



ISSN: 2306-6091

International Journal of Pharmaceuticals and Health Care Research (IJPHR)

IJPHR | Vol.14 | Issue 4 | Oct - Dec 2026

www.ijphr.com

DOI : <https://doi.org/10.61096/ijphr.v14.iss4.2026.708-723>

Formulation and Development of Gastro Retentive Floating Tablets of Lovastatin Using Novel Natural and Synthetic Polymers

Beerla Kavya*¹, V. Lavanya²

Department of Pharamaceutics, Princeton College of Pharmacy, Pocharam, Hyderabad, Telangana

*Corresponding Author: **Beerla Kavya**

Email: princeton.pharmacy@gmail.com



Published on:
14.10.2026
Published by:
Futuristic
Publications
2026| All rights
reserved.



Creative
Commons
Attribution 4.0
International
License.

Abstract: The present study focuses on the formulation and development of gastro retentive floating tablets of Lovastatin using novel natural and synthetic polymers such as ethyl cellulose, ispaggol husk, and fenugreek extract. Lovastatin, a lipid-lowering agent with a narrow absorption window in the upper gastrointestinal tract, benefits from a gastro retentive drug delivery approach to enhance its bioavailability. A series of formulations (F1–F9) were prepared using the direct compression method and evaluated for various pre- and post-compression parameters, including hardness, friability, drug content, floating lag time, total floating duration, and in vitro drug release. Among the developed formulations, F5 was identified as the optimized batch, exhibiting a floating lag time of less than one minute, total buoyancy exceeding 12 hours, and a sustained drug release of 99.56% over 12 hours. The combination of synthetic ethyl cellulose with natural swelling agents like ispaggol husk and fenugreek extract provided an effective matrix system for prolonged gastric retention and controlled drug release. The results suggest that the developed gastro retentive floating tablets of Lovastatin offer a promising strategy to improve therapeutic efficacy and patient compliance.

Keywords: Lovastatin, Ethyl Cellulose, Ispaggol Husk, and Fenugreek Extract

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT).¹ Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, and improves the drug solubility that are less soluble in a high pH environment.² Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs. Over the last few decades, several gastroretentive drug delivery approaches being designed and developed, including: high density (sinking) systems that is retained in the bottom of the stomach³, low density (floating) systems that causes buoyancy in gastric fluid^{4,5,6}, mucoadhesive systems that causes bioadhesion to stomach mucosa⁷, unfoldable, extendible, or swellable systems which limits emptying of the dosage forms through the pyloric sphincter of stomach^{8,9}, superporous hydrogel systems¹⁰ magnetic systems¹¹ etc. The current review deals with floating type gastroretentive drug delivery system.

Basic gastrointestinal tract physiology:

The stomach is divided into 3 regions anatomically: fundus, body, and antrum pylorus. The proximal part is the fundus and the body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states but the pattern of motility is distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle through both stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is divided into following 4 phases.¹²

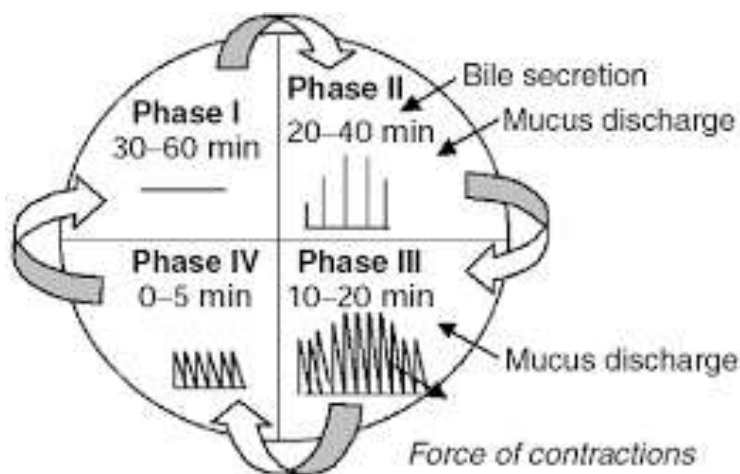


Fig 1.1: Schematic Representation of Interdigestive Motility

Phase I: This period lasts about 30 to 60 minutes with no contractions.

Phase II: This period consists of intermittent contractions that increase gradually in intensity as the phase progresses, and it lasts about 20 to 40 minutes. Gastric discharge of fluid and very small particles begins later in this phase.

Phase III: This is a short period of intense distal and proximal gastric contractions (4-5 contractions per minute) lasting about 10 to 20 minutes these contractions, also known as “house-keeper wave,” sweep gastric contents down the small Intestine.

Phase IV: This is a short transitory period of about 0 to 5 minutes, and the contractions dissipate between the last part of phase III and quiescence of phase

Need For Gastroretention:

- Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).
- Drugs that are less soluble or that degrade at the alkaline pH.
- Drugs that are absorbed due to variable gastric emptying time.
- Local or sustained drug delivery to the stomach and proximal small intestine to treat certain conditions.
- Particularly useful for the treatment of peptic ulcers caused by H.Pylori infections.¹²

Factors controlling gastric retention of dosage forms:

There are several factors that can affect gastric emptying of an oral dosage form which include density, size and shape of dosage form, feeding state, biological factors such as age, gender, posture, body mass index, disease state etc.

1. Effect Of Dosage Form Size & Shape :

Small size tablets are emptied from the stomach during the digestive phase while large size units are expelled during the house keeping waves found that floating unit with a diameter equal or less than 7.5 mm had larger gastric residence time (GRT) compared to nonfloating units but the GRT was similar for floating and non-floating units having a large diameter of 9.9 mm. They found that GRT of nonfloating units were

much more variable and highly dependent on their size which are in the order of small < medium < large units. Moreover, in supine subjects, size influences GRT of floating and non- floating form. Tetrahedron and ring shaped devices have a better GRT as compared with other shapes.^{13,14}

2. Density:

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach¹⁶. Both positions may isolate the dosage system from the pylorus. A density of < 1.0 gm/ cm³ is required to exhibit floating property.¹⁵

3. Gender, Posture & Age:

Generally females have slower gastric emptying rates than male. The effect of posture does not have any significant difference in the mean gastric retention time (GRT) for individuals in upright, ambulatory and supine state. In case of elderly persons, gastric emptying is slowed down.¹⁶

4. Effect of Food & Specific Gravity:

To float FDDS in the stomach, the density of dosage form should be less than gastric content i.e.1.0 g/cm³. Since, the bulk density of a dosage form is not a sole measure to describe its buoyant capabilities because the magnitude of floating strength may vary as a function of time and gradually decrease after immersing dosage form into fluid as a result of development of its hydrodynamic equilibrium. Various studies have shown the intake of food as main determinant of gastric emptying rather than food. Presence of food is the most important factor effecting GRT than buoyancy. GRT is significantly increased under fed condition since onset of MMC is delayed. Studies show that GRT for both floating and non-floating single unit are shorter in fasted subjects (less than 2 hour), but significantly prolonged after meal (around 4 hour).¹²

5. Nature of Meal & Frequency of Food:

Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to fed state, to increase gastric emptying rate and prolonging the drug release. Diet rich in protein and fat can increase GRT by 4-10 hours.¹²

6. Type of Formulation:

Multiple unit formulation show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different release profile or containing incompatible substances and permit a large margin of safety against dosage form failure compared with single unit dosage form.¹³

Future Potential:

Floating dosage form offers various future potential as evident from several recent publications. The reduced fluctuations in the plasma level of drug results from delayed gastric emptying. Drugs that have poor bioavailability because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently thereby maximizing their absorption and improving their absolute bioavailability.

Buoyant delivery system considered as a beneficial strategy for the treatment of gastric and duodenal cancers.

- The floating concept can also be utilized in the development of various anti-reflux formulations.
- Developing a controlled release system for the drugs, which are potential to treat the Parkinson's disease.
- To explore the eradication of *Helicobacter pylori* by using the narrow spectrum antibodies.¹⁴

Classification Of Gastroretentive Drug Delivery System:

The main approaches that have been examined for gastroretentive dosage forms (GRDFs) are: low density of GRDF that cause buoyancy above gastric fluid (Floating system), high density which retain the dosage form in the body of stomach, concomitant administration of drugs or excipients which slow the motility of the GIT, bioadhesion to gastric mucosa, swelling to a large size which prevents emptying of dosage form through the pyloric sphincter.^{17,18}

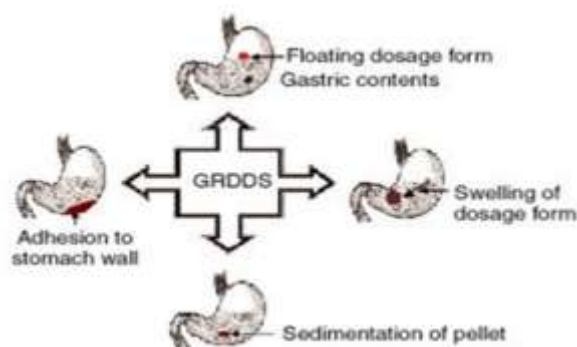


Fig 1.2: Types of Gastroretentive Drug Delivery System

Floating Drug Delivery Systems:

A floating dosage form is useful for drugs acting locally in the proximal gastrointestinal tract. These systems are also useful for drugs that are poorly soluble (or) unstable in intestinal fluids. The floating properties of these systems help to retain in the stomach for a long time. Various attempts have been made to develop floating systems, which float on the gastric contents and release drug molecules for the desired time period. After the release of a drug, the remnants of the system are emptied from the stomach. Based on the mechanism of buoyancy, two different technologies have been used in development of floating drug delivery systems.

These include:

- a) Effervescent system.
- b) Non- Effervescent system.

A) Effervescent Systems:

Effervescent systems¹⁰ include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO₂) 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 evaporate at body temperature. These effervescent systems further classified into two types:

- 1) Gas generating systems.
- 2) Volatile liquid or Vacuum containing systems.

1) Gas Generating Systems:

a) Tablets Intragastric Single layer Floating Tablets or Hydrodynamically Balanced System (HBS):

These formulations have bulk density lower than gastric fluids and thus float in the stomach that increases the gastric emptying rate for a prolonged period,¹⁹ (Fig.3). These are formulated by intimately mixing the gas (CO₂) generating agents and the drug within the matrix tablet. The drug is released slowly at a desired rate from the floating system and the residual system is emptied from the stomach after the complete release of the drug. This leads to an increase in the gastric residence time (GRT) and a better control over fluctuations in plasma drug concentration.

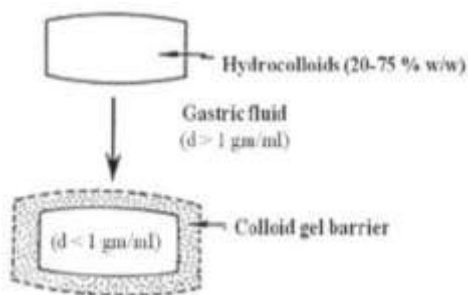


Fig 1.3: Intragastric Single Layer Floating Tablet

Intragastric Bilayer Floating Tablets These are also compressed tablets¹⁹ containing two layers:

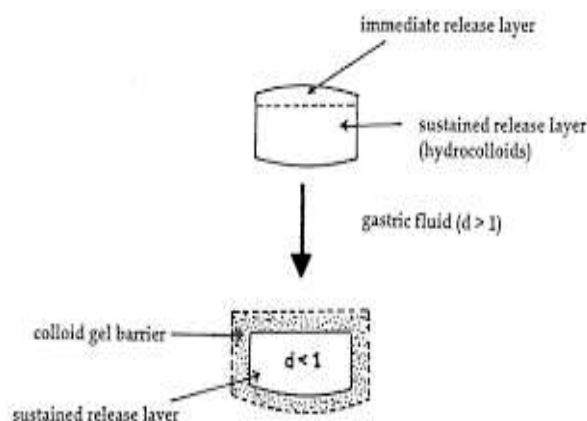


Fig 1.4: Intragastric bilayer floating tablet

- Immediate release layer and
- Sustained release layer.

b) Floating Capsules:

These floating capsules²⁰ are formulated by filling with a mixture of sodium alginate and sodium bicarbonate. The systems float as a result of the generation of CO₂ that was trapped in the hydrating gel network on exposure to an acidic environment.

c) Multiple Unit Type Floating Pills:

These multiple unit type floating pills²⁰ are sustained release pills, known as seeds, which are surrounded by two layers (Fig.5). The outer layer is of swellable membrane layer while the inner layer consists of effervescent agents. This system sinks at once and then it forms swollen pills like balloons which float as they have lower density, when it is immersed in the dissolution medium at body temperature. The lower density is due to generation and entrapment of CO₂ within the system. Key: (a) conventional SR pills; (b) effervescent layer; (c) swellable layer; (d) expanded swellable membrane layer; (e) surface of water in the beaker (37°C).

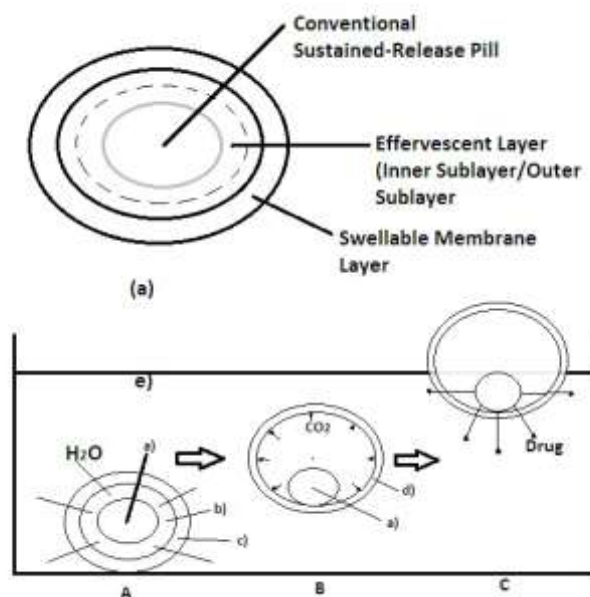


Fig 1.5: (a) A multiple-unit oral floating dosage system. (b) Stages of floating mechanism: (A) penetration of water; (B) generation of CO₂ and floating; (C) dissolution of drug.

d) Floating System with Ion-Exchange Resins:

Floating system using bicarbonate loaded ion exchange resin was made by mixing the beads with 1M sodium bicarbonate solution, and then the semi-permeable membrane is used to surround the loaded beads to avoid sudden loss of CO₂. On contact with gastric contents an exchange of bicarbonate and chloride ions takes place that results in generation of CO₂ that carries beads towards the top of gastric contents and producing a floating layer of resin beads.²⁰

2) Volatile liquid or Vacuum Containing Systems:**a) Intragastric Floating Gastrointestinal Drug Delivery System:**

This system floats in the stomach because of floatation chamber, which is vacuum or filled with a harmless gas or air, while the drug reservoir is encapsulated by a microporous compartment,¹⁹ (Fig.1.6).

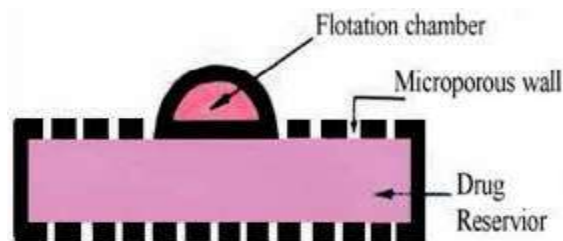


Fig 1.6: Intragastric Floating Gastrointestinal Drug Delivery Device

Inflatable gastrointestinal delivery systems:

Inflatable chamber are incorporated, which contains liquid ether that gasifies at body temperature to inflate the chamber 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,¹⁹ (Fig.7). 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 is released continuously from the reservoir into gastric fluid.

¹MATERIALS

Table: List of materials used in the formulation

List of Chemicals	Manufacturing Company
Entecavir	Procured from Hetero Pharma limited Hyd, provided by SURA LABS, Dilsukhnagar, Hyderabad
PLGA	Merk specialiities Pvt Limited, Mumbai
Ethyl cellulose	M/S Micro labs limited, Hosur. India.
HPMC K4M	Coloron Asia Private Limited; Goa
Dichloro methane (mL)	Qualikems Fine Chem Pvt., Ltd.
Methanol (mL)	Merk specialiities Pvt Limited,Mumbai
Sodium lauryl sulphate (mg)	Merk specialiities Pvt Limited,Mumbai

INSTRUMENTS

Table: List of instruments used

S.NO	Instruments/Equipments	Model and Manufacturer/Supplier
1	UV-Visible spectrophotometer	Lab India, India
2	Electronic weighing balance	Sartorius
4	Magnetic stirrer	Remi Laboratories
5	Dissolution Apparatus	Lab India, Lab India

6	Ultrasonic cleaner	Remi Laboratories
7	FT – IR Spectrometer	Bruker Alpha
8	SEM	SEM (JEOL Ltd.,Japan).

METHODOLOGY

Analytical method development:

a) Determination of absorption maxima:

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

b) Preparation calibration curve:

10mg Lovastatin pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with 10ml 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 10, 20, 30, 40, 50µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 238 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.

7.2. Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality 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. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r \quad \tan \theta = \text{Angle of repose}$$

h = Height of the cone , r = Radius of the cone base

Table 7.1: 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 the mass of the powder divided by the bulk volume and is expressed as gm/cm³. 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. The powder was carefully leveled without compacting and the unsettled apparent volume, V_o , was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where, M = weight of sample

V_o = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the 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. The tapped density was calculated, in gm per L, using the formula:

$$\text{Tap} = M / V$$

Where, Tap= Tapped Density

M = Weight of sample

V = Tapped volume of powder

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:

$$\text{Carr's Index} = [(\text{tap} - b) / \text{tap}] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Table 7.2: 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

7.3. Formulation development of floating Tablets:

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 7mm punch.

FORMULATION OF TABLETS:**Table 7.3: Formulation composition for Floating tablets**

INGREDIENTS (MG)	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lovastatin	20	20	20	20	20	20	20	20	20
Ethyle cellulose	20	40	60	-	-	-	-	-	-
Isapgol husk	-	-	-	20	40	60	-	-	-
Fenugreek extract	-	-	-	-	-	-	20	40	60
Citric acid	10	10	10	10	10	10	10	10	10
Sodium bicarbonate	8	8	8	8	8	8	8	8	8
Micro crystalline cellulose	82	62	42	82	62	42	82	62	42
Magnesium Stearate	6	6	6	6	6	6	6	6	6
Talc	4	4	4	4	4	4	4	4	4
Total Weight	150	150	150	150	150	150	150	150	150

All the quantities were in mg

7.4. Evaluation of post compression parameters for prepared Tablets

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

$$\% \text{ Deviation} = (\text{Individual weight} - \text{Average weight})$$

RESULTS AND DISCUSSION**Analytical Method****a. Determination of absorption maxima**

The standard curve is based on the spectrophotometer. The maximum absorption was observed at 238nm.

b. calibration curve

Graphs of Lovastatin was taken in 0.1N HCL (pH 1.2)

Table 8.1: Observations for graph of Lovastatin in 0.1N HCL

Conc [$\mu\text{g/mL}$]	Abs
0	0
10	0.139
20	0.286
30	0.418
40	0.557
50	0.695

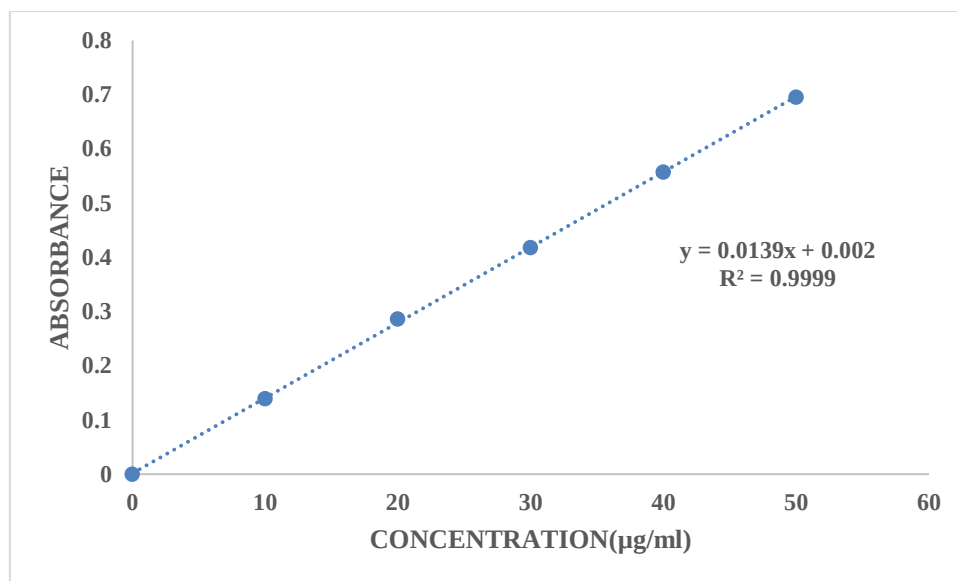


Fig 8.1: Standard graph of Lovastatin in 0.1N HCL

Standard graph of Lovastatin 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 Lovastatin showed good linearity with R^2 of 0.999, which indicates that it obeys “Beer- Lamberts” law.

8.3. Pre formulation parameters of powder blend:

Table 8.2: 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	28.19± 1.20	0.53±0.03	0.63±0.0	15.46 ±0.25	1.22±0.08
F2	16.13±0.19	0.55±0.17	0.49±0.35	14.28±0.28	1.16±0.01
F3	18.04±0.12	0.52±0.15	0.59±0.52	11.86±0.16	1.13±0.02
F4	14.31±0.17	0.47±0.18	0.53±0.42	11.32±0.12	1.12±0.03
F5	15.08±0.23	0.44±0.15	0.51±0.63	13.72±0.18	1.15±0.01
F6	23.12±0.15	0.54±0.12	0.63±0.42	14.28± 0.11	1.16±0.03
F7	15.93±0.15	0.47±0.13	0.55±0.36	14.54± 0.13	1.17±0.01
F8	19.43±0.17	0.41±0.11	0.47±0.33	12.76± 0.25	1.14±0.03
F9	13.64±0.15	0.53±0.12	0.59±0.43	10.16± 0.31	1.11±0.02

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 0.41±0.11 to 0.55±0.17 (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 0.47±0.33 to 0.63±0.42 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 15.46 which show that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 1.11±0.02 to 1.22±0.08 indicating the powder has good flow properties.

8.4. 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.

8.3. In vitro quality control parameters

Formulation codes	Weight variation (mg)	Hardness (kg/cm ²)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time (Hrs)
F1	149.52	3.3	0.63	2.53	98.13	21	7
F2	150.09	3.2	0.51	2.01	99.94	32	9
F3	149.26	3.9	0.46	2.28	97.63	22	10
F4	145.92	3.1	0.61	2.41	98.12	16	9
F5	150.01	3.8	0.39	2.19	99.25	10	12
F6	148.93	3.7	0.32	2.28	98.08	24	10
F7	147.34	3.2	0.77	2.11	97.22	12	9
F8	145.41	3.4	0.66	2.83	99.11	14	6
F9	149.82	3.7	0.54	2.19	96.87	18	8

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

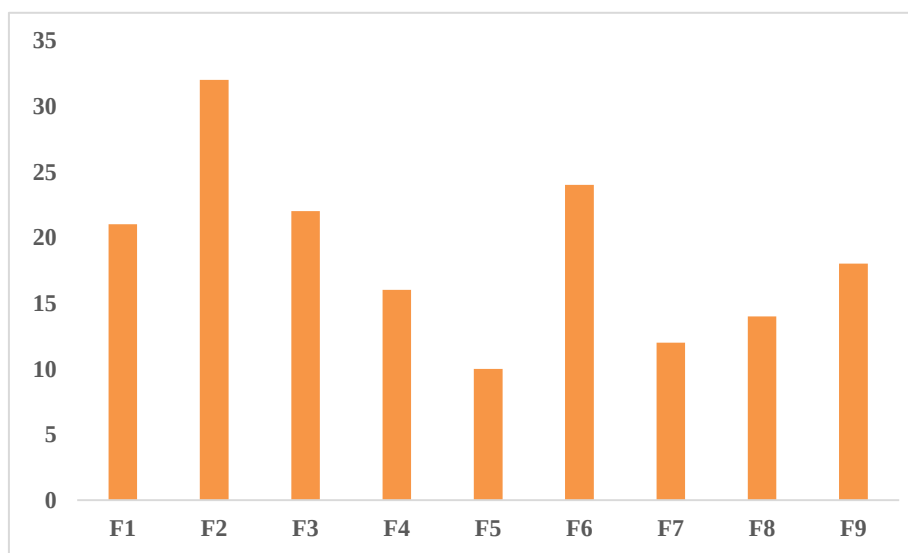


Fig 8.2: Floating lag time (sec)

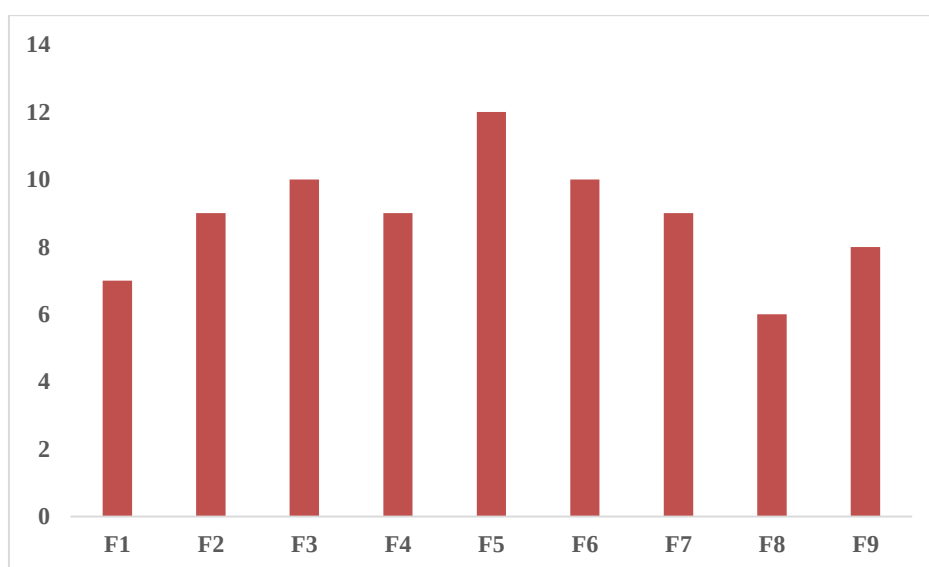


Fig 8.3: Total Floating Time (Hrs)

8.5. In vitro drug release studies

Table 8.4: Dissolution data of Floating tablets

TIME (HR)	CUMULATIVE PERCENTAGE OF DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	21.74	26.98	11.51	16.65	15.42	17.31	19.83	11.16	7.88
2	27.53	33.39	17.91	20.28	19.18	21.24	24.58	17.53	11.61
3	32.21	44.25	24.12	29.68	24.29	28.96	29.75	22.19	17.03
4	39.68	49.1	31.55	34.53	32.32	35.43	35.19	28.08	22.09
5	47.09	54.57	38.90	39.61	37.65	39.92	41.64	34.79	29.11
6	53.36	59.35	43.12	43.01	46.06	43.41	48.25	38.05	37.57
7	61.25	65.89	49.81	48.75	51.89	59.82	54.72	46.38	44.14
8	76.17	71.61	59.36	67.76	58.17	64.59	61.01	54.49	55.39
9	85.81	76.42	63.17	71.24	63.52	71.42	79.78	67.13	65.57
10	97.36	84.31	77.28	86.39	75.61	78.23	83.26	75.94	77.51
11		95.91	91.94	98.48	83.35	88.14	88.48	87.05	82.48
12			98.71		99.56	97.33	96.22	93.46	92.39

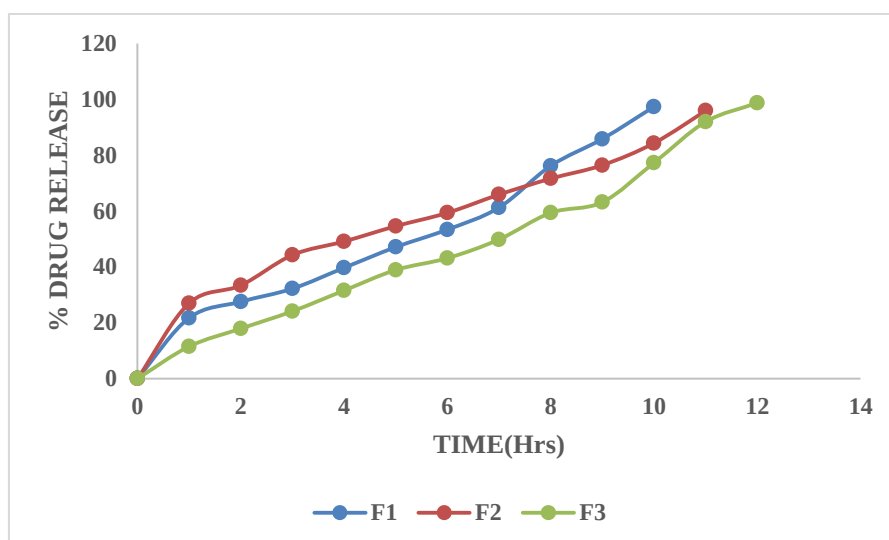


Fig 8.4: Dissolution data of Lovastatin Floating tablets containing Ethyle cellulose

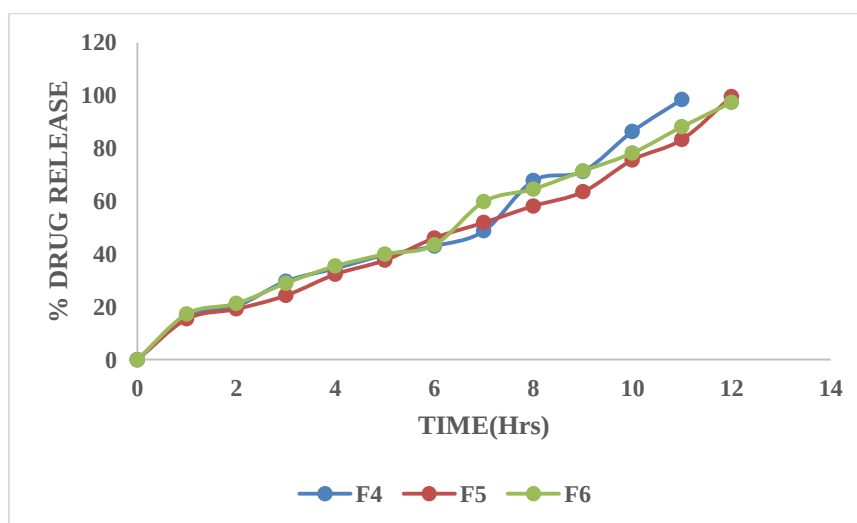


Fig: 8.5 Dissolution data of Lovastatin Floating tablets containing Isapgol husk

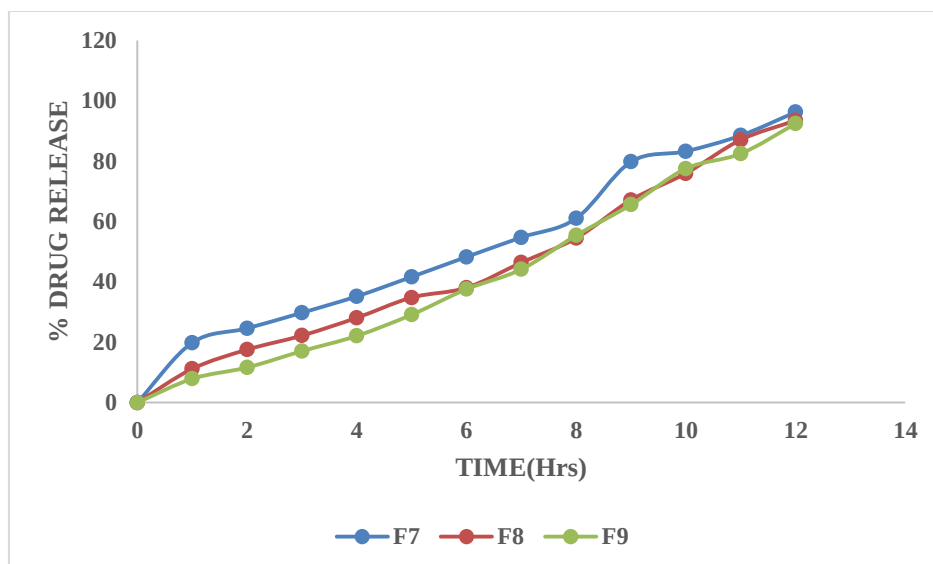


Fig: 8.6 Dissolution data of Lovastatin Floating tablets containing Fenugreek extract

From the dissolution data it was evident that the formulations prepared with Ethyle cellulose as polymer were retarded the drug release 12 hours.

Whereas the formulations prepared with middle concentration of Isapgol husk retarded the drug release up to 12 hours in the concentration 40 mg. In higher concentrations the polymer was unable to retard the drug release.

Whereas the formulations prepared with Fenugreek extract were retarded the drug release in the concentration of 20mg (F7 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.22 % in 12 hours with good retardation.

Hence from the above dissolution data it was concluded that F5 formulation was considered as optimized formulation because good drug release (99.56%) in 12 hours.

Application of release rate kinetics to Dissolution data for optimised formulation:

Table 8.5 Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	% RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE E / 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
15.42	1	1.000	1.188	0.000	1.927	15.420	0.0649	-0.812	84.58	4.642	4.390	0.252
19.18	2	1.414	1.283	0.301	1.908	9.590	0.0521	-0.717	80.82	4.642	4.324	0.318
24.29	3	1.732	1.385	0.477	1.879	8.097	0.0412	-0.615	75.71	4.642	4.230	0.411
32.32	4	2.000	1.509	0.602	1.830	8.080	0.0309	-0.491	67.68	4.642	4.075	0.566
37.65	5	2.236	1.576	0.699	1.795	7.530	0.0266	-0.424	62.35	4.642	3.965	0.676
46.06	6	2.449	1.663	0.778	1.732	7.677	0.0217	-0.337	53.94	4.642	3.778	0.863
51.89	7	2.646	1.715	0.845	1.682	7.413	0.0193	-0.285	48.11	4.642	3.637	1.005
58.17	8	2.828	1.765	0.903	1.621	7.271	0.0172	-0.235	41.83	4.642	3.471	1.170
63.52	9	3.000	1.803	0.954	1.562	7.058	0.0157	-0.197	36.48	4.642	3.317	1.325
75.61	10	3.162	1.879	1.000	1.387	7.561	0.0132	-0.121	24.39	4.642	2.900	1.742
83.35	11	3.317	1.921	1.041	1.221	7.577	0.0120	-0.079	16.65	4.642	2.554	2.088
99.56	12	3.464	1.998	1.079	0.540	8.297	0.0100	-0.002	0.44	4.642	0.761	3.881

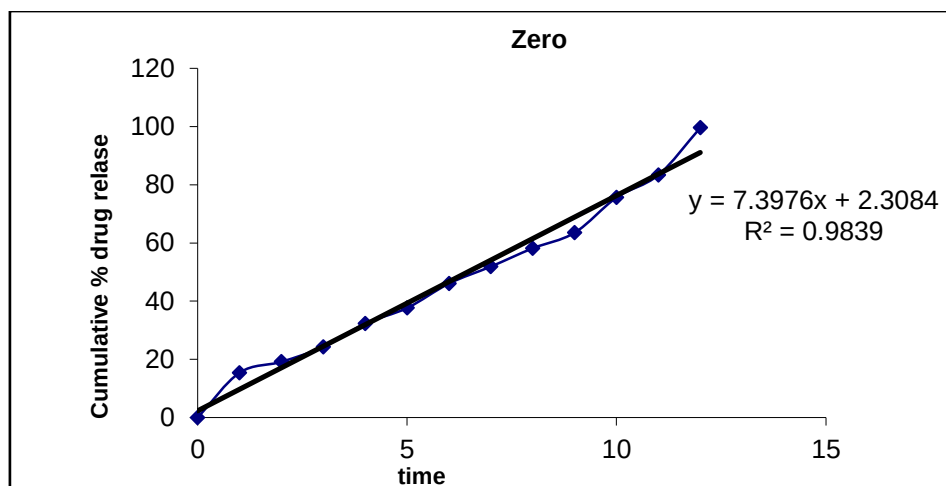


Fig 8.7: Zero order release kinetics

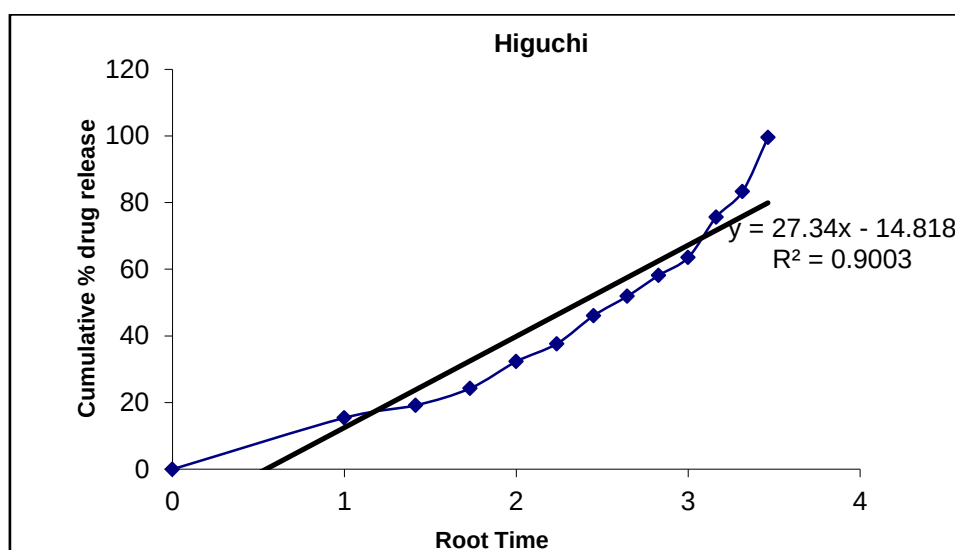


Fig 8.8: Higuchi release kinetics

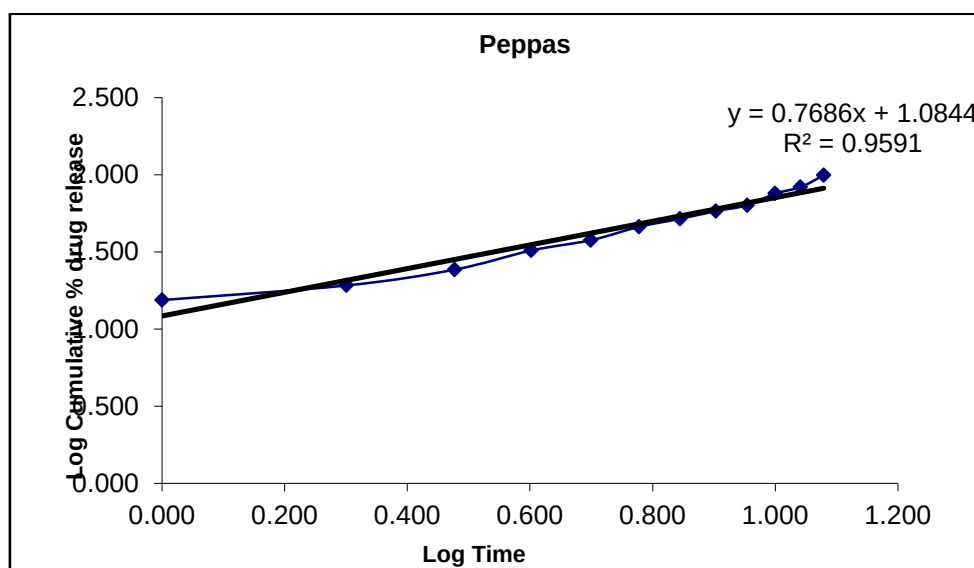


Fig 8.9: Kors mayer peppas release kinetics

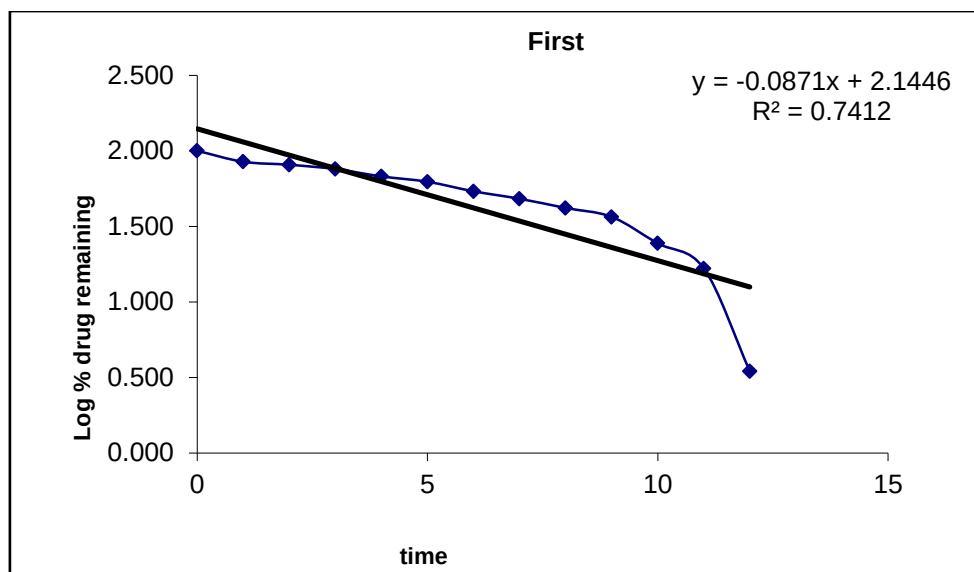


Fig 8.10: First order release kinetics

Optimised formulation F5 was kept for release kinetic studies. From the above graphs it was evident that the formulation F5 was followed Zero order release kinetics mechanism.

8.6. Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy:

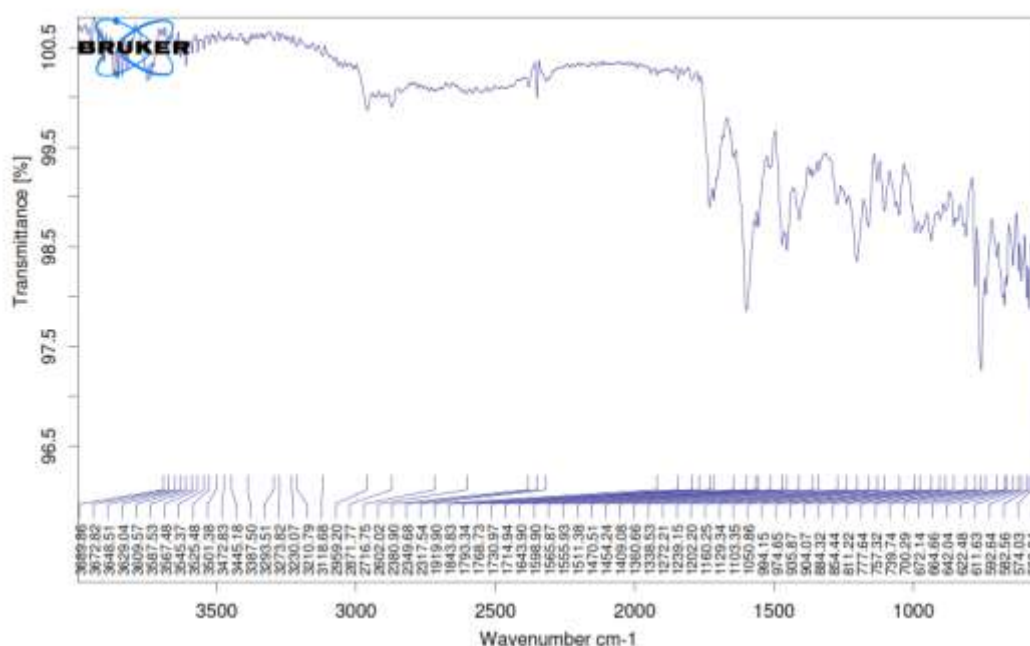


Fig 8.11: FTIR Spectrum of pure drug

CONCLUSION:

Microspheres are prepared with PLGA, Ethyl cellulose and HPMC K4M successfully by the solvent evaporation technique. Microspheres of Entecavir showed excellent mucoadhesivity, % yield, Drug Content, % Drug entrapment efficiency and prolonged drug release up to 12 hours. Microspheres of different size and drug content could be obtained by varying the formulation variables. Thus the prepared microspheres may prove to be potential candidates for oral delivery devices. Formulation Batch E5 showed best appropriate balance between mucoadhesivity and drug release rate, which can be considered as a best fit for microspheres. The polymer ratio (Ethyl cellulose) of 1:2 were selected as best formulation, The formulated system showed sustained release up to 12 h and the system is potentially useful to overcome

poor bioavailability problems associated with Entecavir. Analysis of drug release mechanism showed that the drug release from the formulations the best fit model was found to be zero order release kinetics. Hence it can be concluded that Entecavir loaded Ethyl cellulose Microsphere may be useful to achieve sustained drug release profile suitable for oral administration.

REFERENCES

1. Altaf Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. *Expert Opin Drug Deliv*, 2006; 3(2): 217- 33.
2. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems. *Trop. J Pharm Res*, 2008; 7(3): 1055-66.
3. Rouge N, Allemann E, Gex-Fabry M, Balant L, Cole ET, Buri P, Doelker E. Comparative pharmacokinetic study of a floating multiple-unit capsule, a high density multipleunit capsule and an immediate-release tablet containing 25 mg atenolol. *Pharm Acta Helvetiae*, 1998; 73: 81-7.
4. Streubel A, Siepmann J, Bodmeier R. Multiple unit Gastroretentive drug delivery: a new preparation method for low density microparticles. *J Microencapsul*, 2003; 20: 329-47.
5. Goole J, Vanderbist F, Aruighi K. Development and evaluation of new multiple-unit levodopa sustained-release floating dosage forms. *Int J Pharm*, 2007; 334: 35-41.
6. Shirma S, Pawar A. Low density multiparticulate system for pulsatile release of meloxicam. *Int J Pharm*, 2006; 313: 150-58.
7. Santus G, Lazzarini G, Bottoni G, Sandefer EP, Page RC, Doll WJ, Ryo UY, Digenis GA. An in vitro-in vivo investigation of oral bioadhesive controlled release furosemide formulations. *Eur J Pharm Biopharm* 1997; 44: 39-52.
8. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. *J Control Release* 2003; 90: 143-62.
9. Deshpande AA, Shah N, Rhodes CT, Malik W. Development of a novel controlled-release system for gastric retention. *Pharm Res* 1997; 14: 815-19.
10. Park K. Enzyme-digestible swelling as platforms for longterm oral drug delivery: synthesis and characterization. *Biomaterials* 1988; 9: 435.
11. Fujimori J, Machida Y, Nagai T. Preparation of a magnetically responsive tablet and configuration of its gastric residence in beagle dogs. *STP Pharma Sci* 1994; 4: 425-30.
12. S.U. Zate, P.I. Kothawade, G.H. Mahale, K.P. Kapse, S.P. Anantwar. Gastroretentive Bioadhesive Drug Delivery System: A Review. *International Journal of PharmTech Research Res.* 2(2); 2010: 1227-1235.
13. Desai S, Bolton S. A floating controlled release drug delivery system: in vitro- in vivo evaluation. *Pharm Res.* 1993;10:1321-1325. PubMed DOI: 10.1023/A:1018921830385