0.878*	*0.997*	*0.868*
4	*F4*	*0.998*	*0.763*	*0.938*	*0.996*	*0.861*
5	*F5*	*0.988*	*0.880*	*0.878*	*0.998*	*0.806*
6	*F6*	*0.988*	*0.880*	*0.878*	*0.998*	*0.825*
7	*F7*	*0.995*	*0.832*	*0.912*	*0.990*	*0.877*

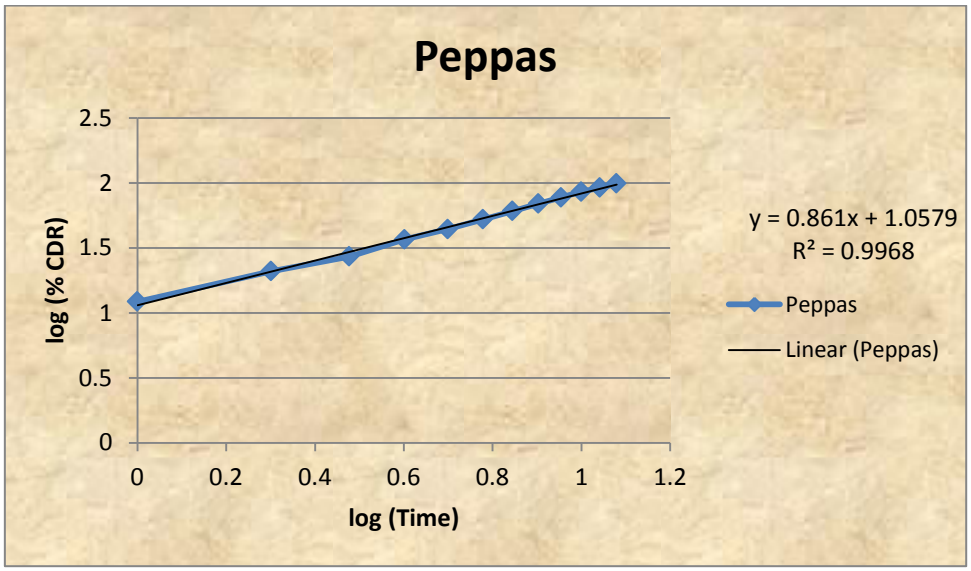
Fig 23: Release Kinetics for Optimized Formulation (F4):

(Ciprofloxacin Hcl + Eudragit 100S+ HPMC K4M)


Zero Order
120
100
80
60
40
20
0
% CDR
0
5
10
15
Time in hrs
y = 8.1409x + 3.2087
R² = 0.9982
Zero Order
Linear (Zero Order)


First order
2.5
2
1.5
1
0.5
0
log % CDR retained
0
5
10
15
Time in hrs
y = -0.1215x + 2.2283
R² = 0.7639
First order
Linear (First order)





COMPARISION WITH INNOVATOR PRODUCT

Percentage Release of Innovator Sample (Cipro XR 500mg) & Prepared Formulation of Ciprofloxacin Hcl floating tablets

Table No -27

S.No	*Time (hrs)*	*Cumulative percentage drug release*	
		Innovator sample	*Optimized formulation of Ciprofloxacin Hcl (F4)*
1	*1*	*10.23*	*12.18*
2	*2*	*16.57*	*20.90*
3	*3*	*24.06*	*27.13*
4	*4*	*31.85*	*36.78*
5	*5*	*38.92*	*44.00*
6	*6*	*47.73*	*52.43*
7	*7*	*55.81*	*60.74*
8	*8*	*62.34*	*69.05*
9	*9*	*70.71*	*77.24*
10	*10*	*79.11*	*85.43*
11	*11*	*88.19*	*91.91*
12	*12*	*95.61*	*98.87*

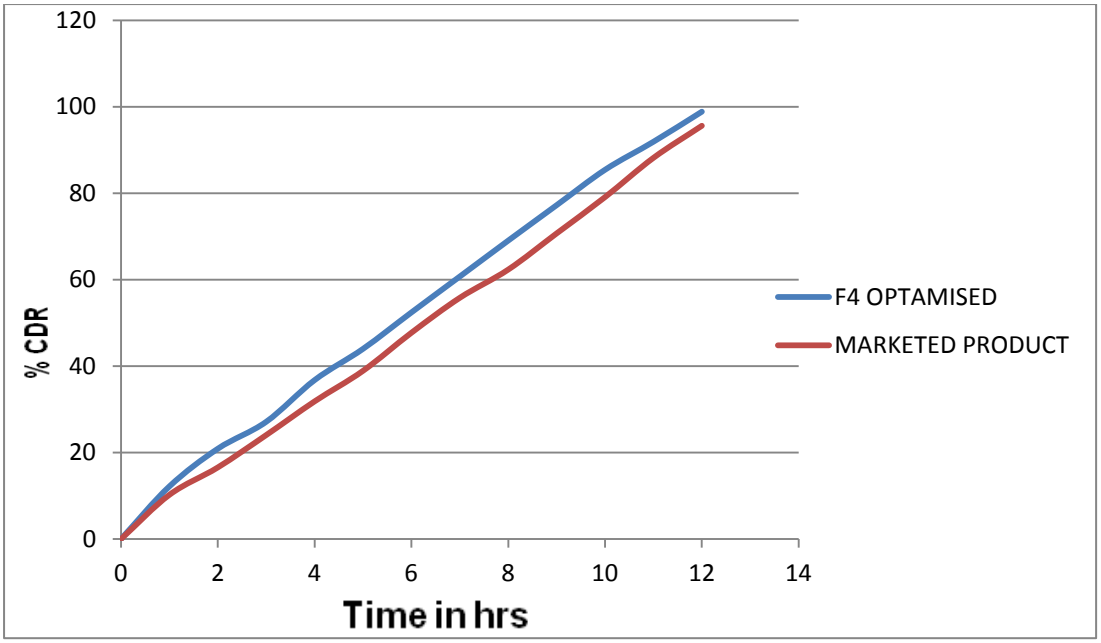


Fig 24: Percentage Release of Innovator Sample (Cipro XR 500mg) & Ciprofloxacin Hcl floating tablets

STABILITY STUDIES

Ciprofloxacin floating tablets (all 7 formulations) were stored at refrigerated temperature (4°C ± 2°C), room temperature (27°C± 2°C) and in programmable envirnomental test chamber (45°C± 2°C) for 45 days.

At the end of 15, 30 and 45 days of storage, the floating tablets were observed for changes in physical appearance analyzed for drug content and subjected to invitro release studies and the result was presented in Table no 28-35

There was no change in the percentage release of ciprofloxacin from all the formulations stored at different temperatures upto 45 days. Tablet evaluation tests were carried out and there were no deviations in all the tests and all are within the limits. It showed that all the formulations are physically stable. There was no change in the drug content (Table no 28 and invitro drug release (Table no 29-35). It showed that all the formulations are chemically stable.

Table No – 28

DRUG CONTENT ESTIMATION AFTER STORING AT DIFFERENT TEMPERATURES

No	Formulation	Drug content*								
		$4^0C\pm 2^0C$			$27^0C\pm 2^0C$			$45^0C\pm 2^0C$		
		15th days	30th days	45th days	15th days	30th days	45th days	15th days	30th days	45th days
1	F1	98.12	98.10	98.11	98.62	98.60	98.60	98.98	98.99	98.99
2	F2	97.73	97.73	97.72	97.20	97.20	97.21	97.43	97.43	97.41
3	F3	98.63	98.64	98.65	98.69	98.69	98.68	98.63	98.64	98.63
4	F4	99.64	99.64	99.63	99.44	99.44	99.45	99.54	99.53	99.54
5	F5	97.80	97.81	97.80	97.87	97.86	97.86	97.68	97.67	97.68
6	F6	97.45	97.47	97.45	97.98	97.97	97.97	97.78	97.79	97.78
7	F7	99.67	99.67	99.68	99.17	99.18	99.17	99.10	99.10	99.11

Table No – 29

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F1

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			4^0C± 2^0C	27^0C ± 2^0C	45^0C± 2^0C	4^0 C± 2^0C	27^0C± 2^0 C	45^0C± 2^0C	4^0C± 2^0C	27^0C± 2^0 C	45^0C± 2^0C
1	1	11.22	11.20	11.82	11.02	11.22	11.44	11.21	11.25	11.88	11.22
2	2	14.3	14.36	14.39	14.33	14.55	14.39	14.31	14.39	14.90	14.54
3	3	19.8	19.45	19.84	19.85	19.89	19.98	19.43	19.86	19.77	19.89
4	4	27.01	26.31	27.09	27.45	27.00	27.08	27.66	27.01	27.66	27.96
5	5	33.73	33.73	33.03	33.73	33.79	33.66	33.79	33.88	33.79	33.70
6	6	39.84	40.24	39.24	39.89	39.76	39.80	39.83	39.80	39.84	39.53
7	7	47.31	47.98	47.31	47.35	47.21	47.34	47.39	47.77	47.36	47.73
8	8	53.04	53.64	53.00	53.44	53.99	53.00	53.32	53.00	53.09	53.84
9	9	63.92	63.09	63.95	63.90	63.09	63.66	63.85	63.93	63.92	63.34
10	10	71.98	70.56	71.99	71.33	71.21	71.32	71.90	71.66	71.84	71.74
11	11	79.81	79.96	79.31	79.80	79.80	79.98	79.56	79.95	79.81	79.81
12	12	88.12	88.10	88.56	88.46	88.16	88.54	88.87	88.13	88.09	88.19

Table No – 30

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F2

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0 C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$
1	1	9.43	9.53	9.99	9.22	9.78	9.21	9.43	8.43	9.54	9.93
2	2	16.13	16.03	16.55	16.18	16.07	16.63	16.10	16.53	16.10	16.53
3	3	21.51	22.58	21.50	21.66	20.57	21.74	21.22	21.89	21.57	21.65
4	4	29.94	29.89	30.90	29.32	29.93	29.97	28.97	29.96	29.90	30.94
5	5	35.93	35.98	35.55	35.23	35.74	35.93	35.55	35.90	35.84	35.91
6	6	41.8	42.80	41.76	41.87	41.88	41.67	41.60	42.76	41.80	41.11
7	7	50.23	50.27	50.32	50.37	51.44	50.24	50.23	50.98	51.85	50.53
8	8	58.17	58.97	57.17	58.10	58.17	58.17	58.18	58.81	58.91	58.97
9	9	68.68	69.55	68.69	68.63	68.69	68.63	67.86	69.67	70.44	67.58
10	10	75.28	75.27	75.52	75.44	75.82	75.67	75.98	75.82	75.33	75.54
11	11	82.13	82.22	83.10	82.24	82.31	82.94	82.63	82.13	82.74	82.56
12	12	90.68	90.66	90.60	90.67	91.76	90.65	90.60	90.68	90.70	90.68

Table No – 31

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F3

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0 C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$
1	1	8.24	8.23	8.25	8.24	8.23	8.22	8.23	8.24	8.21	8.24
2	2	10.38	10.39	10.37	10.36	10.35	10.37	10.38	10.39	10.37	10.36
3	3	13.68	13.66	13.65	13.67	13.69	13.68	13.68	13.67	13.67	13.66
4	4	18.07	18.05	18.08	18.06	18.05	18.09	18.07	18.05	18.06	18.07
5	5	25.66	25.65	25.64	25.65	25.66	25.63	25.66	25.64	25.65	25.61
6	6	30.18	30.19	30.17	30.18	30.19	30.16	30.18	30.17	30.19	30.17
7	7	36.03	36.01	36.02	36.04	36.01	36.03	36.03	36.02	36.05	36.04
8	8	42.04	42.03	42.00	42.01	42.05	42.04	42.04	42.05	42.02	42.03
9	9	51.45	51.46	51.44	51.47	51.46	51.44	51.45	51.46	51.46	51.44
10	10	57.81	57.82	57.80	57.83	57.80	57.82	57.81	57.83	57.80	57.82
11	11	69.91	69.90	69.89	69.92	69.91	69.92	69.91	69.93	69.92	69.94
12	12	73.45	73.44	73.43	73.42	73.41	73.43	73.45	73.44	73.44	73.46

Table No – 32

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F4

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0 C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$
1	1	12.18	12.17	12.15	12.16	12.15	12.19	12.17	12.16	12.15	12.19
2	2	20.09	20.08	20.07	20.10	20.08	20.09	20.10	20.08	20.07	20.06
3	3	27.13	27.14	27.12	27.11	27.12	27.15	27.11	27.14	27.12	27.14
4	4	36.78	36.76	36.77	36.79	36.78	36.75	36.76	36.77	36.76	36.78
5	5	44	44.02	44.01	44.03	44	44.04	44.01	44.04	44.01	44
6	6	52.43	52.44	52.42	52.45	52.44	52.42	52.45	52.44	52.45	52.42
7	7	60.74	60.72	60.73	60.71	60.75	60.71	60.73	60.74	60.70	60.73
8	8	69.05	69.06	69.04	69.02	69.07	69.08	69.06	69.05	69.08	69.02
9	9	77.24	77.25	77.23	77.22	77.25	77.24	77.26	77.23	77.25	77.21
10	10	85.43	85.42	85.44	85.45	85.42	85.41	85.42	85.44	85.41	85.42
11	11	91.91	91.93	91.92	91.90	91.89	91.90	91.93	91.90	91.92	91.94
12	12	98.87	98.86	98.88	98.85	98.84	98.86	98.85	98.84	98.85	98.86

Table No – 33

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F5

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0 C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0 C$	$45^0C\pm 2^0C$
1	1	9.91	9.92	9.93	9.90	9.94	9.95	9.94	9.91	9.92	9.93
2	2	12.83	12.82	12.84	12.82	12.80	12.83	12.82	12.84	12.85	12.80
3	3	16.86	16.87	16.85	16.84	16.87	16.84	16.87	16.85	16.86	16.87
4	4	24.02	24.02	24.01	24.03	24.04	24.02	24.01	24.00	24.01	24.02
5	5	31.16	31.17	31.15	31.14	31.13	31.14	31.17	31.18	31.15	31.13
6	6	37.04	37.04	37.03	37.00	37.01	37.05	37.07	37.06	37.01	37.02
7	7	41.08	41.07	41.06	41.05	41.02	41.04	41.05	41.08	41.07	41.06
8	8	50.23	50.22	50.25	50.21	50.22	50.21	50.20	50.22	50.25	50.24
9	9	58.91	58.93	58.92	58.90	58.91	58.92	58.94	58.90	58.92	58.90
10	10	68.07	68.08	68.06	68.09	68.09	68.06	68.06	68.05	68.07	68.08
11	11	76.14	76.12	76.11	76.13	76.15	76.11	76.13	76.15	76.12	76.13
12	12	85.67	85.68	85.69	85.66	85.65	85.67	85.65	85.66	85.64	85.66

Table no – 34

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F6

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0C$	$45^0C\pm 2^0C$
1	1	10.51	10.50	10.52	10.53	10.54	10.51	10.50	10.53	10.52	10.51
2	2	12.22	12.20	12.21	12.23	12.24	12.25	12.22	12.20	12.21	12.23
3	3	15.27	15.26	15.28	15.25	15.26	15.23	15.24	15.25	15.27	15.29
4	4	21.38	21.35	21.36	21.39	21.38	21.37	21.35	21.36	21.37	21.39
5	5	29.82	29.80	29.81	29.83	29.84	29.85	29.84	29.82	29.81	29.80
6	6	36.17	36.16	36.19	36.18	36.18	36.12	36.13	36.15	36.16	36.15
7	7	40.94	40.93	40.95	40.91	40.92	40.93	40.96	40.94	40.95	40.93
8	8	48.15	48.16	48.17	48.18	48.14	48.11	48.13	48.12	48.15	48.11
9	9	54.02	54.03	54.01	54.02	54.05	54.04	54.01	54.02	54.03	54.00
10	10	62.57	62.56	62.55	62.57	62.58	62.59	62.60	62.58	62.56	62.55
11	11	72.47	72.45	72.46	72.44	72.43	72.42	72.45	72.48	72.46	72.48
12	12	79.93	79.92	79.90	79.92	79.91	79.91	79.94	79.96	79.95	79.93

Table No – 35

STABILITY STUDIES OF DISSOLUTION PROFILE OF FORMULATION F7

S.No	Time in (hrs)	0 days	Percentage drug release (%)*								
			15th days			30th days			45th days		
			$4^0C\pm 2^0C$	$27^0C \pm 2^0C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0C$	$45^0C\pm 2^0C$	$4^0C\pm 2^0C$	$27^0C\pm 2^0C$	$45^0C\pm 2^0C$
1	1	10.98	10.96	10.97	10.98	10.95	10.94	10.92	10.91	10.98	10.94
2	2	19.06	19.02	19.08	19.07	19.05	19.08	19.07	19.05	19.03	19.05
3	3	24.81	24.83	24.82	24.84	24.80	24.78	24.79	24.82	24.81	24.80
4	4	31.04	31.05	31.06	31.03	31.04	31.05	31.00	31.01	31.02	31.02
5	5	39.23	39.24	39.26	39.25	39.24	39.27	39.21	39.20	39.26	39.23
6	6	45.58	45.57	45.56	45.57	45.59	45.55	45.53	45.54	45.56	45.57
7	7	51.08	51.06	51.07	51.04	51.06	51.05	51.06	51.09	51.07	51.06
8	8	61.47	61.49	61.48	61.46	61.47	61.45	61.49	61.48	61.44	61.46
9	9	70.52	70.51	70.53	70.54	70.52	70.50	70.49	70.51	70.52	70.53
10	10	81.64	81.63	81.61	81.62	81.63	81.65	81.67	81.66	81.65	81.63
11	11	87.02	87.00	87.01	87.04	87.06	87.00	87.03	87.04	87.03	87.05
12	12	95.45	95.42	95.43	95.41	95.42	95.44	95.43	95.46	95.44	95.46

IX . SUMMARY AND CONCLUSION

Hydrodynamically balanced tablets of Ciprofloxacin Hcl can be formulated with an approach to increase gastric residence and thereby improves drug bioavailability to the developed floating tablets of Ciprofloxacin Hcl using natural and synthetic polymer HPMC K4M, Eudragit 100S and guar gum with Sodium bicarbonate combination and citric acid as gas generating agent was prepared by wet granulation technique (F1- F7) was achieved.

- Preformulation studies for drug such as angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio were performed and the result showed that all the parameters are within the limits

- Tablets were prepared by wet granulation method and evaluated for generalappearance, hardness test, friability test, uniformity in weight, drug content estimation. All the formulations were found to be good appearance without showing any chipping, capping and sticking defects and other parameters were also passedthe test.

- FTIR Spectroscopic studies indicated that the drug is compatible with all excipients and there is no drug- polymer interactions.

- When comparing all formulation F4 showed optimized drug release of **98.86%** at the end of 12 hours.

- These optimized F4 formulation showed buoyancy lag time of **134 sec**. and floating time of.**12.5 hrs** respectively.

- Data obtained from kinetic treatment revealed F4 formulations follow Koresmayer-peppas model. The 'n' value is **0.861** indicates the non Fickian diffusion.

- From the comparative study of optimized formulation of Ciprofloxacin Hcl (F4) with marketed product (Cipro XR 500mg) shows that F4 is have greater release than marketed product

- All the formulations were subjected for stability studies for 45 days at different temperatures such as room temperature, fridge temperature and acclerated temperature (45°C±2°C). At 15 days interval upto 45 days, the drug content and dissolution studies were carried out. There was no significant change in the drug content and invitro drug release

From the above study, it was concluded that Ciprofloxacin Hcl can formulated as Floating drug delivery system which helps to increase gastric residence timethere by it increases the bioavailability and half life of Ciprofloxacin Hcl.

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