Effect of various polymers on drug release of effervescent floating tablets of paliperidone

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ABSTRACT:
Floating tablets of Paliperidone were developed to prolong gastric residence time, leading to an increase in drug bioavailability. Tablets were prepared by the direct compression method, using polymers such as Tamarind Gum, Carnuba wax and HPMC K15 M. The Fourier transform-infrared spectra revealed that there was no interaction between polymers an drug; hence, they are compatible. The prepared tablets of all the formulations were evaluated for physical characters, hardness and friability, floating lag time, total floating time, drug content and in- vitro drug release. The in vitro release study of the tablets was performed in 0.1 N HCl as a dissolution media. In this research work formulation F5 fulfills all the testing parameters in terms of pre and post compression. And Optimised formulation was showed maximum drug release 99.13 % up to 12 hours. Floating lag time is less 21 sec and total floating time up 12 hours and it was fitted to kinetics of drug release for R^2 value of Zero order release mechanism model is 0.979.
Key words: Paliperidone, Tamarind Gum, Carnuba wax, HPMC K15 M, direct compression method, floating lag time and total floating time.

I. INTRODUCTION

Oral delivery of drugs is the preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in the formulation and cost effective manufacturing process.[1]Many of the drug delivery systems, available in the market are oral drug delivery type systems. Pharmaceutical products designed for oral delivery are mainly immediate release type orconventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration –time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentrations may lead to under medication or overmedication as the C max values fall or rise beyond the therapeutic range
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index , whenever overmedication occurs.[2]

In order to overcome the drawbacks of conventional drug delivery 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.[3]

1.1 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.[4]

Controlled drug delivery or modified drug delivery systems are divided into 4 categories.

1. Delayed release
2. Sustained release
3. Site-specific targeting
4. 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 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 physiologically therapeutically based drug release system. In other words , the amount and the rate of drug release determined by the physiological therapeutic needs of the body.[5]

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. (fig.1).[6]Controlled drug deliveries 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.

Oral delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have an ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action.[7] Thus the objective of the pharmacist is to develop systems that can be as ideal system as possible. Attempts to develop a single dose therapy for the whole duration of treatment have focused attention on controlled or sustained release drug delivery systems. Attention has been focused particularly on orally administered sustained drug delivery systems because of the ease of the administration via the oral route as well as the ease and economy of manufacture of oral dosage form. Sustained release describes the delivery of drug from the dosage forms over an extended period of time. It also implies delayed therapeutic action and sustained duration of therapeutic effect. Sustained release means not only prolonged duration of drug delivery and prolonged release, but also implies predictability and reproducibility of the drug release kinetics. A number of different oral sustained drug delivery systems are based on different modes of operation and have been variously named, for example, as dissolution controlled systems, diffusion controlled systems, ion-exchange resins, osmotically controlled systems, erodible matrix systems, pH independent formulations, swelling controlled systems and the like.

An orally administered controlled drug delivery systems encounters a wide range of highly variable conditions, such as pH, agitation intensity and composition of the GI fluids as it passes down the GIT. Considerable efforts have been made to design oral controlled drug delivery systems that produce more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, like inability to retain and localize the drug delivery system within desired regions of the GIT and highly variable nature of the Gastric emptying process. An important factor, which may adversely affect the performance of an oral controlled drug delivery system, is the G.I transit time. The time for absorption in the GI transit in humans , estimated to be 8-10 hr from mouth to colon, is relatively brief with considerable fluctuation. G.I transit time vary widely between individuals, and depend up on the physical properties of the object ingested and the physiological conditions of the gut. This variability may lead to predictable bioavailability and times to achieve peak plasma levels. One of the important determinants of G.I transit is the residence time in the stomach.

1. Administered one or more times a day
2. Only absorbed in the upper GI regions.
3. Insoluble in water
4. Targeted at sites in the upper GIT
5. Bioavailable through active transport mechanisms
6. Irritating to the mucosa
7. Misbalancing, irritating, or unsafe in the lower GI region.
8. More effective when plasma levels are more constant
9. That is locally active in the stomach
10. That is unstable in the intestinal or colonic environment or degrades in colon.
11. Have low solubility at high values.

1.2 Biological aspects of gastric retention dosage forms

To comprehend the considerations taken in the design of the gastric retention dosage forms and to evaluate their performance the relevant anatomy and physiology of the GIT must be fully understood. The extent of the drug absorption in a segment of the G.I.T depends generally on the rate of absorption as well as on the exposed surface area and time available for drug absorption. The GI transit times of the dosage forms in the various segments of the GIT are listed in table: 1.1. The outer factors influencing absorption are surface area, absorption mechanisms, pH values, enzymes and number of microorganisms.

Table: The transit time of different dosage forms across the segments of GI tract

Transit time (h)		
Gastric	**Small intestine**	**Total**
2.7±1.5	3.1±0.4	5.8

1.2±1.3	3.4±1.0	4.6
0.8±1.2	3.2±0.8	4.0
0.3±0.07	4.1±0.5	4.4

It is well recognized that the stomach may be used as a depot for co0ntrolled release dosage forms. The stomach is J-shaped organ located in the upper left hand portion of the abdomen, just below the diaphragm. The stomach is composed of the following parts.[9,10]

- Fundus
- Body
- Antrum

The proximal stomach made up of the fundus and body regions, serves as a reservoir for ingested materials while the distal region (Antrum) is the major site of mixing motions, acting as a pump to accomplish gastric emptying. The pylorous is an anatomical sphincter situated between the most terminal antrum and the duodenum.

Gastric emptying: [11-14]

The process of gastric emptying occurs in two states:

- Fasting as well as
- Fed states

The pattern of motility is distinct in both states.

In fasting state: An inter digestive series of electrical events occur in a cyclic manner both through stomach and small intestine ever 2 to 3 hrs.[15]This activity is called inter digestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 consecutive phases as[16]

- Phase I (basal phase): It is a period with rare contractions lasting from 40-60 minutes.
- Phase II (preburst phase) : It is a period of similar duration lasting for 40-60 minutes consisting of intermittent action potentials and contractions that gradually increase in intensity and frequency as the phase progresses.
- Phase III (burst phase) : It is short period of intense, large regular contractions lasting for 4-6 minutes .It is this phase which gives the cycle the term housekeeping wave, since it serves to sweep undigested materials out of stomach and down the small intestine.
- Phase IV: It is a brief transitional phase that occurs between phase III and phase I of their two consecutive cycles.

In fed state: The motor activity in the fed state is induced 5-10 min after ingestion of a meal and persists as long as food remains in the stomach. This is also known as digestive motility patter and comprises continuous contractions as in phase II of fasted state. These contractions are not as severe as those in the third phase of the fasted motility pattern. These contractions result in reducing the size of food particles (to<1mm), which are propelled toward the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric emptying rate.[17]

Orally administered controlled release dosage forms are subjected to basically 2 complications that of short residence time and unpredictable gastric emptying, which is affected by age, sex and health condition of a subject. So with extended gastro intestinal residence time, controlled release dosage forms are formulated.

1.3 Factors Affecting Gastric Retention [18]

Density: GRT is a function of dosage form buoyancy that is dependent on the density of a dosage form which affects the gastric emptying rate. A buoyant dosage form should have a density of less than that of the gastric fluids floats. Since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period.[19]

Size: Dosage form units having a diameter of more than 7.5 mm are reported to have an increased gastric residence time compared with those having a diameter of 9.9 mm. Gastric retention time of an dosage form in the fed state can also be influenced by its size. Small tablets are emptied from the stomach during the digestive phase while large size units are expelled during the house keeping waves.[20]

Table: Effect of tablet size on Gastric Emptying time

Tablet size	Gastric emptying time
13 mm	171 ± 13 min
11 mm	128 ± 17 min
7 mm	116 ± 19 min

Shape anddosage form: The six shapes tested (ring, tetrahedron, clover leaf, disk, string, and pellet) displayed different gastric retention times, due to their size and geometry of the systems. The tetrahedron resided in the stomach for longer periods than other devices of a smaller size; likewise extended gastric retention was observed with rigid rings. Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) have a better gastric residence time as compared with other shapes and had been reported to have better GRT 90% -100% retention at 24 hrs compared with other shapes.

Single or multiple unit formulation:
Multiple unit formulation shoe a more predictable release profile and insignificant impairing of performance due o 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.

Effect of buoyancy: On comparison of floating and non floating dosage units , it was concluded that regardless of their sizes the floating dosage units remained buoyant on the gastric contents throughout their residence in the GIT , while the non floating dosage units sank and remained in the lower part of the stomach. Floating units away from the gastro-duodenal junction were protected from the peristaltic waves during digestive phase while the non floating forms stayed close to the pylorus and were subjected to propelling and retropelling waves of the digestive phase.

Materials
Paliperidone-Procured From Orchid Pharmaceuticals, Chennai, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Tamarind Gum-Arvind Remedies Ltd, Tamil nadu, India, Carnuba wax-Arvind Remedies Ltd, Tamil nadu, India, HPMC K15 M -Arvind Remedies Ltd, Tamil nadu, India, Sodium Bicarbonate-Merck Specialities Pvt Ltd, Mumbai, India, Citric acid-Merck Specialities Pvt Ltd, Mumbai, India, Magnesium Stearate- Kerry laboratories, Talc-Kerry laboratories, MCC-S. D. Fine Chem. Labs. (Mumbai, India).

II. METHODOLOGY

Analytical method development:
a) Determination of absorption maxima:
A solution containing the concentration 10µg/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 200-400nm.

a) Preparation calibration curve:

10mg Paliperidone pure drug was dissolved in 10ml of methanol (stock solution 1) 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 10ml 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, 10 µg/ml of per ml of solution. The absorbance of the above dilutions was measured at 235 nm by using UV-Spetrophototmeter 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 the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all theses 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 place 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:

$$\tan \theta = h/r$$

Tan θ=Angle of repose

h= Height of the cone,

r= radius of the cone base

Table 9.1: 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/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 size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10gm powder blend was sieved and introduced into a dry 20ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apartment volume, Vo, was read.

The bulk density was calculated using the formula:
Bulk density= M/Vo
Where,
M= Weight of sample
Vo=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:
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 inter particulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater inter particle 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:
Carr's index = [(tap-b/tap] ×100
Where,B=Bulk density, Tap= Tapped density

Table 9.2: 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 of 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 15min.
3. The powder mixture was lubricated with talc.
4. The tablets were prepared by using direct compression method by using 6mm punch.

FORMUALTION OF TABLETS:

Table 9.3: Formulation composition for floating tablets

INGREDIENTS (MG)	FORMULATION CODE											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Paliperidone	3	3	3	3	3	3	3	3	3	3	3	3
Tamarind Gum	5	10	15	20	-	-	-	-	-	-	-	-
Carnuba wax	-	-	-	-	5	10	15	20	-	-	-	-
HPMC K15 M	-	-	-	-	-	-	-	-	5	10	15	20
Sodium Bicarbonate	10	10	10	10	10	10	10	10	10	10	10	10
Citric acid	8	8	8	8	8	8	8	8	8	8	8	8
Magnesium Stearate	4	4	4	4	4	4	4	4	4	4	4	4
Talc	5	5	5	5	5	5	5	5	5	5	5	5
MCC	65	60	55	50	65	60	55	50	65	60	55	50
Total weight (mg)	100	100	100	100	100	100	100	100	100	100	100	100

All the quantities were in mg

III. RESULTS AND DISCUSSION

Analytical method

A. calibration curve

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 235 nm. Graphs of Paliperidonewas taken in 0.1N HCL (pH 1.2)

Table 10.1: Observations for graph of Paliperidone in 0.1N HCL

Concentration (µg/ml)	Absorbance
0	0
2	0.156
4	0.315
6	0.451
8	0.589
10	0.733

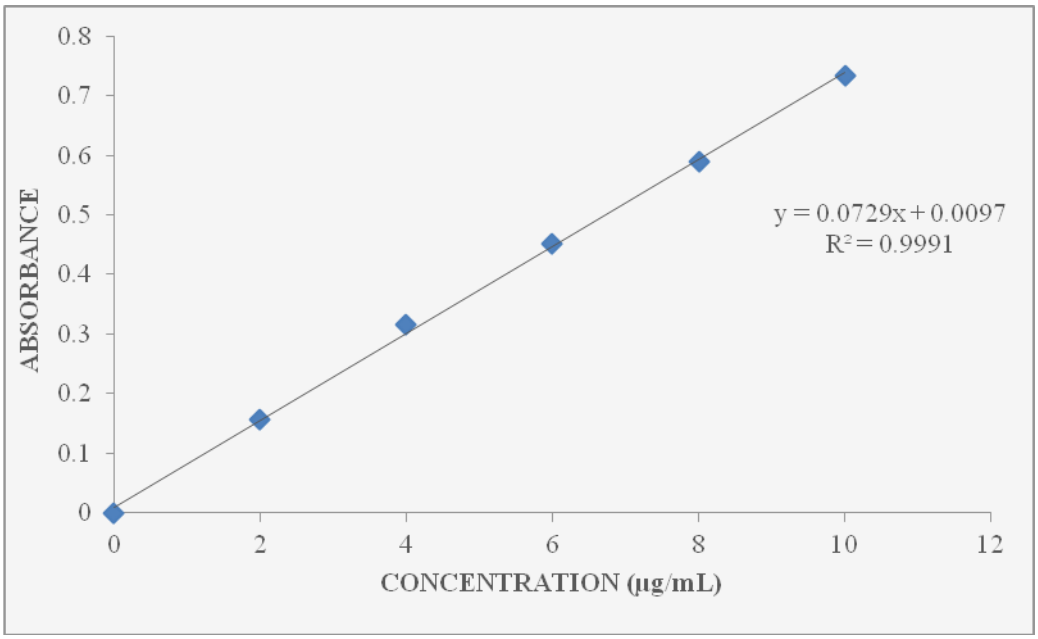

Figure 10.1: Standard graph of Paliperidone in 0.1N HCL

Standard graph of Paliperidone was plotted as per the procedure in experimental method and its linearity is shown in table 10.1 and fig 10.1. The standard graph of Paliperidone showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer-Lamberts" law.

Preformulation parameters of powder blend:

Table 10.2: 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	25.44±0.028	0.4174	0.5158	19.08	1.24
F2	22.66±0.055	0.4315	0.5349	19.33	1.24
F3	24.28±0.064	0.4291	0.5273	18.62	1.23
F4	22.38±0.042	0.4199	0.5194	19.16	1.24
F5	25.30±0.062	0.4394	0.5428	19.05	1.24
F6	21.73±0.040	0.4225	0.5203	18.80	1.23
F7	25.49±0.010	0.4172	0.5164	19.21	1.24
F8	23.93±0.069	0.4275	0.5274	18.94	1.23
F9	22.74±0.026	0.4247	0.5135	17.29	1.21
F10	26.37±0.021	0.4136	0.5164	19.91	1.25
F11	23.52±0.013	0.4156	0.5126	18.92	1.23
F12	21.59±0.012	0.4244	0.5345	20.60	1.26

Tablet powder blend was subjected to various preformulation 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 0.4136 to 0.4394 (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 0.5126 to 0.5428 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 17.29 which show that the powder has good flow properties. All the formulations has shown the Hausners ratio ranging between 1.21 to 1.26 indicating the powder has good flow properties.

8.5. Quality control parameters for tablets:

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

Table 10.3: *In vitro* quality control parameters

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating Lag time (Seconds)	Total floating time (Hours)
F1	98.54	4.8	0.72	3.15	96.41	63	10
F2	99.15	4.1	0.43	3.58	99.73	53	11
F3	96.68	4.5	0.31	3.60	98.59	41	11
F4	97.10	5.3	0.29	3.19	97.13	38	12
F5	99.81	4.9	0.81	3.72	99.14	21	12
F6	97.34	5.1	0.70	3.98	96.87	30	11
F7	98.46	4.7	0.62	3.46	98.15	47	12
F8	99.51	5.0	0.59	3.81	97.50	53	12
F9	97.11	4.3	0.67	3.66	98.07	51	12
F10	99.28	4.8	0.50	3.53	98.10	62	12
F11	96.35	5.1	0.46	3.26	99.01	43	12
F12	98.49	5.3	0.35	3.49	97.76	32	12

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

Figure 10.2: Floating Lag time (Seconds)

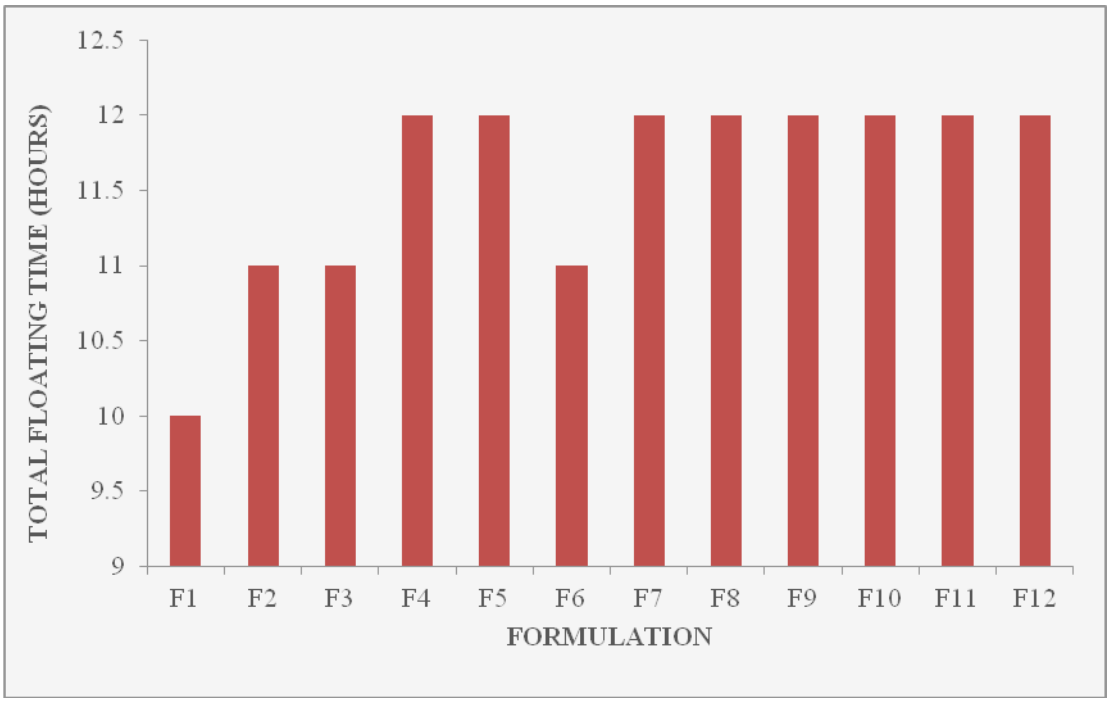

Figure 10.3: Total floating time (Hours)

8.6. *In vitro* drug release studies

Table 10.4: Dissolution data of Paliperidone tablets prepared with Tamarind Gum in different ratios

TIME (H)	F1	F2	F3	F4
0	0	0	0	0
0.5	25.82	20.36	16.01	10.21
1	41.10	28.93	21.25	16.12
2	53.69	32.02	28.43	23.10
3	62.75	40.51	36.15	28.39
4	70.02	47.75	42.28	36.42
5	76.19	53.68	58.90	42.58
6	87.64	58.92	65.76	50.64
7	96.52	71.11	70.82	56.17
8		90.27	78.58	61.53
9		98.03	82.14	66.29
10			86.70	80.17
11			98.19	86.21
12				93.34

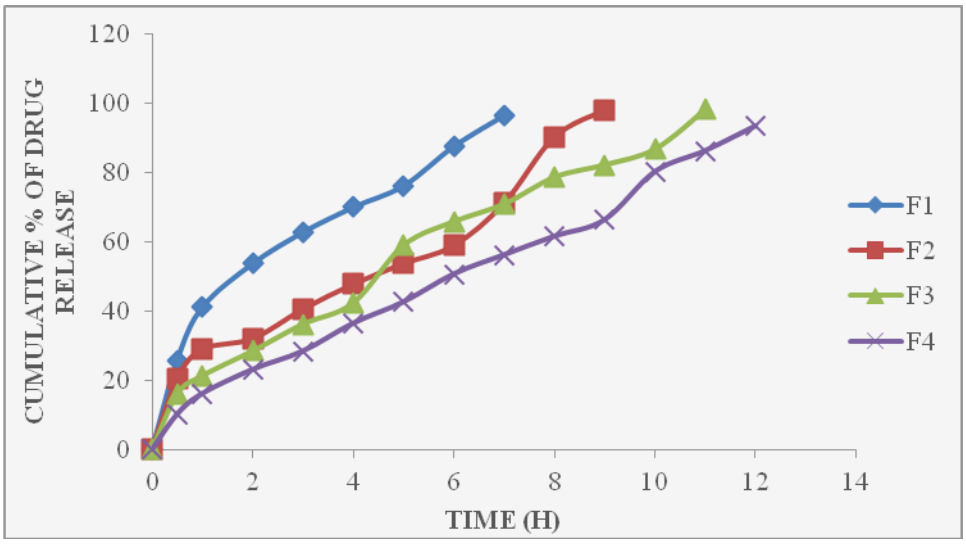

Fig 10.4: Dissolution data of Paliperidone floating tablets containing Tamarind Gum

Table 10.5: Dissolution data of Paliperidone tablets prepared with Carnuba wax in different concentrations

TIME (H)	F5	F6	F7	F8
0	0	0	0	0
0.5	11.32	8.92	06.59	05.75
1	18.83	12.85	10.21	11.92
2	26.92	16.19	19.01	18.56
3	30.71	23.60	26.37	26.55
4	36.42	28.91	34.26	32.09
5	41.96	33.23	39.17	38.27
6	48.38	40.75	43.25	45.86
7	55.72	46.12	48.13	50.17
8	60.65	57.87	53.24	56.29
9	69.56	62.15	58.11	61.93
10	75.90	70.83	67.05	67.82
11	91.76	76.53	72.96	72.14
12	99.13	89.91	86.12	78.56

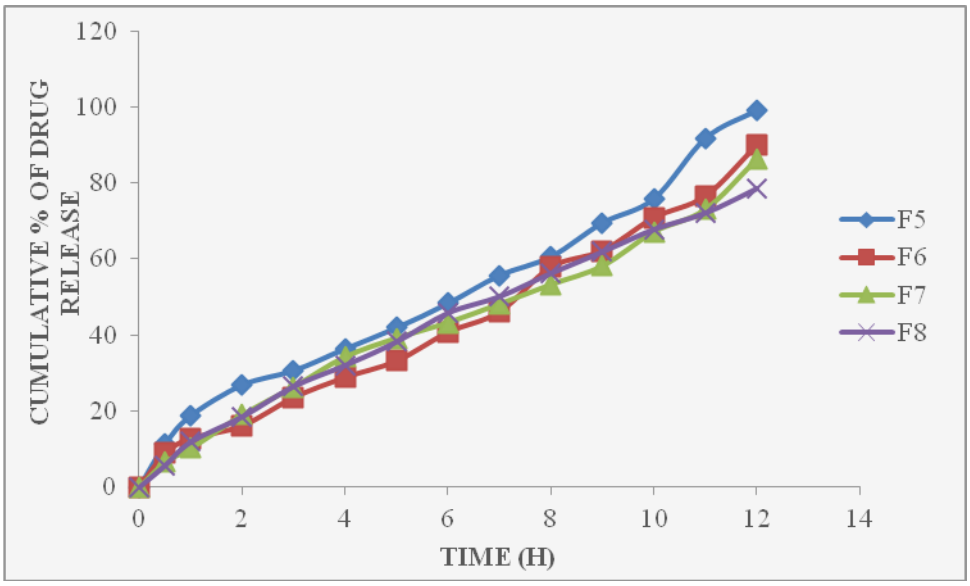

Fig 10.5: Dissolution data of Paliperidone floating tablets containing Carnuba wax

Table 10.6: Dissolution data of Paliperidone by using HPMC K15 M

TIME (H)	F9	F10	F11	F12
0	0	0	0	0
0.5	15.57	10.92	07.49	05.16
1	21.81	16.58	12.05	10.92
2	28.29	20.76	18.36	15.60
3	34.39	26.15	24.11	20.27
4	40.12	31.28	28.89	27.10
5	46.58	37.64	35.56	33.56
6	49.66	43.58	40.11	38.47
7	53.73	46.14	45.78	42.58
8	57.91	51.29	53.19	46.83
9	62.52	57.36	57.27	52.19
10	77.63	64.12	66.93	57.98
11	86.72	70.87	75.12	64.17
12	95.37	90.15	86.06	75.99

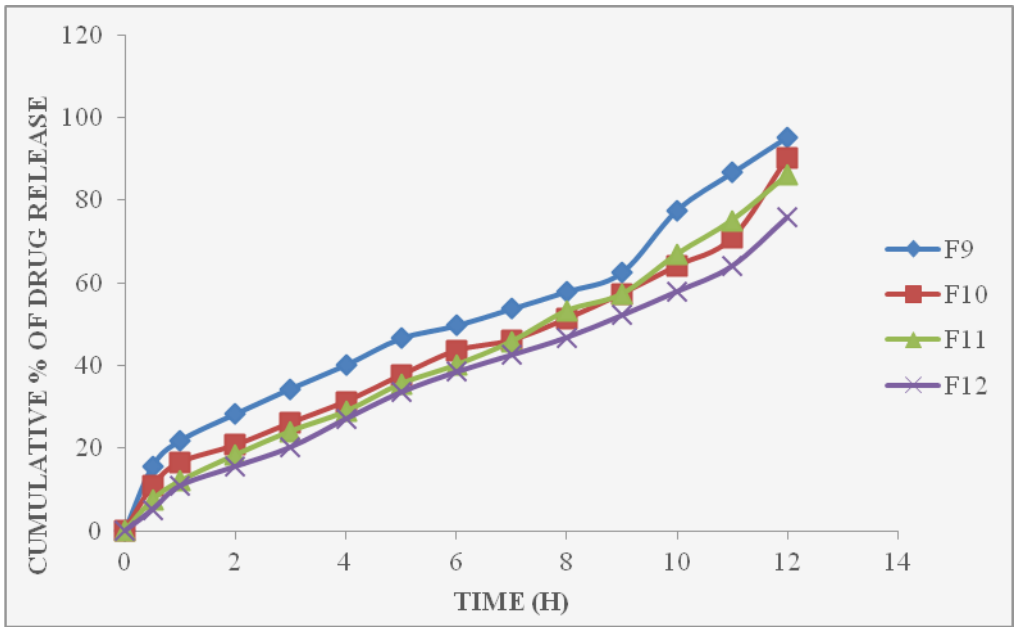

Fig 10.6: Dissolution data of Paliperidone floating tablets containing HPMC K15M

From the dissolution data it was evident that the formulations prepared with Tamarind Gum polymer were retarded the drug release more than 12 hours.

Whereas the formulations prepared with low concentration of Carnuba wax retarded the drug release up to 12 hours. In higher concentrations the polymer was unable to retard the drug release.

Whereas the formulations prepared with low concentration of HPMC K15 M retarded the drug release up to 12 hours. In higher concentrations the polymer was unable to retard the drug release.

Hence from the above dissolution data it was concluded that F5 formulation was considered as optimised formulation because good drug release (99.13 %) in 12 hours.

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

Table 10.7: 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
11.32	0.5	0.707	1.054	-0.301	1.948	22.640	0.0883	-0.946	88.68	4.642	4.459	0.182
18.83	1	1.000	1.275	0.000	1.909	18.830	0.0531	-0.725	81.17	4.642	4.330	0.312
26.92	2	1.414	1.430	0.301	1.864	13.460	0.0371	-0.570	73.08	4.642	4.181	0.461
30.71	3	1.732	1.487	0.477	1.841	10.237	0.0326	-0.513	69.29	4.642	4.107	0.534
36.42	4	2.000	1.561	0.602	1.803	9.105	0.0275	-0.439	63.58	4.642	3.991	0.650
41.96	5	2.236	1.623	0.699	1.764	8.392	0.0238	-0.377	58.04	4.642	3.872	0.770
48.38	6	2.449	1.685	0.778	1.713	8.063	0.0207	-0.315	51.62	4.642	3.723	0.918
55.72	7	2.646	1.746	0.845	1.646	7.960	0.0179	-0.254	44.28	4.642	3.538	1.104
60.65	8	2.828	1.783	0.903	1.595	7.581	0.0165	-0.217	39.35	4.642	3.401	1.240
69.56	9	3.000	1.842	0.954	1.483	7.729	0.0144	-0.158	30.44	4.642	3.122	1.519
75.9	10	3.162	1.880	1.000	1.382	7.590	0.0132	-0.120	24.1	4.642	2.888	1.753
91.76	11	3.317	1.963	1.041	0.916	8.342	0.0109	-0.037	8.24	4.642	2.020	2.622
99.13	12	3.464	1.996	1.079	-0.060	8.261	0.0101	-0.004	0.87	4.642	0.955	3.687

Optimized formulation F5 was kept for release kinetics studies. From the above graphs it was evident that the formulation F5

was followed Zero order release kinetics.

Drug – Excipient compatibility studies
Fourier Transform – Infrared Spectroscopy

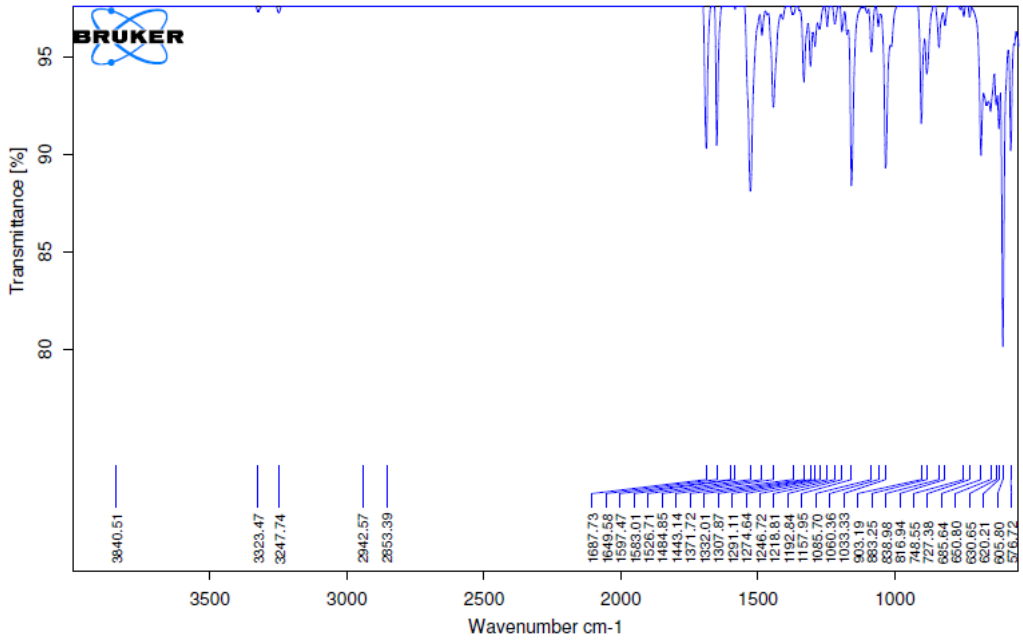

Fig 10.11 :FTIR Spectrum of pure drug

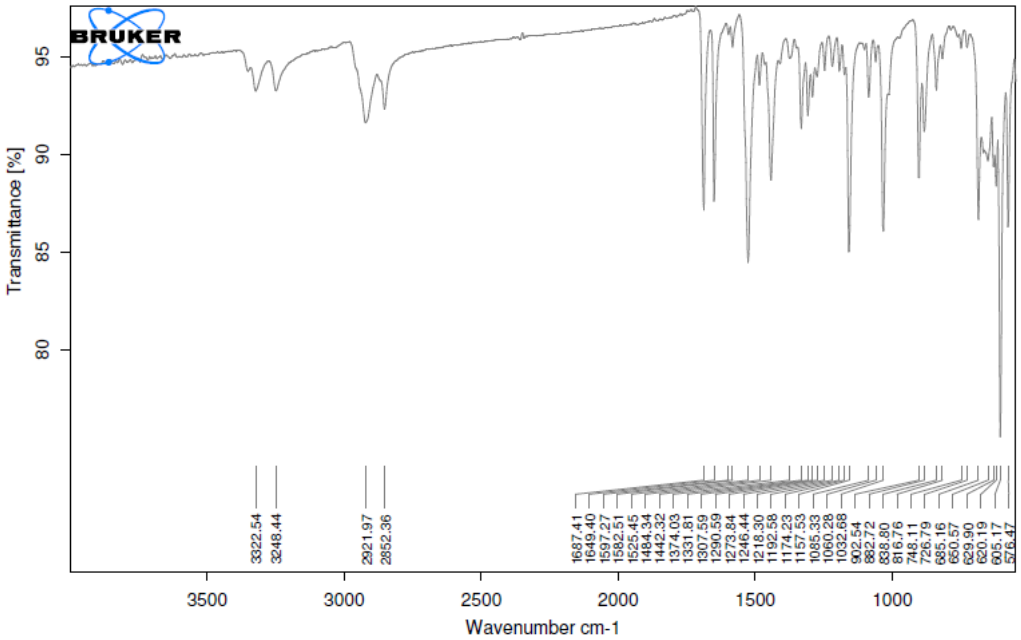

Fig 10.12: FTIR Spectrum of optimized formulation

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.

Paliperidone is 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

In this study, the floating tablets of Paliperidone were prepared by direct compression technique using natural and synthetic polymer containing Tamarind Gum, Carnuba wax and HPMC K15 M. Sodium bicarbonate and Citric acid were used as gas generating agent. Microcrystalline cellulose was used as diluents. Talc and magnesium stearate were used as glidant and lubricant respectively. FTIR spectroscopic studies indicated that the drug is compatible with all the excipients. In the present work, it has been observed from all formulations of precompression and post-compression studies were given within the limit

of values. All the batches showed floating time more than 12 hours which is quite significant for a floating tablet. It is also observed that formulation F5 containing low polymers and gas generating agent shows better controlled release behavior. F5 formulation was considered as optimized with 99.13 % drug release. Hence it can be concluded that the developed formulations F5 formulation is best formulation, it is considered as optimised formulation. From the above graphs it was evident that the formulation F5 was followed Zero order release kinetics.The concept of formulating floating tablets of Paliperidone offers a suitable and practical approach in serving desired objectives of gastro retentive floating tablets.

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