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Research

Formulation And *In Vitro* Characterisation Of Gemifloxacin Floating Tablets

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Abstract

The present study was aimed to formulate and evaluate floating tablets of Gemifloxacin by direct compression method. Gemifloxacin is used as aoral broad-spectrum quinolone antibacterial agent used in the treatment of acute bacterial exacerbation of chronic bronchitis and mild-to-moderate pneumonia. Gemifloxacin is stable in neutral or slightly acidic media. In this study, excipients like Eudragit RSPO, HPMC, Carbopol 974P, sodium bicarbonate and Citric acid were incorporated in a nine different concentrations (F1-F9) along with other excipients (Magnesium Stearate, Talc and Micro crystalline cellulose) to formulate floating tablets by direct compression method. Then all the nine formulations were evaluated for uniformity of weight, hardness, thickness, friability test, floating lag time, drug content and dissolution studies. The dissolution profile of trial-7 (formulation 7) was observed to be better than other formulations. In trial-7Gemifloxacin was formulated as a floating tablet by using Carbopol 974P (32.5 mg) as a matrix forming polymer and sodium bi carbonate (10 mg) as a gas generating agent. Trial-7 formulation showed a good dissolution profile for a controlled period of time which was noticed to be as 99.29% at the end of 12th hour. Thus, it can be concluded that the floating drug delivery system of Gemifloxacin using the appropriate polymers in right amount may enhance the activity ofthe drug by prolonging the gastric residence time or reducing the floating lag time.

Keywords: Gemifloxacin, Eudragit RSPO,HPMC, Carbopol 974P and Floating Tablets.

INTRODUCTION

The aim of drug delivery system is to afforda therapeutic amount of drug to the prope site in the body to attain promptly and thenmaintain desired drug concentration. Theoral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems [1-4]. 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 controlled release systems for better absorption and enhanced bioavailability. One of suchdifficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. The relatively brief gastric emptying time (GET) in humans which normally averages 2-3 h through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose. Sustained releases are dosage forms that provide medication over an extended period of time. Controlled release denotes that the system is able to provide some actual therapeutic control [5]. Controlled release (modified release) dosage forms are growing in popularity. These more sophisticated systems can be used as a means of altering the pharmacokinetic behavior of drugs in order to provide twice or once a day dosage. This is achieved by obtaining a zero-order release from the dosage form. Zero-order release includes drug release from the dosage form that is independent of the amount of drug in the delivery system.

The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion , flotation, sedimentation, expansion, modified shape systems, or by the simultaneous administration of pharmacological agents, that delay gastric emptying. Oral controlled drug release dosage forms should not be developed unless the recommended dosage interval for the controlled release dosage form is longer than that for immediate release dosage form or unless significant clinical advantages for the controlled release dosage form can be justified like the decreased side effects resulting from a lower C max with the controlled release Form as compared to the immediate release or conventional dosage form. In vivo/in vitro evaluation of FDDS has been discussed by scientists to assess the efficiency and application of such systems. Several recent examples have been reported showing the efficiency of such systems for drugs with bioavailability problems.

The concept of floating tablets is mainly based on the matrix type drug delivery system such that the drug remains embedded in the matrix which after coming in contact with the gastric fluid swells up and the slow erosion of the drug without disintegration of the tablet takes place. Sometimes for generating a floating system we even need to add some effervescent or gas generating agent which will also ultimately reduce the density of the system and serve the goal of achieving a floating system. These systems have a particular advantage that they can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the GIT. These systems continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability. Different approaches are currently used to prolong the gastric retention time, like hydro dynamically balanced systems, swelling and expanding systems, polymeric bio-adhesive systems, modified shape systems, high density systems and other delayed gastric emptying devices. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.

Physiology of stomach

The stomach is divided into four major regions: fundus, body, antrum, and pylorus. Its functions are mainly:

- reservoir function: achieved through the flexible volume of the stomach
- emptying function: achieved through low sustained pressure produced by the stomach body
- Mixing and homogenizing function: achieved through stomach contraction that produces grinding.
- Size restriction function: the particle sizes of food emptied through the pylorus is less than 1 millimeter during the fed state.

The stomach is an organ with a capacity for storage and mixing. Its fundus and body region are capable of displaying a large expansion to accommodate food without much increase in the intragastric pressure. Whereas, the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions [11]. Under fasting conditions the stomach is a collapsed bag with a residual volume of 50 ml and contains a small amount of gastric fluid (pH 1-3) and air. Under physiological condition, the gastric absorption of most drugs is insignificant as a result of its limited surface area (0.1-0.2 m2) covered by a thick layer of mucous coating, the lack of villi on the mucosal surface, and the short residence time of most drug in the stomach. Rapid gastric emptying, also called dumping syndrome, occurs when undigested food empties too quickly into the small intestine. Stomach emptying is a coordinated function by intense peristaltic contractions in the antrum. At the same time, the emptying is opposed by varying degrees of resistance to passage of chyme at the pylorus. Rate depends on pressure generated by antrum against pylorus resistance. Chyme = food in stomach which has been thoroughly mixed with stomach secretions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 - 3 hours [12]. This is called the interdigestivemyloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington [13]. PHASE I the quiescent period, lasts from 30 to 60 mins 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 is a short period of intense large regular contractions, termed "housekeeper waves" that sweep off undigested food and last 10-20 min. PHASE IV is the transition period of 0-5 mins between Phase III & I [14.]

Advantages of FDDS

- ✓ FDDS is highly advantageous in the treatment of the disorders related to the stomach. As the prime objective of such systems is to produce a gastro retentive product or a product which has an enhanced retention time in the stomach8.
- ✓ Drugs with considerably short half life can be administered in this manner to get an appreciable therapeutic activity. Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
- ✓ They also have an advantage over the conventional system as it can be used to overcome the adversities of gastric retention time as well as the gastric emptying time.
- ✓ The duration of treatment through a single dose, which releases the an active ingredient over an extended period of time
- ✓ The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.

Disadvantages of FDDS

- ✓ The major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach9
- ✓ 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.
- ✓ Patients should not be dosed with floating forms just before going to bed.
- ✓ Floating system is not feasible for those drugs that have solubility (or) stability problem in gastric fluids.
- ✓ The dosage form should be administered with a minimum of glass full of water (200-250 ml).
- ✓ The drugs, which are absorbed throughout GIT, which under go first-pass metabolism (Nifedipine, Propranolol etc.), are not desirable candidate.

Suitable drug candidates for FDDS

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. In general, appropriate candidates for FDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT1.

- ✓ Drugs with narrow absorption window in GIT, e.g., Riboflavin and Levodopa
- ✓ Drugs that 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, e.g., Amoxicillin Trihydrate

Methods for preparing floating dosage form

Following approaches can be used for preparing floating dosage forms:

- ✓ Using gel-forming hydrocolloids such as hydrophilic gums, gelatin, alginates, cellulose derivatives, etc.
- ✓ Using low-density enteric materials such as methacrylic polymer, cellulose acetate phthalate.
- ✓ By reducing particle size and filling it in a capsule.
- ✓ By forming carbon dioxide gas and subsequent entrapment of it in the gel network.
- ✓ By preparing hollow micro-balloons of drug using acrylic polymer and filled in capsules.
- ✓ By incorporation of inflatable chamber, which contained in a liquid e.g. solvent that gasifies at body temperature to cause the chambers to inflate in the stomach.

Factors affecting the fdds

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. Most of these approaches are influenced by a number of factors that affect their bioavailability and efficacy of the gastro retentive system:

Density: Gastric retention time (GRT) is a function of dosage form buoyancy that is dependent on the density.

Size: Dosage form units with a diameter of more than 7.5 mm are reported to have an increased GRT compared with those with a diameter of 9.9 mm.

Shape of dosage form: Tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT 90% to 100% retention at 24 h 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 h. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with tha 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.

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 h 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 h) is less compared with their age and race matched female counterparts (4.6 ± 1.2 h), regardless of the weight, height and body surface).

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
Anti-cholinergics like Atropine and Propantheline, opiates like Codeine and prokinetic agents like Metoclopramide and Cisapride; can affect floating time.

Pharmacokinetic and pharmacodynamic aspects of fdds
The aim of this section is to delineate these aspects in order to suggest rational selection of drugs for which FDDS would be a beneficial strategy Pharmacokinetic aspects

Absorption window: Validation that the drug is within the category of narrow absorption window agents currently various experimental techniques are available that permit us to verify the absorption properties of the tested molecule, to determine the mechanism of intestinal absorption and to elucidate the permeability at different regions of the GI tract. In the case of absorption by active transporters that are capacity limited, the efficacy of the transport activity may increase following sustained presentation of the drug to the transporting enzymes in comparison to non-control release mode of administration.

Enhanced bioavailability: Once it has been ascertained that the compound in question is defined as narrow absorption window, the possibility of improving bioavailability by continuous administration of the compound to the specific site should be tested. For example, we have found that certain bisphosphonates, including alendronate, are absorbed directly from the stomach. However, the magnitude of this pathway remains modest even in the case where the prolonged gastric retention of the bisphosphonate in rats is produced by experimental/surgical means. On the other hand, the bioavailability of control release (CR) floating systems of Riboflavin and Levodopa are significantly enhanced in comparison to administration of simple CR polymeric formulations. It may be concluded that several different processes, related to absorption and transit of the drug in the gastrointestinal tract, act concomitantly and influence the magnitude of drug absorption. Therefore, in vivo studies are necessary to determine the release profile of the drug from the dosage form that will provide enhanced bioavailability [30].

Enhanced first pass biotransformation: In a similar fashion to increased efficacy of active transporters exhibiting capacity limited activity, the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome P450, in particular CYP3A4) in a sustained manner, rather than by a bolus input.

Improved bioavailability due to reduced P-glycoprotein (P-gp) activity in the duodenum: In apparent contrast to the higher density of CYP3A4 at the upper part of the intestine, P-gp mRNA levels increase longitudinally along the intestine such that the highest levels are located in the colon. Therefore, for drugs that are P-gp substrate and do not undergo oxidative metabolism, such as Digoxin, floating systems may elevate absorption compared to the immediate and CR dosage forms.

Reduced frequency of dosing: For drugs with relatively short biological half-life, sustained and slow input from control release floating system may result in a flip-flop pharmacokinetics and enable reduced dosing frequency. This feature is associated with improved patient compliance, and thereby improves therapy.

Targeted therapy for local ailments in the upper GIT: The prolonged and sustained administration of the drug from the floating systems to the stomach may be advantageous for local therapy in the stomach and the small intestine.

Pharmacodynamic aspects of fdds

Reduced fluctuations of drug concentration: Continuous input of the drug following floating system administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

Improved selectivity in receptor activation: Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations. Reduced counter-activity of the body: In many cases, the pharmacological response, which intervenes with the natural physiologic processes, provokes a rebound activity of the body that minimizes drug activity. Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Minimized adverse activity at the colon: Retention of the drug in the GRDF at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This pharmacodynamic aspect provides the rationale for floating formulation for beta-lactam antibiotics that are absorbed only from the small intestine and presence in the colon leads to development of microorganisms [31]. Evaluation of Floating Tablets The formulated tablets were evaluated for common physical evaluation tests like weight variation, thickness, hardness, drug content and in-vitro dissolution test apart from this the floating tablets also evaluated for floating time, floating lag time and invivo – invitro tests as per following procedures.

Buoyancy / Floating Test: The in vitro buoyancy was determined by floating lag time, as per the method described by a Rosa et al., 1994. Here, the tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT) [32].

In-vitro dissolution study: The tablet was placed inside the dissolution vessel. 5ml of sample were withdrawn at time intervals of 1h, 2h, 3h, 4h, 5h, 6h, 8h, 10 h and 12h. The volume of dissolution fluid adjusted to 900 ml by replacing fresh 5ml of dissolution medium after each sampling. The release studies were conducted with 3 tablets, and the mean values were plotted versus time. Each sample was analyzed at maximum wavelength using double beam UV visible spectrophotometer against reagent blank.

In Vivo Confirmation Of Buoyancy ByUsing Radiographic Studies

For this study the tablets were prepared by replacing half of the amount of drug with barium sulfate. After overnight fasting of three healthy volunteers they were fed with low calorie food and allowed to take water after these tablets were administered orally. Radiographs were obtained at specific time intervals, over these periods volunteers were allowed to take water

MATERIALS

Gemifloxacin-Procured From Hetero Drugs Ltd, Hyderabad, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Eudragit RSPO-Degussa India Ltd. (Mumbai, India), HPMC-Arvind Remedies Ltd, Tamil nadu, India, Carbopol 974P-Merck Specialities Pvt Ltd, Mumbai, India, Citric acid-Laser Chemicals, Ahmedabad, India, Sodium bicarbonate-Merck Specialities Pvt Ltd, Mumbai, India, Micro crystalline cellulose-Merck Specialities Pvt Ltd, Mumbai, IndiaMagnesium Stearate-Apex Chemicals, Ahmedabad, India,Talc-S.D. Fine Chem., Mumbai, India.

Methodology

Analytical method development

Determination of absorption maxima

A solution containing theconcentration 10 µg/ mL drug was prepared in 0.1N HCL UV spectrum was taken using Double beam UV/VISspectrophotometer. The solution was scanned in the range of 200 – 400 nm.

Preparation calibration curve

10mg Gemifloxacin pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 2, 4, 6, 8, 10µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 267 nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2)which determined by least-square linear regression analysis.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured.

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as themass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting.

Tapped density

After carrying out the procedure as given in the measurement of bulk densitythe cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Table 2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of floating Tablets

For optimization of sodium bicarbonate concentration, granules were prepared by direct compression method.

Procedure for direct compression method

1) Drug and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method by using 12mm punch.

Formulation of tablets

Table 3: Formulation composition for Floating tablets

INGREDIENTS (MG)	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Gemifloxacin	320	320	320	320	320	320	320	320	320
Eudragit RSPO	32.5	65	130	-	-	-	-	-	-
HPMC	-	-	-	32.5	65	130	-	-	-
Carbopol 974P	-	-	-	-	-	-	32.5	65	130
Citric acid	5	5	5	5	5	5	5	5	5
Sodium bicarbonate	10	10	10	10	10	10	10	10	10
Micro crystalline cellulose	124.5	92	27	124.5	92	27	124.5	92	27
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
Total Weight	500	500	500	500	500	500	500	500	500

All the quantities were in mg

RESULTS AND DISCUSSION

Analytical Method

Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 267 nm.

calibration curve

Graphs ofGemifloxacin was taken in 0.1N HCL (pH 1.2)

Table 4: Observations for graph of Gemifloxacin in 0.1N HCL

Conc [µg/mL]	Abs
0	0

2	0.125
4	0.248
6	0.364
8	0.475
10	0.586

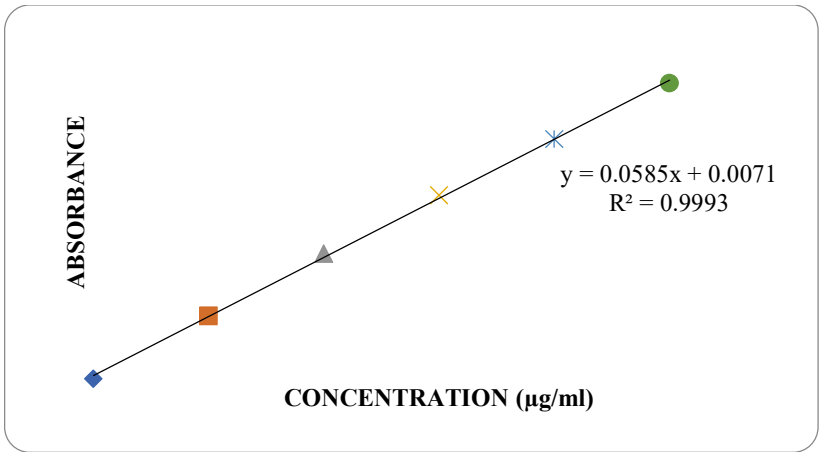

Fig 1: Standard graph of Gemifloxacin in 0.1N HCL

Standard graph of Gemifloxacin was plotted as per the procedure in experimental method and its linearity is shown in Table 8.1 and Fig 8.1. The standard graph of Gemifloxacin showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Preformulation parameters of powder blend

Table 5: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
F1	33º01'±1.18	0.22 ± 0.02	0.25 ± 0.25	13.10±1.14	1.15± 0.15
F2	30º01'±1.37	0.25 ± 0.02	0.29 ± 0.04	13.32±5.22	1.15 ± 0.07
F3	31º09'±2.12	0.26 ± 0..03	0.29 ± 0.02	10.44±3.94	1.11 ± 0.05
F4	34º06'±0.53	0.27± 0.06	0.31 ± 0.07	11.83±2.85	1.13 ± 0.03
F5	34º17'±1.07	0.23 ± 0.01	0.28 ± 0.01	17.04±2.82	1.20 ± 0.04
F6	32º29'±0.91	0.29 ± 0.01	0.33 ± 0.01	7.09 ± 2.82	1.13 ± 0.03
F7	33º21'±0.83	0.24 ± 0.03	0.27 ± 0.03	11.22±4.21	1.12 ± 0.05
F8	33º28'±0.83	0.28 ± 0.01	0.31 ± 0.05	11.55±3.52	1.13 ± 0.04
F9	32º47'±0.62	0.25 ± 0.01	0.27 ± 0.01	10.41±0.27	1.08 ± 0.03

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.22 ± 0.02to 0.29 ± 0.01 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.25 ± 0.25to 0.33 ± 0.01showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 17.04 which shows that the powder has good flow properties.All the formulations has shown the hausners ratio ranging between 1.08 ± 0.03 to 1.20 ± 0.04indicating the powder has good flow properties.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

Table 6: *Invitro* quality control parameters

Formulation codes	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time(Hrs)
F1	499.50	4.9	0.39	5.62	98.14	56	10
F2	498.32	5.6	0.15	5.51	97.24	42	12
F3	495.20	4.1	0.48	5.14	99.51	61	11
F4	498.75	4.8	0.55	5.75	97.21	34	11
F5	496.86	5.6	0.62	5.89	99.56	52	12
F6	497.21	5.2	0.21	5.12	97.35	48	10
F7	499.36	4.8	0.40	5.32	99.22	15	12
F8	500.03	5.4	0.31	5.20	96.36	30	9
F9	497.89	4.2	0.28	5.72	98.57	24	10

All the parameters for SR layer such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

***In Vitro* drug release studies**

Table 7: Dissolution data of Floating Tablets

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	13.58	9.17	8.92	10.80	12.51	19.10	14.21	20.11	11.15
1	18.69	18.25	14.03	15.37	17.92	25.49	20.36	25.34	17.94
2	22.12	24.39	20.62	19.29	22.19	29.82	27.48	30.40	21.67
3	36.34	37.75	26.47	26.40	28.62	37.87	33.24	33.89	25.56
4	44.11	40.28	35.89	33.67	36.51	46.73	48.82	39.90	34.40
5	51.86	47.56	44.56	39.12	43.86	53.87	50.31	45.90	37.58
6	58.27	54.12	49.84	50.74	54.98	62.31	66.17	56.88	41.10
7	67.14	63.29	56.47	57.56	62.26	69.12	73.99	59.34	52.67
8	75.26	68.76	62.35	63.58	68.32	77.58	77.61	67.51	57.25
9	79.98	75.92	68.13	71.75	74.57	81.73	84.50	76.56	65.32
10	83.29	84.27	73.58	75.96	83.34	88.17	89.72	78.49	74.15
11	92.42	90.63	76.21	81.36	86.95	92.52	93.31	80.20	80.52
12	99.16	95.79	82.18	87.24	90.11	98.21	99.29	85.15	90.19

From the dissolution data it was evident that the formulations prepared with Eudragit RSPO as polymer wereretarded the drug release12 hours.

Whereas the formulations prepared with higher concentration of HPMC retarded the drug release up to 12 hours in the concentration 130 mg. In lower concentrations the polymer was unable to retard the drug release. Whereas the formulations prepared with Carbopol 974Pwere retarded the drug release in the concentration of 32.5 mg (F7 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.29% in 12 hours with good retardation. Hence from the above dissolution data it was concluded that F7 formulation was considered as optimised formulation because good drug release (99.29%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation

Table 8: Application kinetics for optimised formulation

Cumulative (%) Release Q	Time (T)	Root (T)	Log(%) Release	Log (T)	Log (%) Remain	Release Rate (Cumulative % Release / T)	1/Cum% Release	Peppas Log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
14.21	0.5	0.707	1.153	-0.301	1.933	28.420	0.0704	-0.847	85.79	4.642	4.410	0.231
20.36	1	1.000	1.309	0.000	1.901	20.360	0.0491	-0.691	79.64	4.642	4.302	0.339
27.48	2	1.414	1.439	0.301	1.860	13.740	0.0364	-0.561	72.52	4.642	4.170	0.471
33.24	3	1.732	1.522	0.477	1.825	11.080	0.0301	-0.478	66.76	4.642	4.057	0.585
48.82	4	2.000	1.689	0.602	1.709	12.205	0.0205	-0.311	51.18	4.642	3.713	0.929
50.31	5	2.236	1.702	0.699	1.696	10.062	0.0199	-0.298	49.69	4.642	3.676	0.965
66.17	6	2.449	1.821	0.778	1.529	11.028	0.0151	-0.179	33.83	4.642	3.234	1.407
73.99	7	2.646	1.869	0.845	1.415	10.570	0.0135	-0.131	26.01	4.642	2.963	1.679
77.61	8	2.828	1.890	0.903	1.350	9.701	0.0129	-0.110	22.39	4.642	2.818	1.823
84.5	9	3.000	1.927	0.954	1.190	9.389	0.0118	-0.073	15.5	4.642	2.493	2.148
89.72	10	3.162	1.953	1.000	1.012	8.972	0.0111	-0.047	10.28	4.642	2.174	2.467
93.31	11	3.317	1.970	1.041	0.825	8.483	0.0107	-0.030	6.69	4.642	1.884	2.757
99.29	12	3.464	1.997	1.079	-0.149	8.274	0.0101	-0.003	0.71	4.642	0.892	3.749

Optimised formulation F7 was kept for release kinetic studies. From the above graphs it was evident that the formulation F7 was followed Kors mayer peppas release kinetics mechanism.

Drug – Excipient compatability studies
Fourier Transform-Infrared Spectroscopy

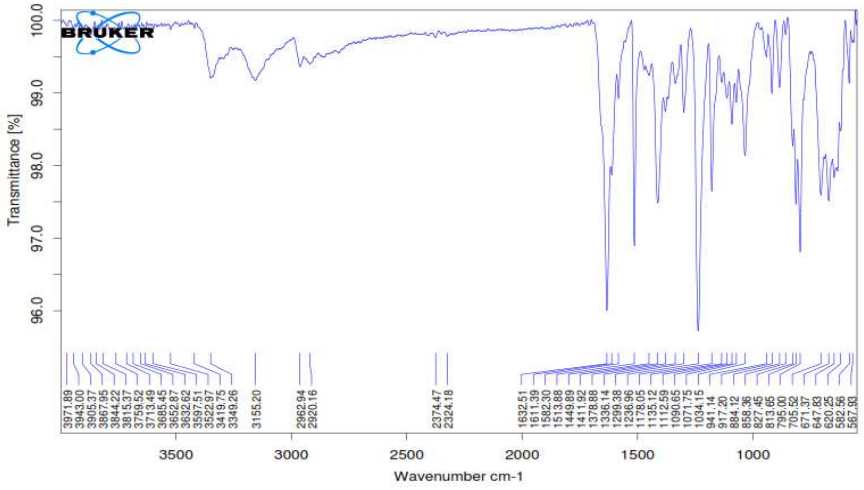

Fig 2: FTIR Spectrum of pure drug

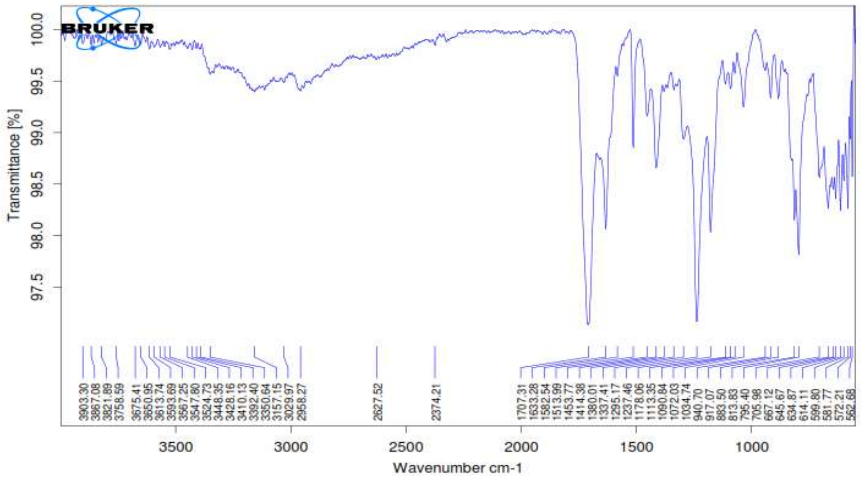

Fig 3: FTIR Spectrum of optimised formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions. Gemifloxacin are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

CONCLUSION

The floating tablets for Gemifloxacin (F1-F9) were successfully prepared using Eudragit RSPO,HPMC and Carbopol 974Pmatrix forming polymer and Sodium bi carbonate and Citric acid as gas generating agent by direct compression method. all the pre compression and post compression parameters are in its limits. The optimized formulation F7 has shown better sustained drug release and which has good floating properties. The release profile of optimized formula, fitted best to korsemeyrpeppas model mechanism.

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