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FORMULATION AND EVALUATION OF GASTRO-RETENTIVE FLOATING TABLETS OF ATENOLOL

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ABSTRACT

The purpose of the present study was to develop gastro-retentive floating tablet of Atenolol. It is a beta-adrenoreceptor antagonist (beta-blocker) used in the treatment of hypertension and angina pectoris. It is incompletely absorbed from the gastrointestinal tract and has an oral bioavailability of only 50% while remaining drug is excreted unchanged in feces. This is because of poor absorption in lower gastrointestinal tract. Therefore, the formulation of Atenolol as a gastro-retentive floating drug delivery system (GFDDS) was thought to be beneficial, with a view to improve its oral bioavailability and therapeutic efficacy. The floating tablets of Atenolol (F1-F9) were prepared by direct compression technique using HPMC of different viscosity grades (K4M and K15M) as the polymers and sodium bicarbonate and citric acid as a gas generating agent, to reduce floating lag time. The blends were evaluated to bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose. The tablets were evaluated to thickness, hardness, diameter, weight variation, and drug content uniformity, friability, floating lag time, effect of hardness on buoyancy lag time and *in-vitro* swelling studies, *in-vitro* drug release studies. *In-vitro* drug release study was performed using USP dissolution test apparatus-II at 50 rpm using 900 ml of hydrochloric acid buffer pH 1.2 maintained at 37±0.5ºC as the dissolution medium. Among the various floating tablet formulations studied, formulation F6 containing drug polymer ratio (1:3) prepared with HPMC K4M & K15M showed promising results releasing 92.63% of the drug in 12 hours with a floating lag time of 30 seconds and floating time of more than 24 hours has been considered as an ideal formulation. FTIR studies indicate that there is no interaction between drug and excipients. Stability study of F6 formulation was performed and that showed no major change in physicochemical parameters, floating properties and drug release profile.

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INTRODUCTION

Oral delivery is the preferred route for drug administration because it is more natural and less invasive than other traditional routes, such as intravenous and intramuscular injection. To achieve maximum bio-availability various techniques are designed in which gastro retentive dosage forms is one among them. The system may be floating; swelling; inflation; adhesion; high-density systems and low density systems that increase the gastric residence time [1].

Floating drug delivery systems (FDDS) were first described by Davis in 1968. These systems were used to prolong the gastric residence time (GRT) of drug delivery systems. They remain buoyant in the stomach for prolonged period of time without affecting the gastric emptying rate of other contents. FDDS is suitable for drugs with an absorption window in the stomach or the upper small intestine, for drugs which act locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid [2, 3].

Atenolol is β-1 cardio selective adrenergic receptor blocker, widely used in the treatment of hypertension and angina pectoris. The drug is insoluble in water and has half-life of six to seven hours with oral bioavailability of 50% [4, 5]. Its molecular formula is $C_{14}H_{22}N_2O_3$. It is a white powder with a molecular weight of 266.34. It is sparingly soluble in water, insoluble in ether and chloroform. It is incompletely absorbed orally, but first pass metabolism is not significant. Because of longer duration of action once daily dose is often sufficient. Side effects related to CNS action are less likely. No deleterious effects on lipid profile have been noted. Effective dose for most individuals falls in a narrow range. It is one of the most commonly used β blockers for hypertension and angina [6].

The purpose of the present study is to develop a gastro-retentive floating tablets for the atenolol drug which would remain in stomach and/or upper part of gastrointestinal tract (GIT) for prolonged period of time with a view to improve bioavailability of the drug as well as its half-life and to control the rate of release of the drug in physiological environment of stomach.

MATERIALS AND METHODS

Materials

The drug Atenolol is provided by as gift sample from IPCA Laboratories Ltd., Vadodara and Hydroxypropylmethyl cellulose (HPMC) of two different viscosity grades (HPMC K4M, HPMC K15M) was gifted samples from Polo pharmaceuticals Ltd Baddi. All other ingredients used were of pharmaceutical grade.

Formulation of floating tablets of atenolol

The floating tablets of Atenolol were prepared by direct compression technique [7]. All the ingredients (Table- 1) used in the formulation were initially passed through sieve 40 separately before mixing. The required quantity of Atenolol and other ingredients except talc and magnesium stearate were weighed out accurately and transferred to a mortar and triturated for thorough mixing. To the above mixture, talc and magnesium stearate was added and further mixed for 2 minutes. Finally the mixture was compressed into tablets of 250 mg each.

Table No. 1: Composition of floating tablets of Atenolol.

Formulation Code	Atenolol (mg)	HPMC K4M (mg)	HPMC K15M (mg)	NaHCO3 (mg)	Citric Acid (mg)	MCC (mg)	Magnesium Stearate (mg)	Talc (mg)
F1	25	25	25	20	10	137.5	2.5	5
F2	25	25	35	20	10	127.5	2.5	5
F3	25	25	45	20	10	117.5	2.5	5
F4	25	35	25	20	10	127.5	2.5	5
F5	25	35	35	20	10	117.5	2.5	5
F6	25	35	45	20	10	107.5	2.5	5
F7	25	45	25	20	10	117.5	2.5	5
F8	25	45	35	20	10	107.5	2.5	5
F9	25	45	45	20	10	97.5	2.5	5

Evaluation of powder

Angle of Repose [8]

Funnel method was used to measure the angle of repose of powder. The accurately weighed powders were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder (2.0 cm above hard surface). The powders were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\mathbf{Tan\theta = h/r} \text{---------- (1)}$$

Therefore, $\theta = Tan^{-1}h/r$

Where, θ = angle of repose,

h= height of the cone, r = radius of the cone base

The results are shown in Table 2.

Bulk Density (Db) [9]

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve no. 20) into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in gm/ml and is given by

$$Db = M/ Vb$$

Where,
M and Vb are mass of powder and bulk volume of the powder respectively. The results are shown in Table 2.

Tapped Density (Dt) [9]

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in gm/ml and is given by

$$Dt = M/ Vt$$

Where, M and Vt are mass of powder and tapped volume of the powder respectively. The results are shown in Table 2.

Compressibility Index [10]

The compressibility index of the power was determined by Carr's compressibility index:

$$\text{Carr's index (\%)} = \{(Dt - Db) \text{ X } 100\}/Dt$$

The results are shown in Table 2.

Hausner's ratio [10]

Hausner's Ratio is an ease of index of powder flow. It is calculated by using the following formula:

$$\text{Hausner's Ratio} = \text{Tapped Density}/ \text{Bulk Density}$$

The results are shown in Table 2.

Evaluation of tablets

Weight variation test [11]

The USP weight variation test is run by weighing 20 tablets individually, calculating the average weight & comparing the individuals tablet weight to the average. The tablets meets the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit. The results are shown in Table 3.

Thickness and Diameter [12]

The thickness and diameter of the tablets were determined using a thickness gauge. Five tablets from each batch were used, and average values were calculated. The results are shown in Table 3.

Hardness [13]

Three tablets of each of the formulations were measured in the hardness test. The hardness was examined using a Monsanto hardness tester. The hardness was measured in kg/cm^2. The results are shown in Table 3.

Friability [14]

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.

$$\% \text{ loss} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100$$

The results are shown in Table 3.

Drug content uniformity [15]

Content uniformity test was carried out as per USP 2009. In this test 30 tablets were randomly selected for the sample and at least 10 of them were assayed individually. Nine of the tablets must contain not less than 85% or more than 115% of the labelled drug content. The tenth tablet may contain less than 75% or more than 125% of the labeled content. If this condition is not meet, the tablets remaining from the 30 must be assayed individually and none may fall outside of the 85% to 115%. The results are shown in **Table 3**.

Floating lag time and duration of floating [11]

Floating characteristics of the prepared formulations were determined by using USP-II paddle apparatus under sink conditions. 900ml of hydrochloric acid buffer pH 1.2 was used as medium and the temperature was maintained to 37±0.5°C thought the study. The time between the introduction of tablet and its buoyancy on the gastric fluid required for the tablet to float on the gastric fluid (floating lag time) and the time during which dosages forms remain buoyant (duration of floating) were measured. The integrity of the test tablets was observed visually during study. The floating lag time and duration of floating of various formulations are shown in Table 4 & Fig.1.

Effect of Hardness on Buoyancy Lag Time [16]

Formulation F-6 was selected to study the effect of hardness on buoyancy lag time. The tablets of batch 6 were compressed at different compression pressures to get the hardness of 5kg/cm^2, 6kg/cm^2, 7kg/cm^2, 8kg/cm^2 and 9kg/cm^2. The tablets were evaluated for buoyancy lag time. The method was same as mentioned in determination of lag time. The results are shown in Table 5 & Fig.2.

***In-vitro* swelling study** [17]

The swelling of polymers used were determined by water uptake. It was observed that the swelling indices were increased with increases in polymer concentration. Usually swelling is essential to ensure floating. For floating tablet, there should be appropriate balance between swelling and water uptake. Tablets were weighed individually and placed separately in basket of dissolution medium containing hydrochloric acid buffer (pH 1.2) solutions 900 ml at 37±0.5°C. At regular intervals 1, 2, 3, 4, 5, 6, 7 and 8 hours, the tablets were withdrawn from the basket and blotted with tissue paper to removed excess surface water and the swollen tablets were reweighed on analytical balance.

Swelling index (SI) of tablets was calculated using the following formula:

$$\% \text{ Swelling Index} = \frac{(\text{Wet weight} - \text{Dry weight})}{\text{Dry weight}} \times 100$$

The results are shown in Table 6 & Fig.3.

***In-vitro* drug release study**

In-vitro dissolution studies were carried out in USP type-II tablet dissolution apparatus using 900 ml hydrochloric acid buffer pH 1.2 as dissolution media. The paddle was rotated at 50 rpm and the temperature was maintained at 37±0.5°C throughout the study. At predetermined time intervals 5 ml of the samples were withdrawn. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5°C. The samples were analyzed for drug releases by measuring the absorbance at 224.8 nm using UV-Visible spectrophotometer.

Analysis of *in-vitro* drug release

The results of *in-vitro* release data were fitted in to following mathematical models for describing the drug release pattern:

Zero order kinetics [18]

Zero order release would be predicted by the following equation:

$$A_t = A_O - K_O t$$

Where,

A_t = Drug release at time t,

A_O = Initial drug concentration,

K_O = Zero-order rate constant (hr^{-1}).

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K_O.

First order kinetics [19]

First order release would be predicted by the following equation:

$$\text{Log } C = \log C_O - K_t/2.303$$

Where,

C = Amount of drug remained at time t,

C_O = Initial amount of drug,

K = First order rate constant (hr^{-1}).

When the data is plotted as log cumulative percent drug remaining versus time yields a straight line, indicates that the release follows First-order kinetics. The constant 'K' can be obtained by multiplying 2.303 with slope values.

Higuchi's Model [20]

Drug released from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation:

$$F_t = Q = A \sqrt{D\,(2C - Cs)\,Cs\,t}$$

Where,
Q = Amount of drug released at time t
D = Diffusion coefficient of the drug in the matrix
A = Total amount of drug in unit volume of matrix
Cs= the solubility of the drug in the diffusion medium
ε = Porosity of the matrix
τ = Tortuosity
t = Time (hrs) at which 'Q' amount of drug is released.
This equation may be simplified if one assumes that D, CS and A are constant. Then equation becomes:

$$Q = K\,(t)^{1/2}$$

When the data is plotted according to above equation i.e., cumulative drug released versus square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to 'K'.

Korsmeyer and Peppas Model [21]

The release rates from controlled release polymeric matrices can be described by the equation proposed by Korsmeyer *et al*.

$$Q = K_1 t^{n}$$

Where,
Q = Percentage of drug released at time t
K = Kinetic constant incorporating structural and geometric characteristics of the tablets
n = Diffusional exponent indicative of the release mechanism.

For Fickian release, n≤0.45 while for anomalous (Non-Fickian) transport, n ranges between 0.45 and 0.89 and for zero order release (caseII transport), n = 0.89 and when n= 0.89, it signifies super case II transport.

Fourier Transforms Infra-Red (FTIR) Spectroscopy

IR spectra of drug in KBr pellets at moderate scanning speed between 4000 to 400 cm-1 was carried out using FTIR. The peak values (wave number) and the possibility of functional group shown in spectra which compare with standard value. The comparison of these results with Atenolol chemical structure shows that sample was pure Atenolol. FTIR study was carried out to check compatibility of drug with polymers.

Stability studies of the most satisfactory formulation [22]

The stability studies were carried out of the most satisfactory formulation as per ICH guidelines. The most satisfactory formulation sealed in aluminium packaging and kept in humidity chamber maintained at 30 ± 2 ^{o}C / 65 ± 5 % RH and 40 ± 2 ^{o}C / 75 ± 5 % RH for two months. At the end of studies, samples were analyzed for the drug content, *in vitro* dissolution, floating behavior and other physicochemical parameters. The results are shown in Table No.10 & 11.

RESULTS:

In present investigation, attempt has been made to formulate gastro-retentive floating tablets of atenolol. Based on Preformulation studies different batches of floating tablets of atenolol were prepared using selected excipients. Powders were evaluated for tests Bulk density, tapped density, compressibility index, Hausner's ratio before being punched as tablets.
The all over result of these studies is shown in following tables:

Table No.2: Micromeritic study of powder mixture of various formulations.

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angle of Repose(°)	25.74	38.69	24.45	33.69	38.96	37.62	39.69	34.51	34.46
Bulk Density (gm/ml)	0.34	0.36	0.38	0.35	0.36	0.34	0.36	0.35	0.36
Tapped Density (gm/ml)	0.41	0.44	0.48	0.44	0.44	0.41	0.44	0.44	0.44
Hausner's Ratio	1.20	1.22	1.26	1.25	1.22	1.20	1.22	1.25	1.22
Carr's Index (%)	17.30	18.18	20.83	20.45	18.18	17.07	18.18	20.45	18.18

Table No.3: Post compression parameters for formulations F1-F9.

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	3.45± 0.2	3.50± 0.2	3.66± 0.20	3.54± 0.30	3.49± 0.20	3.75± 0.20	3.54± 0.20	3.68± 0.30	3.75± 0.20
Diameter (mm)	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2	8.80± 0.2
Hardness(Kg/cm2)	4.80	4.30	5.10	5.20	4.70	4.60	4.60	4.50	5.00
Friability (%)	0.704	0.672	0.558	0.532	0.661	0.672	0.520	0.700	0.807
Weight Variation (mg)	252± 0.09	250± 0.10	251± 0.26	250± 0.05	250± 0.19	252± 0.14	251± 0.16	253± 0.24	252± 0.12
Content Uniformity (%)	99.33	99.83	99.67	99.75	98.70	99.23	99.65	98.91	98.00

Table No.4: Floating lag time and Duration of floating of various formulations.

Formulation Code	Floating lag time (sec)	Duration of floating (hours)
F1	45	>24
F2	30	>24
F3	25	>24
F4	25	>24
F5	30	>24
F6	30	>24
F7	25	>24
F8	25	>24
F9	30	>24

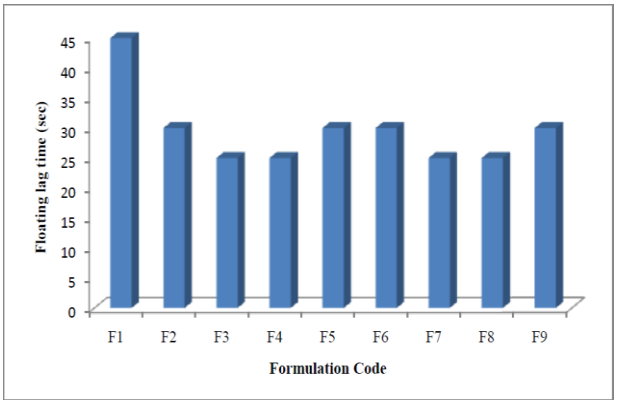

Fig.1: Floating lag time of various formulations.

Table No. 5: Effect of hardness on buoyancy lag time.

Hardness (Kg/m^2)	Buoyancy lag time (seconds)
4	20
5	25
6	30
7	60
8	120

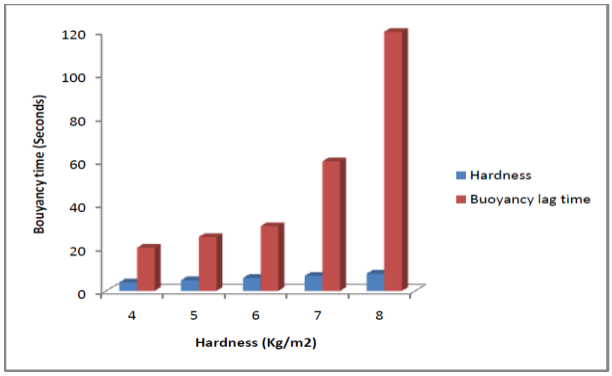

Fig.2: Effects of hardness on buoyancy lag time.

Table No. 6: *In-vitro* swelling study of various formulations.

Time (hour)	Swelling index (% weight gain)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	38.34	83.30	77.89	35.65	45.86	69.65	69.65	57.28	55.82
2	59.77	108.12	97.34	46.63	57.05	79.01	79.01	76.46	91.58
3	66.13	130.87	116.99	55.27	66.12	87.57	87.57	84.58	107.04
4	81.56	136.69	129.23	56.98	66.53	88.57	88.57	101.91	124.14
5	90.20	156.41	151.18	57.06	67.11	103.42	103.42	103.30	128.18
6	95.72	167.01	152.53	58.17	70.98	111.66	111.66	103.90	130.34
7	97.72	169.72	154.27	59.41	71.19	113.93	115.85	104.30	136.28
8	98.12	170.11	155.76	62.75	99.55	115.85	116.67	133.70	137.04

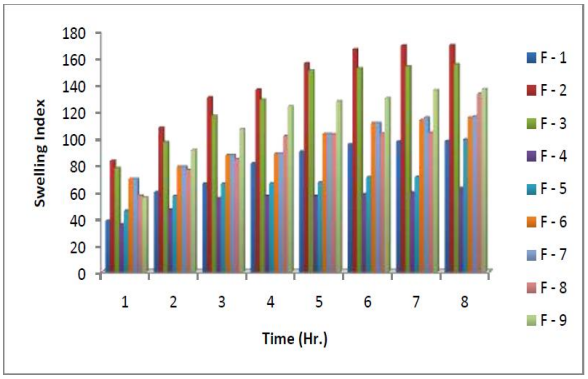

Fig.3: Comparative study of swelling index of various formulations.

Table No.7: *In-vitro* drug release profiles of various formulations: (Zero order and Higuchi model).

Time	√Time	Aten25	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0	0
1	1	62.81	18.98	15.14	17.19	15.31	16.54	18.32	12.11	19.93	18.53
2	1.41	99.17	23.29	20.35	24.51	20.27	22.83	23.74	19.39	26.09	26.62
3	1.732		28.83	26.64	31.32	26.49	28.52	28.46	28.37	33.74	32.28
4	2		33.90	32.95	38.09	30.90	34.12	32.32	36.32	40.49	40.89
5	2.236		38.33	38.29	43.61	38.22	38.58	46.98	43.33	47.53	47.10
6	2.4495		42.44	45.62	54.45	45.25	46.77	55.20	55.14	54.82	55.00
7	2.6457		54.96	59.77	65.35	54.05	55.42	59.84	62.48	63.81	63.81
8	2.8284		65.70	73.91	76.58	65.12	66.18	67.45	70.18	76.16	70.00
9	3		69.85	78.23	80.11	75.94	74.35	76.12	79.10	81.83	76.19
10	3.1622		82.89	83.06	82.53	79.81	80.00	82.99	82.44	85.70	85.63
11	3.3166		87.38	86.12	87.51	84.67	84.99	86.73	84.97	87.55	86.79
12	3.4641		88.60	87.84	91.01	86.72	91.76	92.63	86.98	89.45	89.52

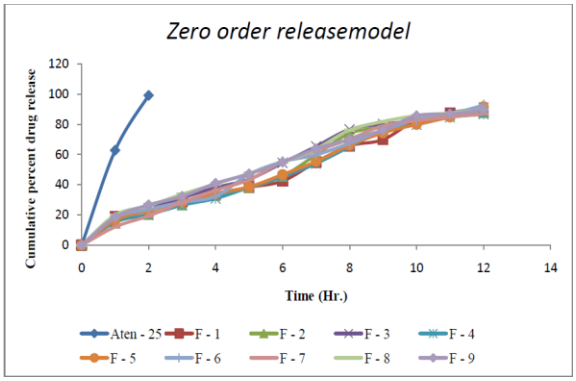

Fig.4: *In-vitro* drug release profile of prepared formulations and marketed product.

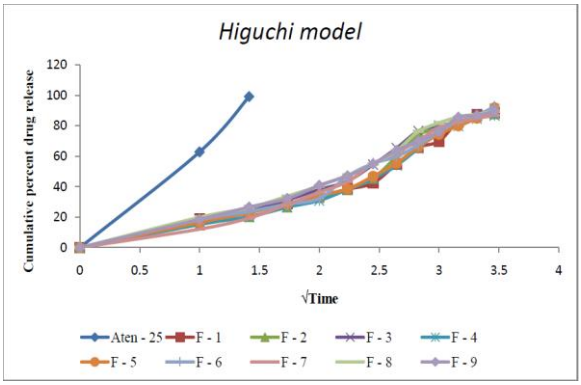

Fig.5: *In-vitro* drug release profile of prepared formulations and marketed product.

Table No. 8. *In-vitro* drug release profiles of various formulations (First order release model):

Time(Hr.)	Aten 25	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	1.397	1.397	1.397	1.397	1.397	1.397	1.397	1.397	1.397	1.397
1	0.968	1.306	1.326	1.315	1.325	1.319	1.310	1.341	1.301	1.308
2	0.686	1.282	1.299	1.275	1.299	1.285	1.280	1.304	1.266	1.263
3		1.250	1.263	1.234	1.264	1.252	1.252	1.252	1.219	1.228
4		1.218	1.224	1.189	1.237	1.216	1.228	1.201	1.172	1.169
5		1.187	1.188	1.149	1.188	1.186	1.122	1.151	1.117	1.121
6		1.158	1.133	1.056	1.136	1.124	1.049	1.049	1.052	1.051
7		1.051	1.002	0.937	1.060	1.047	1.001	0.972	0.956	0.956
8		0.933	0.814	0.767	0.940	0.927	0.910	0.872	0.775	0.875
9		0.877	0.735	0.696	0.779	0.806	0.775	0.718	0.657	0.774
10		0.631	0.626	0.640	0.702	0.698	0.628	0.642	0.553	0.555
11		0.498	0.540	0.494	0.583	0.574	0.520	0.574	0.493	0.518
12		0.454	0.482	0.351	0.520	0.313	0.264	0.512	0.420	0.418

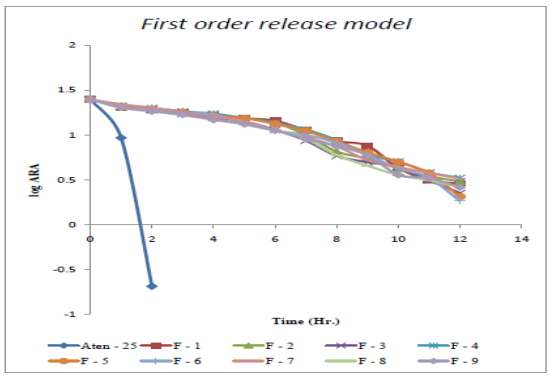

Fig.6: *In-vitro* drug release profile of prepared formulations and marketed product.

Table No. 9. Drug release kinetics of developed formulations.

Formulation Code	R2 value (average)					Mechanism of drug release
	Zero Order	First order	Higuchi	Korsmeyer-peppas		
				R^2	n	
F1	0.980	0.910	0.921	0.939	0.682	Non Fickian anomalous Transport
F2	0.977	0.950	0.923	0.965	0.791	Non Fickian anomalous Transport
F3	0.976	0.955	0.963	0.981	0.724	Non Fickian anomalous Transport
F4	0.986	0.943	0.926	0.966	0.769	Non Fickian anomalous Transport
F5	0.980	0.912	0.934	0.969	0.728	Non Fickian anomalous Transport
F6	0.987	0.929	0.948	0.962	0.713	Non Fickian anomalous Transport
F7	0.979	0.976	0.951	0.993	0.846	Non Fickian anomalous Transport
F8	0.971	0.966	0.963	0.979	0.667	Non Fickian anomalous Transport
F9	0.979	0.961	0.970	0.989	0.764	Non Fickian anomalous Transport

Table No. 10: Drug release profiles of the most satisfactory formulation during stability studies.

TIME (h)	AFTER 30 DAYS		AFTER 60 DAYS	
	A	B	C	D
	F6 (%)	**F6** (%)	**F6** (%)	**F6**(%)
1	19.04±2.19	18.46±1.46	20.12±2.04	18.87±1.61
2	24.12±2.46	23.89±1.76	24.96±2.36	24.13±2.93
3	29.13±2.37	28.74±2.37	30.52±1.21	29.46±1.79
4	33.13±2.22	33.92±2.98	33.87±1.81	34.85±4.45
5	47.22±2.98	48.12±1.37	48.02±3.59	48.89±2.44
6	55.98±1.54	56.43±3.00	56.16±2.20	57.62±2.47
7	60.22±1.10	58.86±0.18	60.97±1.93	59.26±1.92
8	68.55±2.79	66.82±4.78	69.23±3.12	67.32±1.64
9	77.45±1.64	75.85±1.62	78.92±3.45	76.02±2.53
10	83.47±1.66	82.53±1.30	84.22±1.72	83.98±2.56
11	87.92±3.14	89.09±3.11	88.08±3.20	90.34±1.49
12	93.28±0.04	93.54±1.50	93.88±1.73	94.13±0.23

A, C = 30 ± 2 ^{o}C / 65 ± 5 % RH
B, D = 40 ± 2 ^{o}C / 75 ± 5 % RH
All values are mean of 3 readings ± standard deviation

Table No.11: Physicochemical parameters of most satisfactory formulation during stability studies.

Time (Days)		Hardness (kg/cm^2)	Drug content (%)	Floating lag time (seconds)
		F6	F6	F6
0		4.60	99.23	30
30	At 30 ± 2^{o}C 65 ± 5 % RH	4.56 ± 0.33	98.05 ± 0.41	31.54 ± 2.07
	At 40 ± 2^{o}C 75 ± 5 % RH	4.42 ± 0.07	97.12 ± 1.08	31.21 ± 0.76
60	At 30 ± 2^{o}C 65 ± 5 % RH	4.39 ± 0.07	97.84 ± 0.39	31.69 ± 0.74
	At 40 ± 2^{o}C 75 ± 5 % RH	4.87 ± 0.21	98.08 ± 0.23	30.85 ± 0.72

All values are mean of 3 readings ± standard deviation.

CONCLUSION

In the present study, an attempt was made to design and optimize GFDDS of atenolol using HPMC of different viscosity grades (K4M and K15M) as the polymers and sodium bicarbonate as a gas generating agent, to reduce floating lag time. Atenolol is a beta-adrenoreceptor antagonist (beta-blocker) used in the treatment of hypertension and angina pectoris. It is incompletely absorbed from the gastrointestinal tract and has an oral bioavailability of only 50% while remaining drug is excreted unchanged in feces. This is because of poor absorption in lower gastrointestinal tract. So it is selected to prepare a gastro-retentive floating tablet. The objective of the present study is to formulate the GRDFs containing atenolol which would remain in stomach and/or upper part of GIT for prolonged period of time with a view to improve bioavailability of the drug as well as its half-life and to control the rate of release of the drug in physiological environment of stomach. The optimized formulation F6 can be considered as a promising gastro retentive drug delivery system of Atenolol, providing nearly zero order drug release over a period of 12 hours. Therefore, it was concluded that the most satisfactory formulation satisfied the physicochemical parameters, floating properties, drug content requirement, *in vitro* drug release profile requirements and stability requirements. Thus the objectives of the present work of formulating a floating dosage form for atenolol by using different proportions and grades of release rate controlling and gel forming polymers like HPMC has been achieved with success.

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