RESEARCH ARTICLE

Formulation and Development of Bilayer floating Tablet of Selective Drugs as GRDDS

Sreedhar Ranjan Das[1*], Bibhuti Bhusan Panigrahi[2], Manoj Kumar Pani[3]

[1]Sontoshi institute of Pharmaceutical sciences, Manguli, Cuttack., Odisha, India
[2]Professor and Principal, Einstein College of Pharmacy, Bajapur, Khorda, Bhubaneswar, India
[3]Indira Gandhi Institute of Pharmaceutical Sciences, Bhubaneswar, India

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ABSTRACT
The research work based on Bilayer floating tablet of selected drug as Sucralfate and Metoprolol succinate**..** Sucralfate Immediate release layer containing Sucralfate100 mg and total weight with excipients is 300 mg . Metoprolol succinate sustained layer containing Metoprolol succinate 50 mg and total weight with excipients is 200 mg is done. Metoprolol succinate layer (MSF10) the (DSFMS-500mg) produce Average Weight 501.7±0.26 (mg), Thickness 5.99±0.111 mm, Hardness 5.6±0.124KP, Friability 0.543%,FLT 22sec, TFT 18 hrs, Drug Content of Sucralfate 100.02%, Drug Content of Metoprolol Succinate is 99.98%. The TFT. is under acceptance criteria.(18-20hour). So the formulation is the best formulation as GRDDS.
Keywords: Ulcer protective, Sucralfate, Antihypertensive, Metoprolol Succinate, Bilayer floating tablet
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INTRODUCTION

Tablets produce considerable plasma drug[1] concentration and produce better bioavailability[2]. Patients prefer because it is simple to consume. Tablet is most convenience solid dosage form. It can be used to deliver medications directly to the stomach and small intestine. Bioavailability, less drug waste, and increase drug solubility are another factors for consideration.[4] Davis initially described floating systems in 1968.[5,6] The floating mechanism and the bilayertablet idea are integrated in the bilayer floating drug delivery device.[7] Bilayer tablets contain two layers, Immediate release layer[8] which is a layer that is released immediately in the presence of super disintegrant and sustained release layer.[9] The initial dosage happens quickly because gas-generating agent and drug release occur insustained way for an extended period of time. Needs of Bilayer Floating Tablet can be accounted for Improved selectively in receptor activation, Reduced counter activity of the body, Improve bioavailability and providinge better Area Under the Curve (AUC).[10-14]

Mechanism of Bilayer floating tablet

After administration of Bilayer floating tablet the two layers are separated in acid medium of stomach. The immediate release layer disintegrates within few minutes and releases the drug. The time at which the layer start disintegrating is known as Floating Lag Time (FLT) .The sustained release produces bouncy and start floating at upper region for particular period of time and the drug release occurs slowly.[15-17] By characteristic study and compatibility study it is found that both the drugs are FDA, NDA, ANDA approved. They have less drug interaction and compatible to be administrated in case of pregnant women .

MATERIAL AND METHODS

The drug for immediate release layer (Sucralfate) is collected from Bowen Healthcare Ltd Ahmadabad, India and the drug for Sustained release Layer (Metoprolol succinate) is the gift sample from Ravoos Laboratory Ltd.

Preparation of bilayer floating tablet

Preparation of granules of IR Layer

Wet granulation was used to prepare the IR layer for immediate release. Ingredients were measured and sieved using no. 40, the finest available. Proper mixing of materials was performed. Poly sorbate 80 was dissolved in hot water, while SLS was dissolved in cold water. Using the solutions as a granulating fluid is a common use. In the next step, the granulating fluid is used to wet the mixtures. Granulation is then carried out using the RMG granulator. For around 60 minutes, the granules were dried in a Retsch quick drier at 600C to reduce LOD to less than 3%.

Preparation of granules of SR Layer

The wet granulation process was used to create the sustained release SR layer. A complete blending of the 40-mesh polymer with the medication was accomplished. In order to keep the mixture from drying out, the granulating fluid and water were added to the mix (1:9 parts). A tray dryer was used to dry the wet bulk at 500C for around 50 minutes until the percent LOD was less than 2%. Sodium bicarbonate was added to the dried granules, which were then sieved through a 30- mesh screen.

**Author for Correspondence: sreedhardas2009@gmail.com*

Table-1-Composition of Immediate Release layer of Sucralfate in (mg)

S.No	Composition	Quantity per tablet in (mg)									
		F- 1	F- 2	F- 3	F-4	F5	F- 6	F -7	F -8	F -9	F-10
1	Sucralfate	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
2	Crospovidone	0.0	5.840	6,50	7.10	8.0	3.40	8.50	6.0	12.50	3.5050
3	Calcium carbonate	17.50	24.460	25.730	8.20	8.80	5.40	10.20	19.30	1.30	22.970
4	Aerosil	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
5	Lactose MHF	90.0	85.0	80.0	90.0	90.0	85.0	90.0	85.0	90.0	80.0
6	MCC PH 101	75	80	85	90	85	90	80	75	85	85
7	Magnesium stearate	3.8	3	1	2	1	3	1	2	2	1
8	Sodium bicarbonate	10	0	0	0	5	10	5	10	5	5
9	Polysorbate 80	0	0	0	1	0.5	1.5	2	0.5	2.5	0
10	Sodium Luryl Sulphate	0.0	0.0	1.070	0.0	0.0	0.0	0.0	0.0	0.0	0.6250
11	Sunset yellow	2.2	0.20	0.40	0.20	0.40	0.20	0.70	0.70	0.20	0.40

Table 2 : Composition of Sustained Release Layer Metoprolol Succinate (mg)

S.No.	Composition	Quantity per tablet in (mg)									
		F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9	F-10
1	Metoprol	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0
2	Hydro Propyl MethylCellulose	50	50	50	50	45	50	45	45	50	50
3	Sodium Bicarbonate	50	-	-	-	50	-	-	-	50	-
4	Aerosil	-	50	-	-	-	50	-	-	-	50
5	EudragitRSPO	-	-	50	-	-	-	50	-	-	-
6	EudragitRLPO	-	-	-	50	-	-	-	50	-	-
7	EudragitRS100	25	-	25	-	25	-	25	-	25	-
8	NA CMC	-	25	-	25	-	25	-	25	-	25
9	Sodium alginate	15	15	15	15	15	15	15	15	15	15
10	HPC	5	5	5	5	10	5	10	10	5	5
11	Talc	5	5	5	5	5	5	5	5	5	5

Bulk density and Tapped density

The granules (W) were placed separately into a graduated measuring cylinder. The initial (bulk) volume (VB) was noted. Granules were kept in the tapped density tester USP and subjtapping is done at a rate of 200 drops/min. The difference between the initial and final volumesmust be less than 2%

Bulk density= ρB = W/vB

Tapped density, ρT =W/v

Compressibility Index

Carr's Index or Compressibility Index

(CI) = 1- ρB / ρT *100

The CI value below 15% indicates good flow of the powder and above 30%indicates poor flow property of the powder.

Hausner's Ratio

Hausner's Ratio= ρT/ ρB

Below 1.25 indic good flow property and above 1.25 indicates poor flow property of the powder.

Angle of Repose

The granules and the powder were passed separately through the funnel which is fixed in a stand at a height of 2.5 inch. up to conical pile will touch the tip of the funnel.

Angle of repose

(θ) = Tan-1 (Height of pile / radius of pile)

RESULTS AND DISCUSSION

The pre formulation study shows: The angle of repose- 24o-260 , Bulk density 0.500 to 0.526 g/ml, Taped density 0.547-0.676 g/ml, Compressibility Index 17.57-26.20 %, Hausner's Ratio 1.229-1.314 , %LOD 2.13-2.86%. The flow property of the lubricated granules of Sustained release layer shows the angle of repose 24o-33o, bulk density 0.298 to 0.397 g/ml, Taped density 0.403-0.510 g/ml, Compressibility Index 25.67-32.45 %, Hausner's Ratio 1.392-1.493 , %LOD 1.73-1.92%. The average weight of Sucralfate immediate release formulations is 205-207mg, thickness 3.01- 3.53mm, hardness 5.45-5.75KP, Friability is less than 1, average TFT is 22 second and % of drug release is 99.49%. The SF3 shows drug release 100.73% but TFT is 26 second which is over limit. SF10 produce FLT (Floating Lag Time) 21 second shows drug release 99.49% which remain in limit. The average weight of Metoprolol Succinate sustained release formulation is 295-296mg, thickness 2.45-3.92 mm, hardness 6.96-9.34 KP, Friability is less than 1, average TFT is 16-18 hours and % of drug release is 97-101%. The MSF2 shows drug release 100.61% but TFT is 16 hour which is under limit. MSF6 produce TFT 18 hours shows drug release 100.01% which remain in limit. Swelling index of Metoprolol Succinate sustained release formulation is 182% to 221 % after 18 hours. The MSF10 shows highest Swelling index 220.61%.Accelerated Stability Study of Sucralfate immediate release shows only in SF2 slide black spot arises but other

Table 3: Result of Post compression of Sucralfate immediate release layer

Formulations	Tablet Average weight (mg)	Tablets Average thickness (mm)	Tablets Average Hardness(KP)	Tablets Average Friability (%)	Average (TFT)in second	Average Drug Content (%)
F1	214.2±.572	03.63±.024	5.18±.068	0.148	21	88.98
F2	206.6±0.541	3.53±0.008	5.87±0.214	0.159	22	99.33
F3	206.8±0.699	3.18±0.021	5.62±0.370	0.159	26	100.73
F4	205.2±0.441	3.18±0.024	5.51±0.228	0.398	24	99.57
F5	206.4±0.401	3.00±0.045	5.39±0.220	0.081	21	95.12
F6	207.3±0.410	3.10±0.045	5.11±0.109	0.198	23	99.45
F7	205.8±0.543	3.41±0.07	5.79±0.155	0.298	24	98.43
F8	206.6±0.321	351±0.006	5.43±0.279	0.299	23	97.54
F9	205.2±0.500	3.20±0.010	5.45±0.109	0.292	22	99.96
F10	206.5±0.327	3.01±0.001	5.49±0.056	0.299	21	99.49

Table 4: Composition of the Bilayer Floating Tablet (DSFMS-500mg)

S. No	Selected formulation SF9	Ingredients (mg)	Selected Formulation MSF10	Ingredients (mg)
1	Sucralfate	100	Metoprolol Succinate	50
2	Crospovidone	12.50	HPMC K 100M	50
3	Calcium carbonate	1.30	Sodium bicarbonate	-
4	Aerosil	1.50	Aerosil	50
5	Lactose MHF	90	Eudragit RSPO	-
6	MCC PH 101	85	Eudragit RLPO	-
7	Magnesium Stearate	2	Eudragit RS100	-
8	Sodium bicarbonate	5	Na CMC	25
9	Polysorbate 80	2.5	Sodium alginate	15
10	SLS	0	HPC KLUCEL HF	5
11	Sunset Yellow	0.2	PVPK 90	QS
12	Purified Water	qs	Ethyl cellulose	QS
13	Total wt	0	TALC	5
	Total Weight	300	IPA	QS
			Purified Water	QS
			Total weight	200

formulations shows better stability. Accelerated Stability Study of Metoprolol Succinate layer shows MSF3,MSF5 and MSF6shows stability problems but other formulations shows better stability.

CONCLUSION

Comparing all the evaluated parameters and stability studies it is confirmed that SF10 andMSF9 are the best formulations. So Bilayer Floating Tablet DSFMS is composed ofSF10 and MSF9.

Table 5: Evaluation parameters compared with acceptance criteria

S. No.	Parameter	Observed Value	Acceptance criteria
1	Description	Yellow color SR layer white color IR layer	Yellow colorSR layer white color IRlayer
2	Average Weight(mg)	501.7±0.26	490-510
3	Thickness (mm)	5.99±0.111	5-6
4	Hardness (KP)	5.6±0.124	4-6
5	% Friability	0.599	Less than 1
6	FLT (sec)	22	15-25
7	TFT (hr)	18	18-20
8	Drug content Sucralfate (%)	100.02%	95%-105%
9	Drug content Metoprolol succinate (%)	99.98%	90%-110%

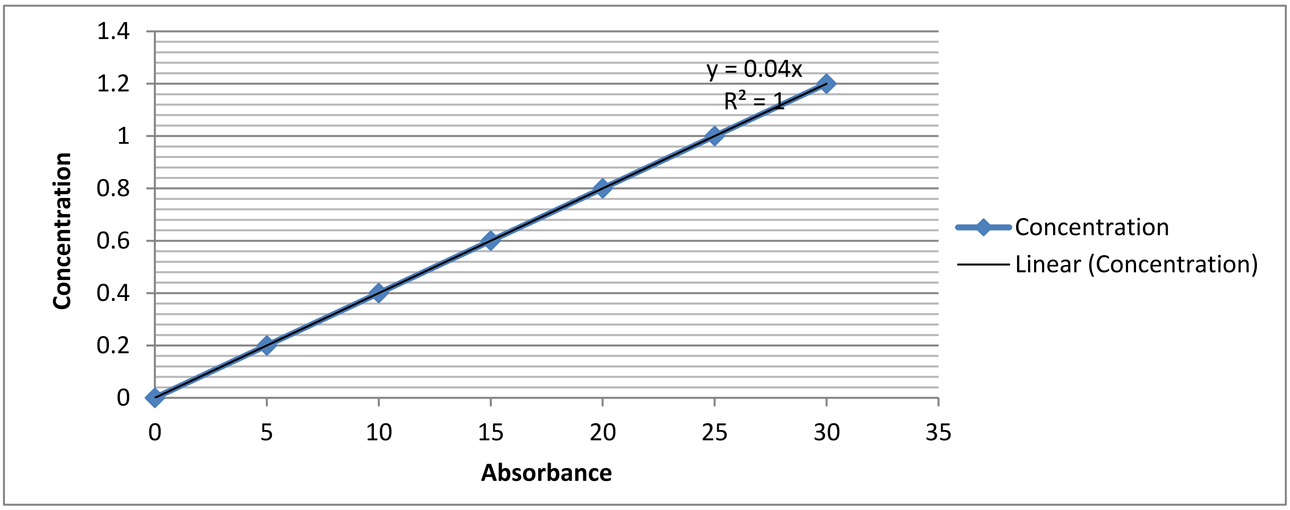

Figure 1: Drug release study of Sucralfate

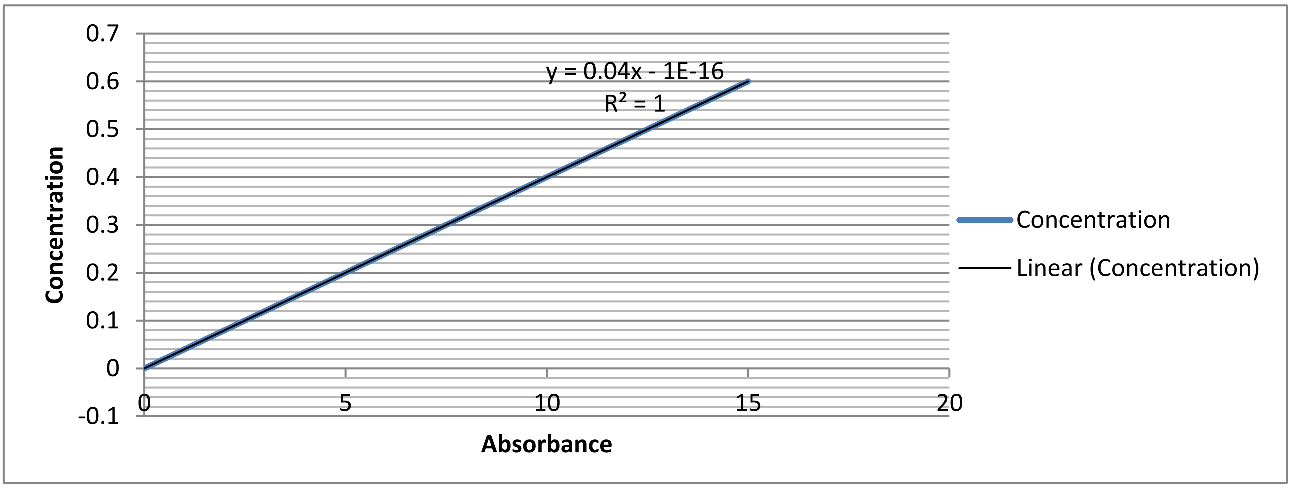

Fig 2: Drug release study of Metoprolol Succinate

Table 6: *In vitro* evaluation study of DSFMS after 90 days of stability studies

S No	Parameters	Initial evaluation results	15 days	30days	60days	90days
1	Average Weight(mg)	501.70±0.260	499.1±0.21	500.7±0.12	497.7±0.15	501.6±0.36
2	Thickness (mm)	5.99±0.111	5.98.±0.013	5.97.±0.021	5.99±0.115	5.98±0.121
3	Hardness (KP)	5.6±0.124	5.6±0.111	5.6.0±0.321	5.6±0.453	5.7±0.132
4	% Friability	0.599	0.657	0.768	0.923	0.599
6	TFT (hr)	18	18	18	18	18
7	FLT(SEC)	22	23	22	22	22
8	Drug Content in % (Sucralfate)	100.02	101.03	102.04	100.06	100.04
9	Drug Content in % (Metoprolol succinate)	99.85	99.87	98.85	99.75	99.98

Metoprolol succinate layer (MSF10) the (DSFMS-500mg) produce Average Weight 501.7±0.26 (mg), Thickness 5.99±0.111 mm, Hardness 5.6±0.124KP, Friability 0.543%, FLT 22sec, TFT 18 hrs, Drug Content of Sucralfate 100.02%, Drug Content of Metoprolol Succinate is 99.98%.

After 90 days the Stability Study Average Weight 501.6±0.36 (mg), Thickness 5.99±0.121 mm, Hardness 5.7±0.132KP, Friability 0.599%, FLT 22sec, TFT 18 hrs, Drug Content of Sucralfate 100.04%, Drug Content of Metoprolol Succinate is 99.98%.

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