Research Article

Formulation Development and Evaluation of Gastroretentive Bilayer Floating Tablets of Simvastatin and Telmisartan

B. Prabakaran*, K. Elango, K. Ramesh Kumar, D Jaison

College of Pharmacy, Madras Medical College, Chennai – 03, India.

ABSTRACT

The objective of this present investigation is to design and evaluate the gastroretentive bilayer floating tablets of Simvastatin as controlled release and Telmisartan as immediate release. The combination therapy of Telmisartan and Simvastatin is useful in serious cardiovascular adverse effect such as hypertension, congestive heart failure and exacerbation of angina which may occur along with increasing cholesterol level in the blood, while the fixed dose combination remain the preferable choice to the patient as compared to the individual dosage form. Bi-layer tablet is suitable for sequential release of two drugs in combination, two incompatible substances and also for controlled release of drug. The bilayer tablets are prepared using different super disintegrants like Sodium Starch Glycolate, Cross Carmellose Sodium, Crospovidone for Telmisartan immediate release and xanthan gum, guar gum and HPMC K4M for Simvastatin controlled release. Sodium Bicarbonate is used as a gas generating agent. The precompression parameters like angle of repose, bulk density, tapped density; compressibility index and hausner's ratio were studied. The tablets were characterized by physical and chemical parameters such as tablet Uniformity of weight, thickness, hardness, diameter, friability, drug content, swelling index and In vitro drug release. The optimized formulation based on all the parameter T-3(Crospovidone) was selected for immediate release layer, S-5(Xanthan gum and HPMC K4M) for controlled release layer and bilayer tablets were prepared. The dissolution data was subjected to various release kinetic models to understand the mechanism of drug release.

Keywords: Gastroretentive floating tablets, bilayer tablets, simvastatin, telmisartan

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***Address for correspondence:**
B. Prabakaran,
College of Pharmacy, Madras Medical College, Chennai – 03, India.
E-mail: praba9966@gmail.com, elangopharm16@gmail.com

1. INTRODUCTION

Oral route is the most often route for administration of drug. Tablets are the most convenient oral dosage form and preferred by patient and physicians [1]. Bilayer tablet is suitable for sequential release of two drugs in combination in which one layer is sustained release and another layer is immediate release [2]. Floating drug delivery systems is one of the important approaches to achieve gastric retention to obtain sufficient drug bioavailability [3]. Hypertension and hypercholesterolemia frequently coexist and may require concomitant drug treatment [4].

Simvastatin is a member of lipid-lowering agent. It is a potent inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase which catalyzes the conversion of HMG-CoA to mevalonate, an early rate-determining step in cholesterol biosynthesis. Simvastatin has absorption window in upper G.I. tract and as a result display low bioavailability (5%). Therefore, gastro retentive drug delivery system might be advantageous for Simvastatin [5].

Telmisartan is used to treat hypertension by blocking the hormones angiotensin thereby relaxing blood vessels, causing them to wide. Telmisartan is an angiotensin receptor blocker (ARB), which show high affinity for the angiotensin II type 1 (AT1) receptors, has longer duration of action and has the longest half- life of any ARB (24 hours). The bioavailability of telmisartan is poor at about 45%, due to extensive first pass hepatic metabolism [6].

The combination therapy of simvastatin and telmisartan may be useful and effective in

some situations, particularly in serious cardiovascular adverse effects such as severe hypertension, congestive heart failure, and/or exacerbation of angina which may occur along with increasing the cholesterol level in the blood. The use of statin in combination with antihypertensive drugs may improve BP control in patients, with uncontrolled hypertension and high serum cholesterol level [4].

2. MATERIALS AND METHODS

2.1. Materials

Simvastatin (Medopharm Ltd); Telmisartan (Pharma French Ltd);Xanthan gum, Guar gum, HPMC K4M, Sodium starch glycolate, Croscarmellose sodium, Crospovidone, Lactose, PVP K30, Talc and Magnesium stearate (Kniss Laborataries); Sodium bicarbonate and Citric acid (Indian Research products) were of analytical grade.

2.2. Formulation of bilayer tablets

The formulation of bilayer tablets was carried out in two stages. The immediate release layer was prepared by wet granulation method using different super disintegrants (Sodium Starch Glycolate, Cross Carmellose sodium and Crosspovidone) [5] and the controlled release layer prepared by direct compression using xanthan gum, guar gum and HPMC K100M as the release retarding polymers and sodium bicarbonate was used as a gas generating agent [7,8]. The optimum concentration of above ingredients was determined under experimental conditions and on the basis of trial preparation of tablets. Bilayer tablets were prepared on rotary tablets compression machine [8,9]. First the controlled release layer was precompressed on compression machine manually and the immediate release layer was loaded on top of the precompressed layer and compressed with 9 mm punch on compression machine automatically. Composition of immediate release and controlled release layer are shown in (**Table 1 and Table 2**).

2.3. Evaluation of preformulation parameters [11-13]:

2.3.1. Fourier Transform infra-red spectroscopy (FT-IR)

The powdered samples of the tablets were mixed thoroughly with previously dried potassium bromide (IR grade) are compressed so as to form transparent pellets. The samples were scanned from 4000 to 400 cm^{-1} at ambient temperature.

Table 1: Formulation table for immediate release of Telmisartan tablets

S.No.	INGREDIENTS	T1	T2	T3
1	Telmisartan	40	40	40
2	Sodium starch glycolate	06	-	-
3	Croscarmellose sodium	-	04	-
4	Crospovidone	-	-	03
5	Lactose	43.5	45.5	46.5
6	PVP K30	03	03	03
7	Purified water	Q.S	Q.S	Q.S
8	Talc	5	5	5
9	Magnesium stearate	2.5	2.5	2.5

Average weight of each tablet = 100mg

Table 2: Formulation table for Simvastatin floating tablets

S.No	Ingredients	S-1	S-2	S-3	S-4	S-5	S-6	S-7	S-8	S-9
1	Simvastatin	20	20	20	20	20	20	20	20	20
2	Xanthan gum	120	80	40	60	70	-	-	-	-
3	Guar gum	-	-	-	-	-	40	80	120	150
4	HPMC K4M	40	40	40	40	40	40	40	40	40
5	Sodium Bicarbonate	50	50	50	50	50	50	50	50	50
6	Citric acid	10	10	10	10	10	10	10	10	10
7	Lactose	28.5	68.5	108.5	88.5	78.5	108.5	68.5	28.5	-
8	PVP K30	09	09	09	09	09	09	09	09	09
9	Talc	15	15	15	15	15	15	15	15	15
10	Magnesium stearate	7.5	7.5	7.5	7.5	7.7	7.5	7.5	7.5	7.5

Total weight of the tablet = 300 mg

2.3.2. Angle of Repose

The angle of repose of granules or powder blend of each layer of each formulation was determined by fixed funnel method. The granules or blends were poured through funnel separately until the apex of pile so formed just touches the tip of the funnel. The angle of repose was measured using the formula,

$\tan\theta = h/r$: h – height of pile ; r = radius of pile

2.3.3. Bulk density

Bulk density was determined by placing the powder blend in a measuring cylinder and the total volume was measured and total weight of powder was measured. Bulk density was calculated using formula,

Bulk density (BD) = Weight of powder/Bulk volume

2.3.4. Tapped Density

The tapped density was obtained by dropping the cylinder onto a hard wooden surface. The tapping was continued until no further change in volume was noted, tapped density was calculated using formula

Tapped density (TD) = Weight of powder/Tapped volume

2.3.5. Carr's or Compressibility index

Carr's or Compressibility index (CI) was calculated using the formula,

% CI = [(TD – BD)* 100] / TD

2.3.6. Hausner's Ratio

Hausner's ratio is a number that is correlated to the flowability of powder and powder blend. It was calculated using the formula,

Hausner's ratio = TD / BD

2.4. Evaluation of postcompression parameters [12-14]:

2.4.1. Uniformity weight

20 tablets were selected randomly. Average weight of the tablet was determined. These tablets were individually weighed and the weight of individular tablets was compared with average weight.

2.4.2. Thickness

The thickness of the tablet was measured using Vernier Caliper. A total of 5 tablets were randomly selected and thickness was measured.

2.4.3. Hardness

The resistance of the tablets to break under conditions of storage, transportation and handling before usage depends on hardness of tablets which was measured by Monsanto hardness tester. The hardness was measured in terms of kg/cm^2.

2.4.4. Friability

Tablets pre-weighed were placed in Roche Friabilator and rotated for 4 minutes at 25 rpm. Percentage friability was determined by the formula,

% Friability = [(initial weight – final weight) / initial weight] * 100

2.4.5. Drug Content [15]

10 tablets were powdered, powder equivalent to the average weight was taken in a 100 ml standard flask and dissolved with 5 ml of ethanol and made upto 100 ml with 0.1N HCl. The solution was filtered and 10ml of filtrate was diluted with 0.1N HCl in a 100ml flask. From above solution 10ml was taken and diluted with 0.1N HCl in 100ml volumetric flask. The absorbance of the resulting solution containing Telmisartan was measured spectrophotometrically at 291 nm using 0.1N HCl as blank. The concentration was obtained using calibration curve. The same procedure was used for Simvastatin at 238nm. The drug content for bilayer tablets was estimated using simultaneous equation method. The mean percent drug content was calculated as an average of three determinations.

***2.4.6. In-vitro* floating studies**

Floating characteristics of the prepared formulations were determined using USP paddle apparatus at a speed of 50 rpm in 900ml of 0.1N HCl solution (pH=1.2) at 37 ± 0.2^0c for 24 hours. The time between the introduction of tablet and its buoyancy on the 0.1 N HCl (floating lag time) and the time during which the dosage form remain buoyant (floating duration) were measured. Also, the matrix integrity of the tablets during the study was visually monitored.

***2.4.7. In-vitro* drug release study**

The release of Telmisartan was determined using USP Type II (Paddle) dissolution apparatus under sink condition. The dissolution medium was 900 ml of a 0.1N HCl solution (pH=1.2), at 37^0c±0.2^0c and the stirring speed was 50 rpm. The *in-vitro* release studies were carried out for 1 hour with 10 minutes interval. The absorbance of the solution was recorded at 291 nm using UV spectrophotometer.

The release of Simvastatin was determined using USP Type II (Paddle) dissolution apparatus under sink condition. The dissolution medium was 900 ml of a 0.1N HCl solution (pH=1.2), at 37^0c±0.2^0c and the stirring speed was 100 rpm. The *in-vitro* release studies were carried out for 24 hours. The absorbance of the solution was recorded at 238 nm using UV spectrophotometer.

The release of bilayer tablets was determined using USP Type II (Paddle) dissolution apparatus under sink condition. The dissolution medium was 900 ml of a 0.1N HCl solution (pH=1.2), at 37^0c±0.2^0c and the stirring speed was 100 rpm. Aliquot of the solution was collected at specific interval were replaced with fresh dissolution medium. The Telmisartan and Simvastatin were analyzed spectrophotometrically at 291 nm and 238 nm respectively using simultaneous equation method.

2.4.8. Swelling Studies

The swelling property of floating tablets was determined by placing the tablet in the dissolution test apparatus containing 900ml of 0.1N HCl (pH 1.2) and maintained at 37±0.5ºC. At periodic intervals, the tablets were taken out and the weight gain in each tablet was checked using electronic weighing balance. The swelling characteristics were expressed in terms of the percentage water uptake according to the equation,

SI = [(Weight of tablet at time t – Weight of tablet at time 0) / Weight of tablet at time 0]* 100

2.4.9. Curve fitting analysis [16]

Mathematical models such as Zero order, First order, Korsemeyer Peppas, Higuchi and Hixson Crowel were applied to the observed release profile data to analyze the rate, mechanism and pattern of the drug release.

3. RESULTS AND DISCUSSION

3.1. Fourier Transform Infra-Red Spectroscopy of Telmisartan, Simvastatin and formulation

The IR spectrum of Telmisartan exhibited distinctive peaks at 3405.90 cm^{-1} owing to O-H stretching of the Carboxylic acids and at 1635.71 cm^{-1} because of C=O stretching as shown in (**Fig. 1**). The IR spectrum of Simvastatin exhibited distinctive peaks at 3471.18 cm^{-1} owing to O-H stretching of the Alcohols and at 1242.26cm^{-1} because of C-O stretching as shown in (**Fig. 2**). The formulation containing the Telmisartan and Simvastatin do not interact with each other and with that of excipients present (**Fig. 3**)

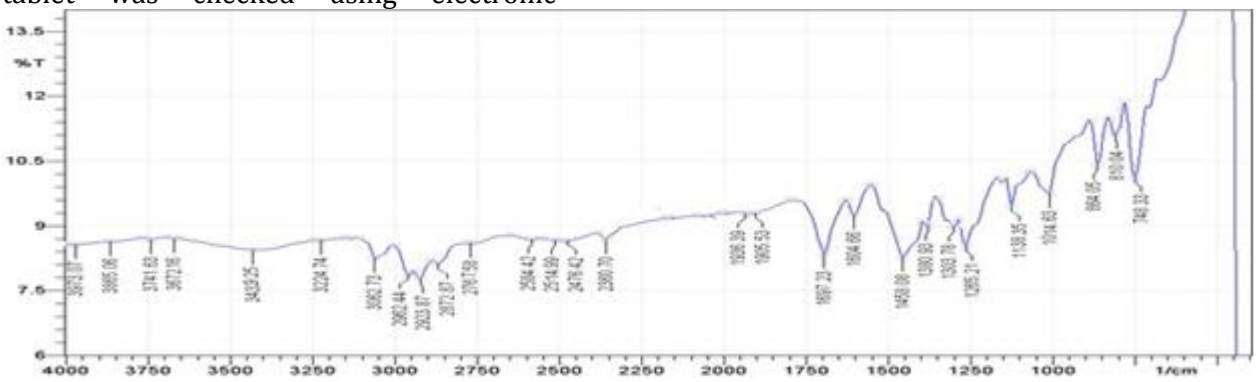

Figure 1: FTIR graph of Telmisartan

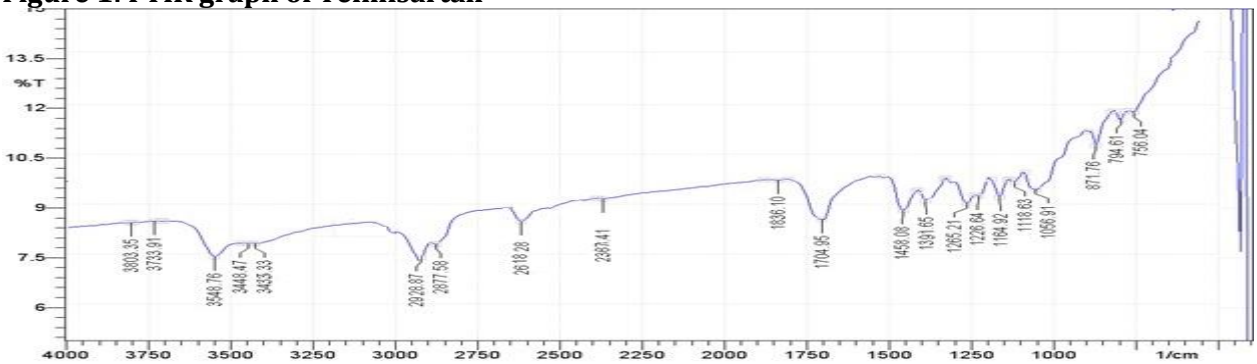

Figure 2: FTIR graph of Simvastatin

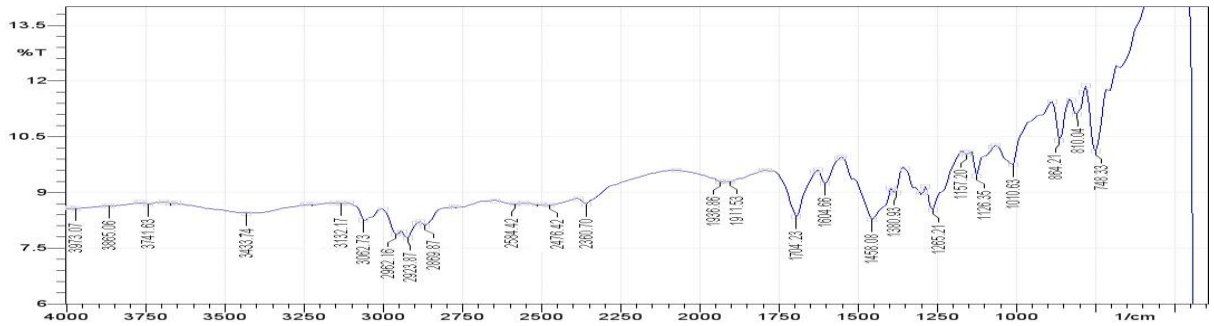

Figure 3: FTIR graph of formulation containing Simvastatin and Telmisartan

3.2. Preformulation study of Telmisartan immediate release (IR) granules:

The drug and the formulated blends were evaluated for Precompression parameters. The result shows poor flow property. So wet granulation technique was used for preparing IR granules of Telmisartan. The results are given in (**Table 3**).

Table 3: Precompression study of immediate release (IR) granules

Formulation	Bulk density* g/cm³	Tapped density* g/cm³	Compressibility index*(%)	Hausner's ratio*	Angle of repose* (degree)
T-1	0.500 ±0.0011	0.555 ±0.0027	09.99 ±0.0234	1..111 ±0.0034	34.28 ±0.1009
T-2	0.606 ±0.0012	0.666 ±0.0032	09.09 ±0.0204	1.101 ±0.0034	34.12 ±0.1267
T-3	0.555 ±0.0011	0.588 ±0.0025	5.550 ±0.0245	1.050 ±0.0036	32.17 ±0.1048

*MEAN±S.D (n=3)

The bulk density of IR granules ranged from 0.500 to 0.606 g/cm³ and tapped density ranged from 0.555 to 0.666 g/cm³. The compressibility index of the IR granules ranged from 05.55 to 09.99% and Hausner's ratio ranged from1.050 to 1.111. All the formulations showed good compressibility. The angle of repose of IR granules ranged from 32.17 to 34.28. The formulated IR granules were showed good flow property.

3.3. Characterization of Telmisartan IR tablets

The formulated telmisartan tablets were evaluated for Post compression parameters. The results are given in (**Table 4**).

Table 4: Post compression parameters of Telmisartan IR tablets

Parameters	T-1	T-2	T-3
Uniformity of weight(mg)**	100.90±0.2567	100.75±0.2314	**100.73±0.2034**
Thickness* (mm)	3.000±0.0005	3.000±0.0004	**3.000±0.0004**
Hardness* Kg/cm²	4.04±0.2012	4.08±0.2123	**4.04±0.2011**
Friability *	0.170±0.0034	0.242±0.0043	**0.141±0.0042**
Disintegration time* (minutes)	7.34±0.0153	8.22±0.0127	**3.46±0.0187**
% Drug content *	98.55±0.0064	96.77±0.0043	**99.00±0.0069**

**MEAN±S.D (n=20)*MEAN±S.D (n=3)

The weights of tablets ranged from 100.73 to 100.90 mg. The values are uniform and were within the pharmacopeial limits. Mean thickness of tablets is uniform in all formulations. The hardness for tablets ranged from 4.04 to 4.08 Kg/cm². All the formulations were uniform and possed good mechanical strength with sufficient hardness. The friability range from 0.14 to 0.24 and all values were below 1%. The disintegration time for T1, T2 and T3 formulation was 7, 8, and 3 minutes respectively. The drug content of all formulations was within limits.

3.4. In-vitro Dissolution Studies

The *invitro* dissolution of immediate release formulations of Telmisartan is given in the (**Fig. 4**).

The *invitro* drug release for T1, T2 and T3 formulation was at 45, 55 and 30 minutes respectively. From the *invitro* dissolution study the formulation T-3 was found to be optimum and selected for bilayer floating tablets.

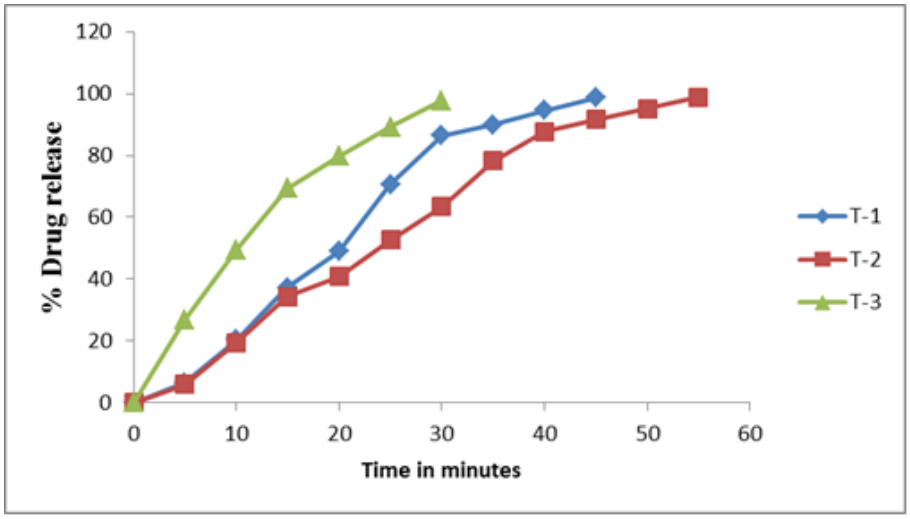

Figure 4: *In-vitro* dissolution of immediate release formulation of Telmisartan

3.5. Preformulation study of Simvastatin controlled release (CR) granules: The drug and the formulated blends of floating Simvastatin are evaluated for Precompression parameters. The results are given in the (**Table 5**).

Table 5: Precompression study of drug and formulated blends

Drug formulation	Bulk density* g/cm³	Tapped density* g/cm³	Compressibility index*(%)	Hausner's ratio*	Angle of repose* (degree)
Simvastatin	0.228 ±0.0043	0.300 ±0.0012	23.93±0.0265	1.310±0.0045	43.23 ±0.5369
S-1	0.523 ±0.00455	0.683 ±0.0045	23.41 ±0.0537	1.302 ±0.0033	33.73 ±0.4382
S-2	0.522 ±0.0023	0.672 ±0.0056	25.27±0.0372	1.321 ±0.0145	34.34 ±0.2456
S-3	0.512 ±0.0045	0.678 ±0.0078	25.99 ±0.0286	1.341 ±0.0237	34.99 ±0.3462
S-4	0.521 ±0.0042	0.622 ±0.0065	23.22±0.0265	1.284 ±0.0342	32.14 ±0.3521
S-5	0.502 ±0.0035	0.620 ±0.0087	20.89±0.0242	1.124 ±0.0342	28.24 ±0.4852
S-6	0.527 ±0.0023	0.666 ±0.0154	20.80±0.0743	1.250 ±0.0234	32.27 ±0.3482
S-7	0.534 ±0.0054	0.627 ±0.0098	20.72±0.0275	1.272 ±0.0127	32.07 ±0.2964
S-8	0.532 ±0.00532	0.622 ±0.0054	22.28±0.0434	1.230 ±0.0045	32.14 ±0.3929
S-9	0.542 ±0.0054	0.626 ±0.0087	21.22±0.0445	1.245 ±0.0544	33.27 ±0.5225

*MEAN±S.D (n=3)

The bulk density of CR granules ranged from 0.228- 0.534 g/cm³ and tapped density ranged from 0.300- 0.683 g/cm³. The compressibility index of the CR granules ranged from 14.22-25.99% and Hausner's ratio ranged from 1.111-1.341. All formulation showed good compressibility. The angle of repose of CR granules ranged from 26.27- 43.23. The formulated CR granules were showed good flow property.

3.6. Characterization of Simvastatin floating tablets

The formulated Simvastatin tablets are evaluated for Postcompression parameters. The results are given in the (**Table 6 and Table 7**).

The weights of tablets ranged from 300.12 to 301.85 mg. The weight of tablets within the pharmacopeial limits. Mean thickness of tablets is uniform in all formulations. The hardness for tablets ranged from 5.00 to 5.08 Kg/cm². All the formulation were uniform and possed good mechanical strength with sufficient hardness. The friability ranged from 0.10 to 0.28 and all values are below 1%. The drug content of all formulations is within limits. The floating duration ranged from 06 to >24 hours and the floating lag time ranged from 18 to 58 seconds. The formulation S-5 exhibited optimum floating behavior when compared with all the other formulations.

***3.7. In-vitro* Dissolution Studies**

The *in-vitro* dissolution of Simvastatin floating tablets is given in the (**Table 8 and Fig. 7**).

Table 6: Post compression parameters of Simvastatin floating tablets

Formulation	Uniformity of weight(mg)**	Thickness (mm)*	Hardness* Kg/cm²	Friability*	% Drug content*
S-1	300.70±0.0256	4.00±0.0013	5.04±0.0045	0.162±0.0238	98.40±0.0463
S-2	301.85±0.0453	4.00±0.0023	5.04±0.0076	0.140±0.0053	99.19±0.0535
S-3	301.35±0.1563	4.00±0.0021	5.08±0.0046	0.251±0.0043	97.60±0.0546
S-4	300.21±0.1206	4.00±0.0012	5.04±0.0086	0.210±0.0034	98.67±0.0453
S-5	300.18±0.0854	4.00±0.0007	5.00±0.0098	0.101±0.0021	99.79±0.0587
S-6	301.00±0.0354	4.00±0.0004	5.04±0.0532	0.220±0.0064	97.20±0.0965
S-7	300.35±0.1536	4.00±0.0012	5.00±0.0663	0.251±0.0083	98.25±0.0437
S-8	300.70±0.0325	4.00±0.0007	5.04±0.0453	0.280±0.0062	98.76±0.0436
S-9	300.12±0.0325	4.00±0.0006	5.00±0.0754	0.261±0.0063	99.12±0.0427

**MEAN±S.D (n=20) *MEAN±S.D (n=3)

Table 7: Floating characteristics of Simvastatin floating tablets

Buoyancy parameter	S-1	S-2	S-3	S-4	S-5	S-6	S-7	S-8	S-9
Floating lag time (seconds)	58	47	45	37	18	42	52	58	54
Floating duration (Hours)	>24	>24	12	20	22	06	10	12	12

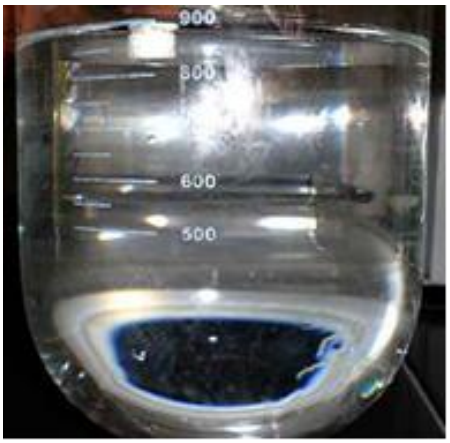

Figure 5: Buoyancy at 30 minutes

Figure 6: Buoyancy at 24th hour

Table 8: *In-vitro* dissolution study of Simvastatin floating tablets

TIME (Hours)	CUMULATIVE % DRUG RELEASE								
	S-1	S-2	S-3	S-4	S-5	S-6	S-7	S-8	S-9
0.5	4.33	4.93	5.97	5.91	**5.89**	18.71	14.12	7.23	6.65
1	6.17	6.98	8.40	7.87	**7.67**	29.12	21.02	13.16	8.59
1.5	8.75	10.13	12.31	10.87	**10.22**	42.65	29.64	17.20	12.79
2	11.43	13.73	14.86	12.24	**12.07**	57.18	37.09	21.36	15.60
3	15.64	17.59	21.56	18.53	**17.04**	70.79	46.88	28.86	22.48
4	19.27	20.63	28.46	22.03	**22.27**	84.26	57.23	35.81	29.20
5	23.29	24.35	37.22	26.76	**25.02**	**98.38**	76.78	45.54	38.88
6	27.20	29.17	46.20	31.05	**29.82**		88.57	57.05	48.02
7	30.65	35.61	54.94	36.01	**35.44**		**97.79**	68.80	57.05
8	34.36	40.28	64.89	42.43	**40.27**			84.04	66.81
9	37.45	45.84	71.34	47.16	**45.18**			93.67	75.16
10	42.23	51.41	81.74	54.03	**50.56**			**98.21**	85.33
11	45.55	58.45	89.74	62.26	**56.68**				**97.18**
12	49.68	64.37	**98.43**	69.37	**62.11**				
16	54.67	69.07		81.27	**73.27**				
20	59.24	75.32		92.34	**85.59**				
22	63.89	79.98		**101.32**	**94.77**				
24	**68.06**	**85.02**			**99.97**				

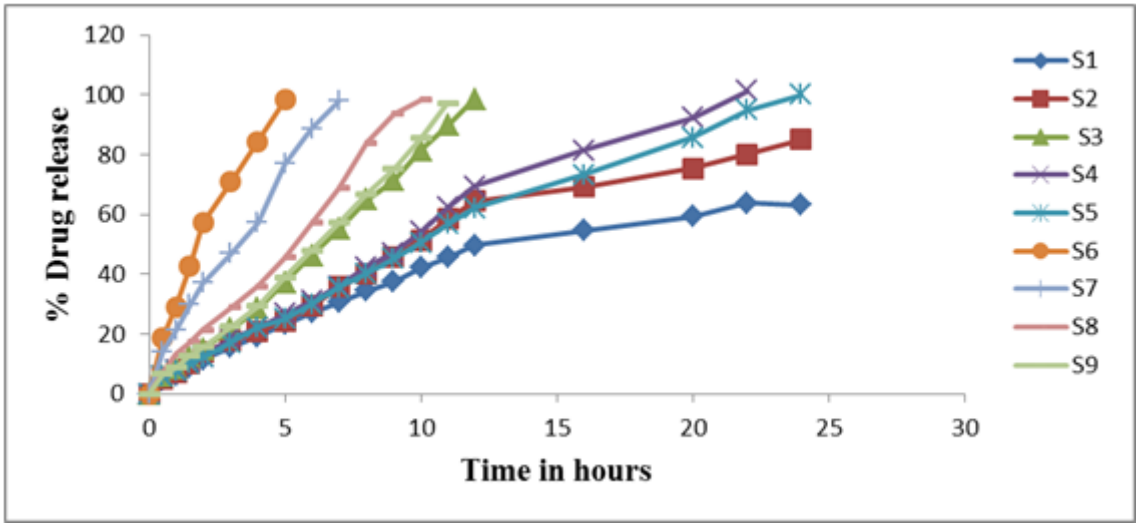

Figure 7: *Invitro* dissolution study of Simvastatin floating tablets

The of *invitro* dissolution of Gastro-retentive floating tablets showed that the formulation S-6, S-7, S-8 and S-9 containing guar gum released the entire drug at 5, 7, 10 and 11 hours respectively. The formulations S-1 and S-2 containing xanthan gum controlled the drug release from the floating tablet for more than 24 hours and formulation S-3,S-4 and 3-5 released for 12, 22 and 24 hours respectively. From above results the formulation S-5 was found optimum and selected for bilayer floating tablets.

3.8. Gastroretentive Bilayer floating tablets:

The optimized formulations T-3 and S-5 were combined together to develop gastroretentive Bilayer Floating Tablets (BFT) of Simvastatin and Telmisartan immediate release. The post compression parameters of the developed BFT are given in (**Table 9**) and are within the limits. The average weight was 402 mg (±5 %), Hardness was 5.9 kg/cm^2 (withstand mechanical stress), Friability was 0.10% (<1 %) and the drug content of Telmisartan and Simvastatin was 99.72 % and 101.02 % respectively (90 to 110 %).

Table 9: Post compression study of bilayer tablets

PARAMETERS		BILAYER TABLETS
Uniformity of weight (mg)		402± 0.1039
Thickness (mm)		5 ± 0.0012
Diameter (mm)		9 ±0.000
Hardness (kg/cm^2)		5.90 ± 0.0146
Friability (%)		0.10 ± 0.0019
Floating lag time (secs)		14
Floating duration (hours)		>24
Drug content (%)	Telmisartan	99.72
	Simvastatin	101.02

The *in-vitro* dissolution study of bilayer floating tablets is given in (**Fig. 8**).

The Telmisartan released completely at the end of 30 minutes, whereas Simvastatin released completely at 24 hours in a controlled manner.

The dissolution data from table was fitted into several release kinetics and the regression coefficient values and n value are shown in the (**Table 10**). This shows that the release follows Zero order kinetics and the 'n' value of 0.8347 indicates non-fickian transport.

The Swelling of BFT given in (**Table 11**), shows that the swelling index of the tablet increases with increase in time upto 12 hours. At the end of 24th hour swelling index of tablet is reduced, this may be attributed

to the erosion of biodegradable polymer Xanthan gum. This indicates that the drug will remain in the gastric region till drug is released from the delivery system and promotes evacuation after its release.

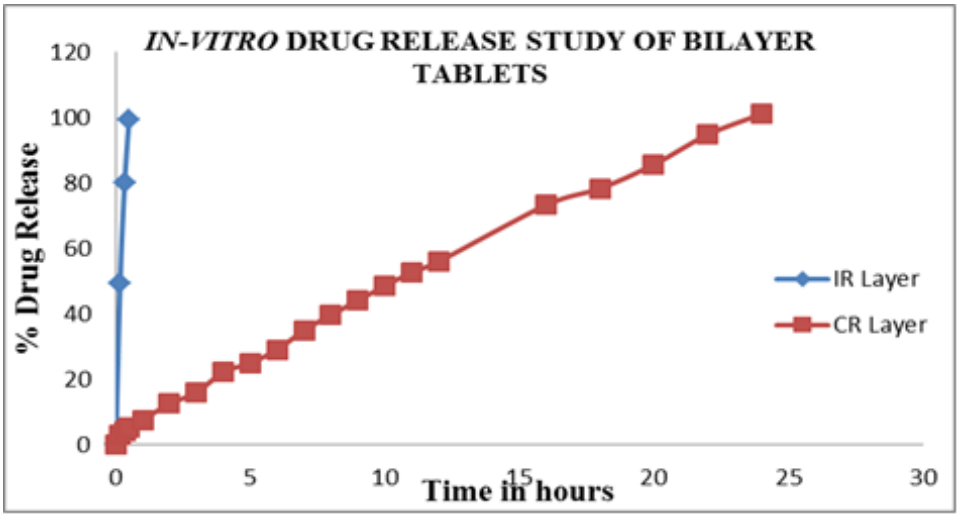

Figure 8: *In-vitro* dissolution study of bilayer floating tablets

Table 10: Release kinetics of BFT

Release Kinetics type	Zero order	First order	Higuchi	Hixson	Korsmeyer Peppas	'n'
	0.9955	0.8199	0.9522	0.9364	0.9967	0.8347

Table 11: Swelling Index of bilayer floating tablets

Time in hours	% Swelling
0	0
1	36.27
2	88.56
4	142.34
6	177.33
8	214.72
10	251.21
12	298.52

CONCLUSION

The prepared tablets showed satisfactory results for various evaluation tests such as tablet dimension, hardness, friability, weight uniformity, drug content and *in-vitro* dissolution study. The optimized formulation based on all the parameter T-3(Crospovidone) is selected for immediate release layer and S-5(Xanthan gum and HPMC K4M) was selected for controlled release layer. The drug release mechanism was found to be non fickian; dependent on both drug diffusion and polymer relaxation. The bilayer tablets of Telmisartan and Simvastatin may be useful in serious cardiovascular adverse effect such as hypertension, congestive heart failure and exacerbation of angina.

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