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Research Article

FORMULATION AND IN-VITROEVALUATION OF GASTRO RETAINTIVE BI-LAYERED FLOATING TABLET OF SUCRALFATE AND METOPROLOL SUCCINATE

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A R T I C L E I N F O

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A B S T R A C T

Formulation and evaluation and selection of best formulation of 500 mg Bi-Layer Floating Tablet having 214 mg Ulcer protective Sucralfate as Immediate Release Layer and 286mg of antihypertensive Metoprolol Succinate as Floating Sustained Release layer.Best formulations are selected from 15 formulations of Sucralfate and 10 formulations of Metoprolol Succinate according to pre formulation study , in vitro evaluation, accelerated stability study. Then Bi Layered Floating Tablet is compressed and In vitro evaluation is done. In presence of major amount of Crospovidone, Lactose MFL,MCC PH 101,Sodium Bicarbonate, HPC-L the immediate release formulation of Sucralfate (SF10) produce DT 6.29± 0.047 min ,Drug content 99.95% in presence of acid medium of stomach. In presence of majore amount of HPMC K 100,Sodium Bicarbonate ,Aerosil, Udragit the cotrolled release layer (MSF6) produce drug release 102.11% in upper intestine This formulation(SF10 + MSF6) generate maximum prolonged gastro retention and satisfy GRDDS in patients having Stomach Ulcer with Hypertension in pregnancy and lactation.

INTRODUCTION

Bi-layer Floating Tablet comes under floating system which was described by Davis-1986[1]It contain Immediate release layer which deliver initial dose by increasing lag time[3] Another layer is Sustained release layer which remain in gastric region[2] for several hours and prolong the gastric resistance time and produce buoyancy[3]and improve bioavailability at high PH environment

Bilayer floating drug delivery system is combined principle of Bi –Layered Tablet as well as floating mechanism[4] Drug absorption from G.I.T depends upon contact time with intestinal mucosa[5] Bi-layered Tablet materials involve both the compressibility and consolidation[4] Bi-Layered tablet contain immediate and sustained release layer[6] The incorporated drug remain in gastric region for several hours and produce prolong gastric resistance time and improve bioavailability .It reduce drug waste and enhance the solubility of drug[7] . The drug release slowly at desired rate and increase GRT .and better control of fluctuations in plasma drug concentration[8]Both Sucralfate and Metoprolol succinate produce minor drug interaction in pregnancy and lactate mother[9] Both the drugs are administrated in empty stomach in presence of acid medium[9]. They act at stomach as well as at upper part of small intestine and produce better bioavilability [10]

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The present study deals with optimization and in vitro evaluation of Bi-Layered Floating Tablet prepared by the selected formulation from15 formulations of Sucralfate and 10 formulations of Metoprol succinate and to produce better GRDDS

MATERIALS AND METHODS

According to different properties and uses of various exepients are taken in different ratios to formulate and optimize Bi-layered Floating Tablet of Sucralfate and Metoprolol Succinate.

Preparation of Granules

Preparation of Sucralfate Granules

The15 formulations of Sucralfate IR tablets were prepared by wet granulation method**.** The required ingredients were weighed accurately and passed through 40 mesh. The sieved materials were then mixed well in a poly bag for about 30 minutes. The surfactants, SLS and polysorbate80 were dissolved in cold and hot water respectively to use as granulating fluid. To moisten the blend, either water or surfactant solution was used as granulating fluid. The wet mass was granulated in RMG granulator. The granules were then dried in a Retsch rapid dryer at 60^0C for about 60 minutes until the % LOD becomes less than 3%. The dried granules were then passed through 40 mesh and then lubricated by mixing with the lubricant (which was previously passed through 60 mesh) in a polybag for about 15 minutes. The flow properties of the lubricated granules were determined.

Table 1 Composition of Immediate release Sucralfate layer of Bilayered Floating Tablet (SF1-SF9)

	INGREDIENTS	QUANTITY PER TABLET IN MG								
		SF 1	SF 2	SF 3	SF 4	SF 5	SF 6	SF 7	SF 8	SF 9
1	SUCRALFATE	100	100	100	100	100	100	100	100	100
2	CROSPOVIDONE	0	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
3	CALCIUM CARBONATE	23	25	25	25	0	25	0	0	0
4	AEROSIL	1	1	1	1	1	1	1	1	1
5	LACTOSE MHF	31.25	31.25	31.25	31.25	31.25	31.25	31.25	31.25	31.25
6	MCC PH 101	48.45	45.2	44.575	44.575	74.575	49.575	49.575	49.825	46.075
7	MAGNESIUM STEARATE	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
8	SODIUM BICARBONATE	5	5	5	5	0	0	25	25	25
9	POLYSORBATE 80	0	0	0	0.625	0.625	0.625	0.625	0.375	0.375
10	SLS	0	0	0.625	0	0	0	0	0	0
11	SUNSET YELLOW	0.312	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125
12	PURIFIED WATER	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
	TOTAL WT OF TABLET	214.5	214.5	214.5	214.5	214.5	214.5	214.5	214.5	214.5

Table 2 Composition of Immediate release Sucralfate layer of Bilayered Floating Tablet :(SF10-SF-15)

Sl No	INGREDIENTS	QUANTITY PER TABLET IN MG					
		SF 10	SF 11	SF12	SF 13	SF 14	SF 15
1	SUCRALFATE	100	100	100	100	100	100
2	CROSPOVIDONE	6.25	6.25	3.75	8.75	6.25	6.25
3	AEROSIL	1	1	1	1	1	1
4	LACTOSE MFL	31.20	31.20	31.20	31.20	31.20	31.20
5	MCC PH101	48.575	43.575	48.575	43.575	52.325	39.825
6	MAGNESIUM STEARATE	0.5	0.5	0.5	0.5	0.5	0.5
7	SODIUM BICARBONATE	25	25	25	25	18.75	31.25
8	POLYSORBATE 80	0.375	0.375	0.375	0.375	0.375	0.375
9	HPC-L	1.25	6.25	3.75	3.75	3.75	3.75
10	SUNSET YELLOW	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125
11	PURIFIED WATER	q.s	q.s	q.s	q.s	q.s	q.s
	TOTAL WEIGHT	214	214.	214.	214.	214.	214.

Table 3 Composition of sustained Release Metoprolol Succinate layer of Bilayered Floating Tablet

SL. NO	INGREDIENTS	QUANTITY PER TABLET IN MG									
		MSF1	MSF2	MSF3	MSF4	MSF5	MSF6	MSF7	MSF8	MSF9	MSF10
1	METOPROLOL SUCCINATE	50	50	50	50	50	50	50	50	50	50
2	HPMC K 100M	75	100	100	100	100	100	100	100	100	75
3	SODIUM BICARBONATE	100	100	100	100	100	100	100	100	100	100
4	AEROSIL	3	3	3	3	3	3	3	3	3	3
6	EUDRAGIT RSPO	30	30	-		-	-	-	-	-	30
7	EUDRAGIT RLPO	-	-	30		-	-	-	-	-	-
8	EUDRAGIT RS100	-	-		30	-	-	-	-	-	-
8	Na CMC	25	-	-	-	30	-	-	-	-	20
9	SODIUM ALGINATE	-	-	-	-		30	-	-	-	-
10	HPC KLUCEL HF	-	-	-	-	-	-	30	-	-	-
11	PVPK 90	-	-	-	-	-	-	-	30	-	5
12	ETHYL CELLULOSE	-	-	-	-	-	-	-	-	30	-
13	TALC	3	3	3	3	3	3	3	3	3	3
14	IPA	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
15	PURIFIED WATER	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
	TOTAL WEIGHT	286	286	286	286	286	286	286	286	286	286

Table 4 Flow properties of lubricated granules of Sucralfate

Formulation Code	Angle of Repose (Θ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	%LOD
SF1	27.53	0.507	0.687	26.20	1.314	2.13
SF2	27.82	0.521	0.622	21.31	1.248	2.86
SF3	26.27	0.546	0.694	21.33	1.254	2.68
SF4	25.43	0.454	0.547	17.17	1.186	2.26
SF5	26.13	0.503	0.629	20.03	1.264	2.28
SF6	25.52	0.506	0.634	20.19	1.257	2.74
SF7	26.19	0.502	0.609	17.57	1.229	2.78
SF8	26.33	0.526	0.676	22.25	1.229	2.92
SF9	26.23	0.501	0.615	18.54	1.310	2.73
SF10	26.28	0.500	0.627	20.25	1.263	2.78
SF11	26.31	0.507	0.625	18.88	1.239	2.91
SF12	26.48	0.505	0.623	18.94	1.221	2.64
SF13	16.06	0.511	0.624	22.11	1.284	2.68
SF14	25.73	0.505	0.616	18.02	1.229	2.89
SF15	26.33	0.511	0.620	17.58	1.212	2.77

Table 5 Flow properties of lubricated granules of Metoprolol Succinate:

Formulation Code	Angle of Repose (Θ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	%LOD
MSF1	31.36	0.374	0.531	29.56	1.419	1.74
MSF2	22.53	0.343	0.514	33.26	1.498	1.89
MSF3	32.72	0.368	0.508	27.55	1.380	1.93
MSF4	32.39	0.348	0.492	29.26	1.475	1.83
MSF5	32.66	0.341	0.503	32.20	1.475	1.79
MSF6	32.73	0.356	0.502	29.08	1.410	1.87
MSF7	32.61	0.342	0.479	28.60	1.400	1.92
MSF8	32.53	0.353	0.497	28.97	1.407	1.90
MSF9	33.04	0.359	0.509	29.46	1.417	1.76
MSF10	32.44	0.331	0.481	31.18	1.453	1.96

Table 6 Accelerated Stability Study of Sucralfate Lubricated Granules

Granules	After 7 days	After 15 days	After 30 days	Aftrer 45Days	After 60 Days	After 90 Days
SF1	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF2	No Change	No Change	No Change	No Change	No Change	Rare black spots
SF3	No Change	No Change	No Change	No Change	No Change	Stick at the wall
SF4	No Change	No Change	No Change	No Change	No Change	No change
SF5	No Change	No Change	No Change	No Change	No Change	No change
SF6	No Change	No Change	No Change	No Change	No Change	Started caking
SF7	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF8	No Change	No Change	No Change	No Change	No Change	Odour change
SF9	No Change	No Change	No Change	No Change	No Change	No change
SF10	No Change	No Change	No Change	No Change	No Change	No change
SF11	No Change	No Change	No Change	No Change	No Change	No change
SF12	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF13	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF14	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF15	No Change	No Change	No Change	No Change	No Change	Slide yellowish

Table 7 Accelerated Stability Study of Sucralfate Lubricated Granules:

Granules	After 7 days	After 15 days	After 30 days	Aftrer 45Days	After 60Days	After 90 Days
MSF1	No Change	No Change	No Change	No Change	No Change	Rare black spot
MSF2	No Change	No Change	No Change	No Change	No Change	No change
MSF3	No Change	No Change	No Change	No Change	No Change	No change
MSF4	No Change	No Change	No Change	No Change	No Change	No change
MSF5	No Change	No Change	No Change	No Change	No Change	No change
MSF6	No Change	No Change	No Change	No Change	No Change	No change
MSF7	No Change	No Change	No Change	No Change	No Change	No change
MSF8	No Change	No Change	No Change	No Change	No Change	No change
MSF9	No Change	No Change	No Change	No Change	No Change	No change
MSF10	No Change	No Change	No Change	No Change	No Change	Rare black spot

Table 8 Post compressional parameters of the formulated Sucralfate layer of Bilayered floating tablet.

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (KP)	% Friability	Disintegration Time (min)	% Drug Content
SF4	209.2±0.441	3.18±0.024	5.51±0.228	0.398	0.46±0.690	99.57
SF5	211.4±0.601	3.04±0.036	5.68±0.130	0.079	9.28±0.132	98.15
SF9	211.2±0.500	3.19±0.010	5.97±0.179	0.316	1.3±0.066	100.14
SF10	218.5±0.527	3.01±0.021	5.81±0.116	0.396	1.22±0.115	100.56
SF11	215.2±0.737	3.19±0.038	6.15±0.263	0.317	23.96±0.853	100.3

Table 9 Post compressional parameters of the formulated Metoprolol Succinate layer of Bi layered floating tablet.

Formulation Code	Average weight(mg)	Thickness (mm)	Hardness (KP)	% Friability	% Drug content	FLT (SEC)	TFT (HR)
MSF2	283.8±0.527	3.28±0.009	8.87±0.138	0.092	101.61	16	>20
MSF3	281.4±0.707	3.28±0.010	8.77±0.115	0.144	101.87	27	>20
MSF4	279.3±0.881	3.29±0.010	7.86±0.091	0.145	98.22	30	>20
MSF5	281.0.±0.500	3.25±0.014	8.86±0.121	0.131	100.65	18	>20
MSF6	283.9±0.527	3.29±0.007	8.71±0.147	0.197	100.91	28	>20
MSF7	281.2±0.707	3.28±0.019	8.87±0.150	0.105	100.83	27	>20
MSF8	283.8±0.527	3.28±0.011	8.87±0.076	0.183	98.65	30	>20
MSF9	280.4±0.667	3.27±0.030	7.8±0.089	0.105	99.88	53	>20

Table 10 Swelling index values observed from Metoprolol Succinate tablets:

TIME (HR)	SWELLING INDEX %							
	MSF2	MSF3	MSF4	MSF5	MSF6	MSF7	MSF8	MSF9
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	96.0	83.5	82.7	105.7	114.2	71.1	110.2	68.9
2	113.7	106.1	108.1	128.0	160.4	100.5	152.7	102.6
3	153.5	147.6	148.4	155.5	187.4	149.2	181.3	129.5
4	165.3	164.7	173.7	178.6	197.0	153.5	199.9	138.4
5	188.6	184.3	188.5	193.3	216.1	164.5	209.9	150.3
6	190.2	190.3	189.7	200.1	226.7	184.2	222.5	171.5
7	203.1	202.0	202.6	209.9	239.8	191.4	237.1	177.5
8	215.0	210.5	209.2	212.4	214.3	211.2	242.7	187.4

Table 11 Composition of formulation of Optimized Sucralfate and Metoprolol Succinate (SFMS) Bi Layered Floating Tablet.

SL No	Ingredients (mg)	SF 10	Ingredients (mg)	MSF6
1	SUCRALFATE	100	METOPROLOL SUCCINATE	50
2	CROSPOVIDONE	6.25	HPMC K 100M	100
3	AEROSIL	1	SODIUM BICARBONATE	100
4	LACTOSE MFL	31.25	AEROSIL	3
5	MCC PH101	48.575	EUDRAGIT RSPO	30
6	MAGNESIUM STEARATE	0.5	EUDRAGIT RLPO	-
7	SODIUM BICARBONATE	25	EUDRAGIT RS100	-
8	POLYSORBATE 80	0.375	Na CMC	-
9	HPC-L	1.25	SODIUM ALGINATE	-
10	SUNSET YELLOW	0.3125	HPC KLUCEL HF	-
11	PURIFIED WATER	q.s	PVPK 90	-
	TOTAL WEIGHT	214	ETHYL CELLULOSE	-
12			TALC	3
13			IPA	Q.S
14			PURIFIED WATER	Q.S
15			TOTAL WEIGHT	286

Table 19 Post compressional parameters observed from the bilayered tablets of SFMS

SL. NO.	Parameter	Observed Value
1	Average Weight (mg)	494.7±0.866
2	Thickness (mm)	5.89±0.136
3	Hardness (KP)	8.3±0.348
4	% Friability	0.646
5	FLT (sec)	785
6	TFT (hr)	>20
7	DT of sucralfate layer	2.02±0.157

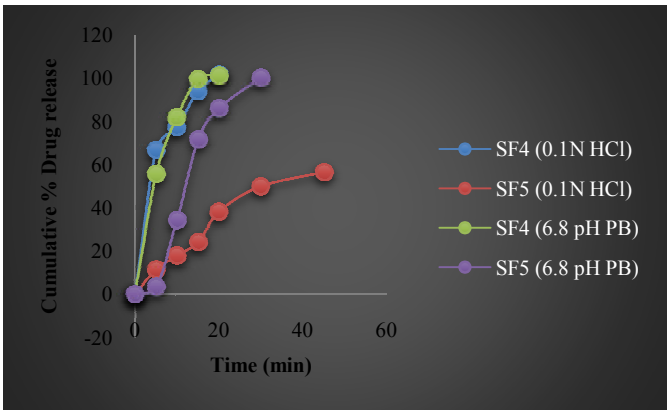

Figure 1 Cummulative drug release study of SF4 and SF5 in presence of 0.1 HCL and 6.8 Phosphate buffer.

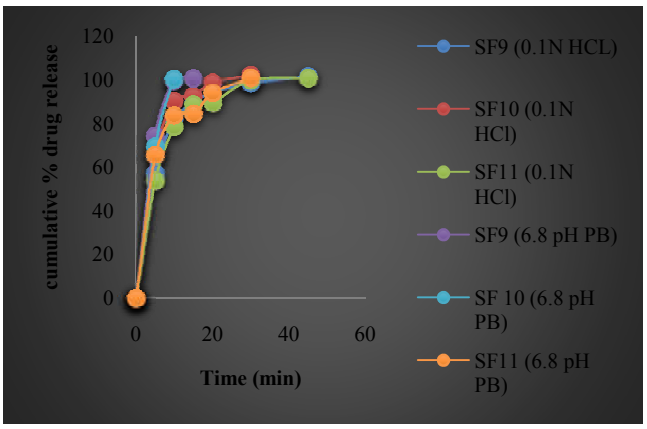

Figure 2 Cummulative drug release study of SF9,SF10 and SF11 in presence of 0.1 HCL and 6.8 Phosphate buffer.

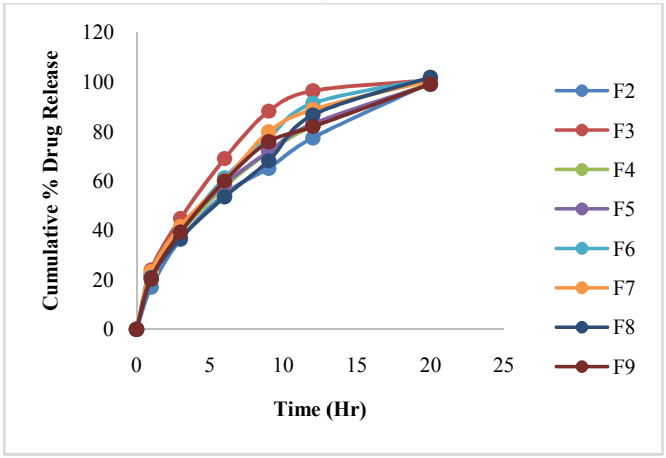

Figure 3 Cummulativ drug release study of (MSF2,MSF3,MSF4,MSF5,MSF6,MSF7,MSF8,MSF9) in presence of 0.1 HCL.

Preparation of Metoprolol Succinate granules

The Metoprolol Succinate floating SR tablets were prepared by wet granulation method. The drug and polymer which were previously passed through 40 mesh were mixed thoroughly in a polybag for 20 minutes. The blend was moistened with granulating fluid *i.e.,* water and IPA (1:9 parts). The wet mass was passed through 24 mesh and then dried in a tray dryer at 50^0C for about 50 minutes until the % LOD becomes less than 2%. The dried granules were passed through 30 mesh and mixed with sodium bicarbonate in a polybag for 10 minutes. To this talc (previously passed through 60mesh) was added and mixed well for 10 minutes. The flow properties of the lubricated granules were evaluated.

Flow Properties of Lubricated granules

The lubricated granules obtained from wet granulation of Sucralfate and Metoprolol Succinate with different excipients are evaluated for flow properties like bulk density, tapped den

Bulk density and Tapped density (g/ml)

The previously weighed pure drug or granules (W) were placed separately into a graduated measuring cylinder and the

initial (bulk) volume (V_B) was noted. It was placed in the tapped density tester USP and subjected to constant tapping at a rate of 200drops/min until the difference between the initial and final volumes should be less than 2%. It was recorded as the final (tapped) volume (V_T) and various flow properties were calculated with the following formulae.

Bulk density, $\rho B = \frac{W}{VB}$ Tapped density, $\rho T = \frac{W}{VT}$

Compressibility Index

It was calculated by using the following formula

Carr's Index or Compressibility Index (CI) = $1-\frac{\rho B}{\rho T} * 100$

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

Hausner's Ratio: It is calculated by the following formula;

Hausner's Ratio= $\frac{\rho T}{\rho B}$

The Hausner's ratio below 1.25 indicates good flow property and above 1.25 indicates poor flow property of the powder.

Angle of Repose (Θ): It was determined by using a funnel whose tip was fixed at a constant height (H) of 2.5cm from horizontal surface. The granules and the powder were passed separately through the funnel until the tip of the conical pile touches the tip of the funnel. The radius of the base of the conical pile is measured as R (cm). It is determined with the formula;

Angle of repose (θ) = Tan^{-1} (height /radius).

Acclerater stability study of Lubricated Granules:

Acclerated stability study is done of lubricated granules 10 gm of each formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 3 months. The granules were packed in 85mm HDPE bottles with an oxygen adsorbent, and a desiccant containing silica gel with cotton as filler. The granules were withdrawn after the regular interval of stability period, and evaluated for physical properties**.**

Discard of Unstable Formulation

After Acclerated stability study the unstable formulations are discarded and remain formulations are selected for further studies.

Flow Properties of Lubricated Granules of selected Formulations after 90 days of Stability Studies

The lubricated granules obtained from wet granulation of Sucralfate and Metoprolol Succinate with different excipients are evaluated for flow properties like bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose.

Preparation of Tablet

Preparation of Sucralfate (IR) layer in BIlayer Floating Tablet

The lubricated granules were then compressed by using 16 station tablet compression machine (CADMACH) with 7mm plane round shaped punches.

Preparation of Metoprolol Succinate (SR) tablet

The lubricated granules were compressed by 16 station tablet compression machine (CADMACH) with 13.1mm round concave punches

Evaluation of tablets

The Post comprisal parameters like hardness, thickness,% friability, disintegration time were evaluated for all the prepared tablets. The drug content was determined for all the batches. Dissolution studies were conducted for all formulations.

Weight variation

Twenty tablets were collected randomly and the average weight and individual weight was calculated. The % weight variation was calculated with the following formula.

%Weight variation= Average weight-individual weight/individual weight x100

Thickness

The thickness of the ten tablets was measured in mm by using Vernier calipers.

Hardness

The hardness of the ten tablets was measured by using Varian V K200 Tablet Hardness Testerand is given in the units of KP.

% Friability

Ten tablets were carefully dedusted prior to testing and weighed accurately (Wo). The tablets were placed in the drum of Roche Friabilator (USP). The drum was rotated for 100 times at a speed of 25rpm. The tablets were collected, re-dedusted and accurately weighed (W1). It is calculated form the following formula;

% Friability= $1-\frac{W1}{W0} * 100$

Disintegration Test

The disintegration study was performed for sucralfate tablets by using disintegration apparatus Thermonik DT Tester (USP). For this water was used as the disintegration medium. 6 tablets were placed in 6 tubes of the disintegration apparatus. The time (min) taken for the tablets to disintegrate was noted.

Floating lag time (FLT)

The MS tablets were placed in a beaker containing 250ml of 0.1N HCl and the time (sec) required to float the tablet was observed and recorded as FLT**.**

Total floating time (TFT)

The time (hr) up to which the MS tablet remains buoyant was noted and recorded as TFT.

Determination of swelling index of Metoprolol Succinate Tablets

The previously weighed (W1) tablet was placed in USP apparatus type-I which was immersed in a bowel containing 900ml of 0.1N HCl and maintained at 37 ± 0.2^0C. The tablets

were removed from the basket at regular intervals of time (up to 8hrs with 1 hr interval) and placed on a blotting paper to remove the excess medium The tablet was reweighed (W2). The studies were repeated for all formulations in triplicate. The swelling index was calculated as Swelling Index = W2-W1/W1 x 100

Determination of drug content of Sucralfate and Metoprolol Succinate Formulations

Ten SF tablets were weighed accurately and then crushed well in a clean motor and pestle. The powder equivalent to 25mg of the drug was weighed (Ws) and then transferred to a 100ml volumetric flask. 50ml methanol was added and sonicated for 5 minutes at 27^0C. Then the volume was made up to 100ml using methanol (V4). From this 4ml (V5) was transferred to a 100ml volumetric flask and the volume was made up to 100ml (V6) with 0.1N HCl (pH 1.2). The flask was agitated for 5 minutes and then the sample was analyzed for drug content at 281nm using UV Spectrophotometer. The drug content was calculated using the following formula.

% Drug Content= $\frac{AS}{AS} * \frac{W}{V1} * \frac{V2}{V3} * \frac{V4}{WS} * \frac{V6}{V5} * \frac{AW}{L} * P$

Where,
AS= Test absorbance
AS= Standard Absorbance
W= Weight of standard drug (25mg)
V1= Volume of solvent added to standard stock solution (100ml)
V2, V3= Dilution of the standard stock solution (4ml of stock solution diluted to 100ml with solvent)
AW= Average weight of the tablet (mg)
L= Label claim of the drug (10mg)
P = Potency of sucralfate (91.4%).

Release Kinetic profile of Sucralfate and Metoprolol Succinate

Formula for determination of percentage of release of drug from in vitro dissolution testing:
Concentration of drug (µg/ml)= (slope × absorbance) ± intercept

Amount of drug released mg/ ml = Concentration × Dissolution bath volume × dilution factor/1000.
Cumulative percentage release (%) = Volume of sample withdrawn (ml)/bath volume (v) × P (t – 1) + Pt
Where Pt = Percentage release at time t
Where P (t – 1) = Percentage release previous to 't'

Acclerated stability study of formulation of Sucralfate and Metoprolol Succinate.

Acclerated stability study is done of 10 Tablets of each formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 90 Days..The tablets were packed in 85mm HDPE bottles with an oxygen adsorbent, and a desiccant containing silica gel with cotton as filler. The granules were withdrawn after the regular interval of stability period, and evaluated for physical properties**.**

Selection of best formulation of Sucralfate and Metoprolol Succinate.

According to Accelerated stability study of lubricated granules and Post compressional parameters and Accelerated stability study of compressed tablets one formulation of Sucralfate and one formulation of Metoprolol Succinate is selected.

Preparation of Bi-layered tablets of SFMS

Sucralfate layer and Metoprolol Succinate layer, Bilayered Floating tablets were prepared.The Bi-Layered tablets of Sucralfate and Metoprolol Succinate (SFMS) were compressed using 13.1mm round concave punches using a Bi-Layered Tablet Compression Machine. The granules of Metoprolol Succinate were placed first and pre-compressed with slight hardness of about 4-5KP. Then the granules of Sucralfate were placed and compressed with a final hardness of about 12-14 KP. The compression of Bi-Layered Tablet is based upon Composition of optimized Sucralfate layer and composition of optimized Metoprolol Succinate layer ,

The post compressional parameters of SFMS tablets

The post compressial parameters ; Average weight, Thickness, Hardness,% friability, FLT, TFT, DT of Sucralfate Layer is determined**.**

Acclerated Stability study of SFMS bi Layered Tablets

10 Tablets of SFMS Bi-layered tablets were subjected to accelerated stability studies at 45^0C and 75% RH for a period of 90 Days. The tablets of SFMS were packed in 85mm HDPE bottles with an oxygen adsorbent, a molecular sieve and a desiccant containing silica gel with cotton as filler.

RESULT AND DISCUSSION

Flow Proreties of Lubricated Granules

The lubricated granules obtained from wet granulation of Sucralfate and Metoprolol Succinate with different excipients are evaluated which produce better flow properties .

Accelerated stability study of Lubricated Granules

Acclerated stability study is done of lubricated granules 10 gm of each formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 90 days it is found that (SF4,SF5,SF9,SF10,SF11) produce better stability and (MSF2,MSF3,MSF4,MSF5,MSF6,MSF7,MSF8,MSF9) produce better stability.

Evaluation of Tablets

The Post compressional parameters of Sucralfate Tablets

It shows all the selected formulations of Sucralfate fulfil the parameters of post compressial studies.

The Post compressional parameters of Metoprolol Succinate Tablets

Buoyancy study of Metoprolol Succinate

In vitro Buoyancy study of selected formulations of MSF,it produce better Floating Lag Time Total FloatingTime and other parameters of post compressial studies.

Swelling index of Metoprolol Succinate

Swelling index values observed that at it is gradually increasing according to increase of time period. .All the formulations produce near abut 200 % at 8 hours.

Drug content of Sucralfate and Metoprolol Succinate Tablets

Avrage drug content of Sucralfate formulations is (99.57+98.15+100.14+100.56+100.3=498.72/5=99.74 %)
Avrage drug content of Metoprolol Succinate formulations is (101.61+101.87+98.22+100.65+100.91+100.83+98.65+99.88 =802.62/8=100.32 %)

Selection of best Formulation of Sucralfate and Metoprolol Succinate

According to Accelerated stability study of lubricated granules and post compressional parameters and cumulative drug release study of compressed tablets **SF10 and MSF6** are selected as best formulations.

The Accelerated Stability study of Granules of Optimized Formulations

The accelerated stability study of granules of optimized formulation of Sucralfate and Metoprolol Succinate provide there is no change in physical parameters after 90 days.

Post compressional parameters of SFMS Bilayered Floating Tablet

After optimization of Sucralfate and Metoprolol Succinate formulations The Bilayered Floating Tablet is prepared and post compressional parameters are studied and found that the Disintigration Time of Sucralfate is 2.02±0.157 in Stomach medium and F.L.T of Meto proplol Succinate is 785 sec and T.F.T is >20 hours.

CONCLUSIONS

The result of present study indicate that after various types of in vitro and in vivo evaluation from 15 formulations of Sucralfate and 10 formulations of Metoprol Succinate ,the combination of formulations (SF10+MSF6) provide the better properties of Bi layer floating tablet. The present study can generate a new scope in optimization of formulations and clinical trials and can produce better identification in Gastro Retentive Drug Delivery System.

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