Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

DESIGN AND CHARACTERIZATION OF GASTRO RETENTIVE FLOATING TABLETS OF SUMATRIPTAN SUCCINATE

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ABSTRACT

The aim of this study was to for mulate and evaluate sumatriptan floating drug delivery system. The floating tablets of Sumatriptan were prepared by using HPMCK15M, HPMCE15LV, Carbopo l940 polymers. The pre compression and post compression evaluation were performed asperpharmacopoeial standards. The tablets were prepared by direct compression method. Dissolution measurements were carried out in a (USP) dissolution testing apparatus II. Compatibility study was performed by FTIR. The compatibility study of the prepared Sumatriptan floating tablets confirms that there is no interaction between the drug and polymers used. The cumulative drug release was performed in order of kinetics. The drug release kinetics was observed by Non-fickian diffusion mechanism. The floating lag time were found to be significantly increased with the increasing concentration of the polymers. When compared to the other formulation depends on dissolution profile HPMCE15 was shows better effect. The release kinetic data implies that here lease mechanism of all the formulations was Non-fickian. It may be used to extended period of drug release for at least 12h, that's way improving the bioavaibility and patient compliance.

KEYWORDS

Sumatriptan Gastro retentive, Floating drug delivery and Sustained release.

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INTRODUCTION

The aim of controlled release and sustained release to increase the therapeutic effectiveness of drug by its site of action and reduce the dose and delivery of drug is uniformed[1]. The current controlled release technology had madeitpossible to release drug sata constant release rate for longer periods of time ranging from daystoyears[2]. However, this benefit had not satisfied a variety of important drugs that (i)

are locally active in the stomach, (ii) have an absorption window in the stomach or in the upper small intestine, (iii) are unstable in the intestinal or colonic environment, or (iv) exhibit low solubilities at high pH values[3]. The dosage form significantly prolonged gastric residence and controlled release. Besides being able to continually and sustainably deliver drugs to the small lintestina lab sorption window, the improvements provided from GRDDS include: achieving a greater and prolonged the rapeutic effect and thus reducing the frequency of administration periods, providing a more effective treat men to flocal stomach disorders, and minimizing both lower-tract in activation of the drug and drug effects on the lower intestinal flora[4].

Floating drug delivery systems (FDDS) or hydro dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach based on high density and low density of polymers[5]. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach[6]. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. The gastric content are needed to buoy anent of system[7]. Many buoy ant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres[8].

Sumatriptan is widely prescribed as an anti migraine. It is a selective agonist of vascular serotonin ((5-hydroxytryptamine; 5-HT) type 1-like receptors. It is an effective and popular drug for relieve migraine symptoms[9]. Sumatriptan is al so used for treatment of relieve head ache, pain, and other symptoms. There commended dose of Sumatriptan is 25 mgorally. As biological halflife shorter it is poor candidate for sustained release drug delivery system[10]. Thus a sustained release dosage form of Sumatriptan is desirable, as biological half-life of Sumatriptan is about (2.5 hours). This favors development to fsustained release formulation[11].

Traditional oral sustained formulations have a drawback that it cannot release a drug at specific site. Its absorption window is either in colon or through the GIT. This leads to poor absorption of drug, and this affects the therapeutic effect of the drug. Sumatriptan is a pro-kinetic drug and it acts mainly on GIT and CNS[12]. It has more prominent effect on upper part GIT. And sustained release dosage forms are designed to complement the pharmaceutical activity of medicament in order to achieve better selectivity and longer duration of action. So Sumatriptan is chosen for the present study[13].

A serotonin agonist that acts selectively at 5HT1 receptors. It is used in the treatment of migraine disorders. A transdermal patch version of sumatriptan is currently in phase I trials in the U.S. The 5-HT_{1B} and 5-HT_{1D} receptors function as auto receptors, which inhibit the firing of serotonin neurons and a reduction in the synthesis and release of serotonin upon activation. After sumatriptan binds to these receptors, adenylacyclase activity is inhibited via regulatory G proteins, increases intracellular calcium, and affects other intracellular events[14]. This results in vasoconstriction and inhibition of sensory nociceptive (trigeminal) nerve firing and vaso-active neuropeptide release[15].

MATERIAL AND METHODS

Materials

Sumatriptan was a generous gift from Spectrum Pharma labs Hyderabad, Hydroxyl propyl methyl cellulose, Carbopol 940, Avicel, Sodium bicarbonate, Lactose, Mg-Stearate, Talc, Hydrochloric acid were obtained from S.D fine chemicals, Mumbai.

Methods

Preparation of Sumatriptan floating tablets by compression method

Sumatriptan floating was prepared by direct compression technique using drug and variable concentration of polymers (HPMCK4M, HPMCE15LV, Carbopol 940, Sodium Bicarbonate, MCC, Lactose, Mg-stearate, and Talc). The respective powders and optional additives were

blended thoroughly with a mortar and pestle. The powder blended was then lubricated with Mg-stearate and purified talc and then compressed on a tablet punching machine.
Total weight = 200mg

RESULTS AND DISCUSSION

Drug – excipients compatibility studies

The IR spectrum of pure drug was found to be similar to the standard spectrum of Sumatriptan. Compatibility studies were performed through FTIR spectroscopy. The IR spectrum of pure drug and physical mixture of drug and polymer was studied. The character is tic absorption peaks of Sumatriptan obtained were obtained at 4000-500cm-1. It has been observed that there is no chemical interaction between Sumatriptan and polymer's used. It was observed that peak obtained in spectra drug and polymers. Which show there were nointer action between drug and polymers?.

Standard calibration curve of Sumatriptan using 0.1 N HCL

100mg drug was accurately in 100ml volumetric flask. It was dissolved in 0.1N HCL to gives 1000µg/ml. the standard stock solution stock solution was then serially diluted with 0. 1NHCL to get 1 to 10µg/ml of Sumatriptan. The absorbance was measured against 0. 1NHCL as blankat 225nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Different Drug Release Kinetics Model for Sumatriptan Floating Tablets

Regression coefficients fit to different drug release kinetics models for Sumatriptan floating tablets. The present study is an attempt to develop floating tablets of Sumatriptan, with different polymers which hre leases a therapeutic amount of Sumatriptan to the proper site in the body and also to achieve and maintain the desired Sumatriptan concentration. Direct compression method was used for formulation of floating tablets, also different types of polymers like HPMC (HPMCK15M, HPMCE15LV), Carbopol 940 were studied. These polymers were widely used gel forming polymers. There lease rate could effectively be modified by varying the "polymer" concentration. By using HPMCE15LV they gave optimum FLT as well as long acting effect. It was found that the tablet formulation retarded the drug release for12h as desired.

The results of the drug-excipients compatibility by FTIR studies revealed that there was nochemical interaction between the pure drug and excipients. The Pre compression parameters like bulk density, tapped density, Carr's index and angle of repose were determined. The final formulation showed acceptable flow properties. The post compression parameters like the thickness, hardness, friability, weight variation, content uniformity, FLT and TFT and *In vitro* release, were carried out and the values were found to be within IP limits. Thus it is summarized and concluded that HPMC E15LVcan be successfully used in formulation of Sumatriptan sustained release gastro retentive floating tablets.

Table No.1: Formulation of Sumatriptan floating Tablets

S.No	Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	DRUG	25	25	25	25	25	25	25	25	25	25	25	25
2	HPMCE 15 LV	---	---	---	25	30	45	20	20	20	---	---	---
3	HPMC K15M	25	30	45	---	---	---	---	---	---	20	20	20
4	CARBOPOL 940	---	---	---	---	---	---	10	15	20	10	15	20
5	MCC	65	65	65	65	65	65	65	65	65	65	65	65
6	$NAHCO_3$	20	20	20	20	20	20	20	20	20	20	20	20
7	MG -STERATE	2	2	2	2	2	2	2	2	2	2	2	2
8	TALC	3	3	3	3	3	3	3	3	3	3	3	3
9	LACTOSE	60	55	40	60	55	40	55	50	45	55	50	45

Table No.2: Pre-Compression Evaluation of Sumatriptan Floating Tablets

S.No	Formulation code	Angle of repose (θ)±SD	Bulk density $_3$ (gm/cm) ±SD	Tapped density $_3$ (gm/cm) ±SD	Hausnerratio (HR)±SD	Carr index (Ic)±SD
1	F1	22.46±0.726	0.221±0.010	0.261±0.010	1.180±0.010	15.398±0.596
2	F2	24.08±0.556	0.223±0.020	0.260±0.010	1.150±0.060	15.794±0.359
3	F3	22.49±0.471	0.232±0.016	0.270±0.026	1.190±0.010	16.018±0.640
4	F4	22.64±0.746	0.250±0.010	0.267±0.015	1.127±0.005	11.707±0.514
5	F5	23.68±0.312	0.232±0.011	0.300±0.010	1.198±0.009	16.678±0.560
6	F6	22.84±0.665	0.220±0.010	0.262±0.011	1.127±0.006	11.407±0.513
7	F7	22.26±0.825	0.210±0.010	0.262±0.010	1.180±0.010	15.397±0.593
8	F8	21.76±0.645	0.230±0.011	0.250±0.010	1.190±0.010	16.016±0.640
9	F9	21.68±0.346	0.221±0.005	0.281±0.012	1.204±0.004	17.657±0.734
10	F10	22.79±0.934	0.227±0.010	0.266±0.005	1.175±0.005	15.000±0329
11	F11	22.91±0.471	0.230±0.010	0.270±0.010	1.170±0.010	14.828±0.550
12	F12	22.89±0.520	0.225±0.011	0.260±0.010	1.165±0.030	15.399±0.594

All the values are expressed as mean± SD. (n=3)

Table No.3: Post Compression Evaluation of Sumatriptan floating tablets

S.No	Formulation code	Weight variation Average wt in (mg)±SD	Hardness (Kg/cm^2) ±SD	Diameter in(mm) ±SD	Thickness in(mm) ±SD	Friability (%)±SD	Drug content uniformity (%)±SD
1	F1	199.58±0.933	4.258±0.208	9.32±0.577	2.238±0.058	0.756±0.057	99.686±0.613
2	F2	200.4±0.882	4.942±0.115	9.31±0.577	2.141±0.067	0.584±0.055	97.571±0.407
3	F3	196.6±0.825	4.856±0.115	9.64±0.577	2.231±0.055	0.757±0.015	99.040±0.819
4	F4	200.05±0.887	5.063±0.155	9.00±0.000	2.250±0.000	0.670±0.010	99.487±0.147
5	F5	200.3±0.833	4.800±0.200	8.66±0.577	2.271±0.057	0.769±0.011	98.590±0.391
6	F6	200.2±0.951	4.942±0.115	8.64±0.577	2.119±0.010	0.764±0.090	97..350±0.306
7	F7	199.98±0.887	4.864±0.115	9.00±0.000	2.235±0.049	0.740±0.060	98.741±0.228
8	F8	200.2±0.833	4.464±0.115	8.65±0.577	2.874±0.052	0.767±0.011	98.148±0.503
9	F9	200.15±0.812	4.734±0.115	8.64±0.577	2.886±0.057	0.660±0.010	98.435±0.119
10	F10	200.1±0.852	4.942±0.115	8.65±0.577	2.254±0.000	0.778±0.017	97.421±0.355
11	F11	200.14±0.812	4.643±0.115	9.00±0.000	2.200±0.100	0.660±0.010	95.514±0.130
12	F12	200.13±0.745	4.800±0.200	8.64±0.577	2.350±0.100	0.780±0.010	96.162±0.678

All the values are expressed as mean± SD. (n=3)

Table No.4: *In-Vitro* Drug Release Studies

Time	% Cumulative release											
	FT1	**FT2**	**FT3**	**FT4**	**FT5**	**FT6**	**FT7**	**FT8**	**FT9**	**FT10**	**FT11**	**FT12**
1	9.16	7.10	7.78	14.88	15.16	10.05	11.68	9.78	8.56	11.21	12.24	11.54
2	12.38	11.51	11.21	21.91	22.73	17.87	18.89	10.89	12.42	18.43	14.53	14.73
3	19.44	15.34	16.73	27.18	29.08	25.44	23.08	15.74	16.27	27.81	22.54	22.16
4	23.68	20.32	20.13	38.42	34.02	33.54	30.34	18.36	22.52	37.54	31.24	26.83
5	31.71	27.38	23.52	45.73	42.08	38.61	37.73	22.06	27.56	48.62	42.24	34.74
6	37.85	33.78	29.29	51.54	50.83	49.14	44.74	27.15	34.78	57.64	46.45	45.34
7	42.21	36.61	37.56	62.31	58.52	58.08	51.74	36.17	38.36	67.56	52.14	54.7
8	47.76	44.81	45.54	71.33	68.35	65.21	59.77	43.84	47.57	71.53	63.84	60.3
9	60.53	53.52	52.54	75.81	73.76	68.48	66.52	54.53	55.48	77.61	71.24	66.46
10	69.39	63.31	61.08	83.44	80.85	76.30	72.05	65.73	63.36	81.41	75.33	72.42
11	73.37	71.64	69.75	89.24	85.81	82.14	78.20	73.43	73.41	86.56	81.45	77.54
12	80.40	77.42	74.62	95.08	91.63	88.68	87.49	81.24	78.47	91.63	84.65	82.74

All the values are expressed as mean± SD. (n=3)

Table No.5: Kinetics Drug Release Studies

S.No	Formulation code	Zero order	First order	Higuchi	Peppas
		r^2	r^2	r^2	r^2
1	F4	0.983	0.902	0.979	0.987

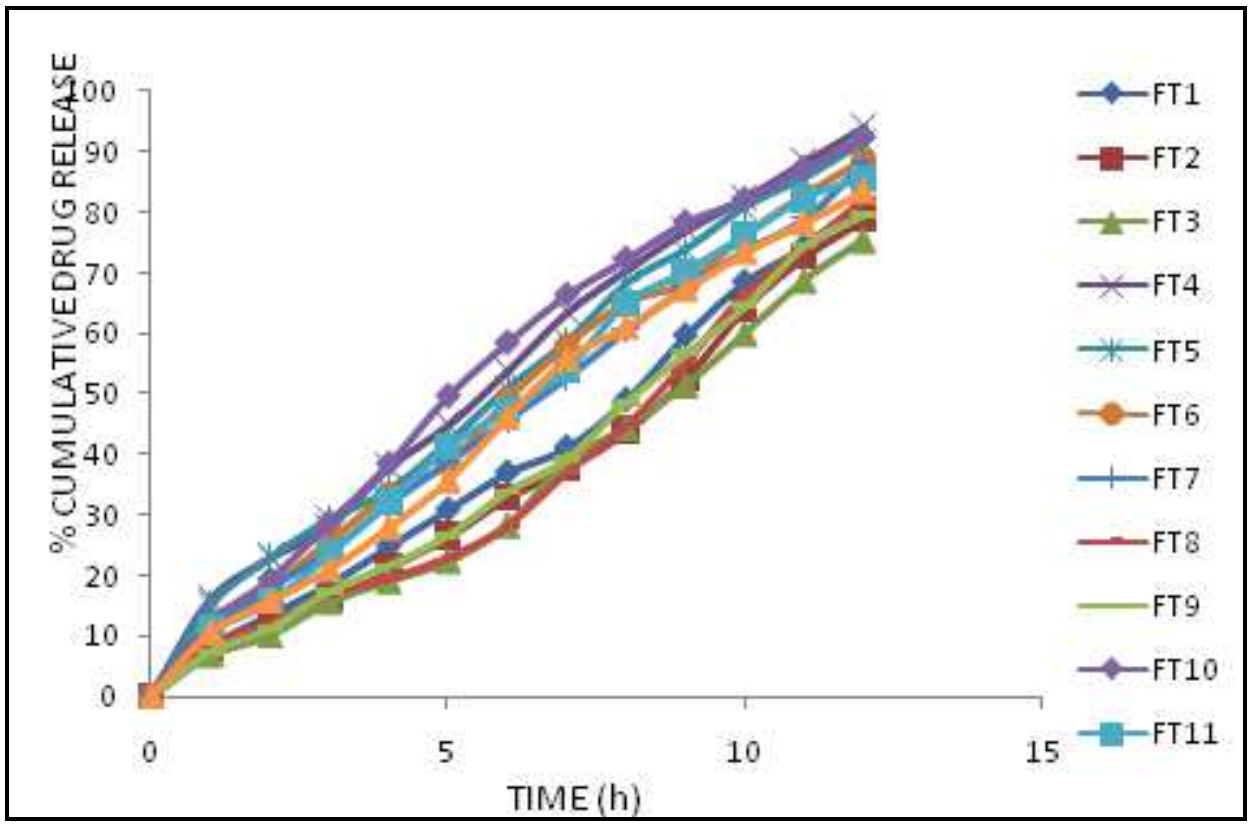

Figure No.1: *In-vitro* drug release profile of Sumatriptan floating tablets of batches F1 to F12.

Drug Release kinetics of Sumatriptan F4

Time(h)	F4
0	0
1	14.886
2	21.914
3	27.188
4	38.424
5	45.731
6	51.542
7	62.312
8	71.331
9	75.814
10	83.443
11	89.242
12	95.089

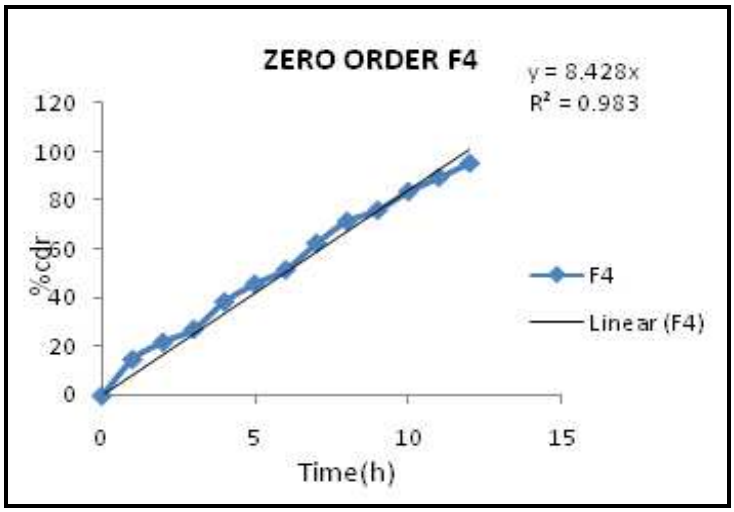

Figure No.2: Zero order release kinetics

First order release kinetics data of Sumatriptan floating tablets

Time	Log % cdr remaining
1	1.930001001
2	1.892573176
3	1.86220296
4	1.789411474
5	1.734551819
6	1.685365486
7	1.575972562
8	1.457412545
9	1.383564049
10	1.218981649
11	1.03173154
12	0.691169934

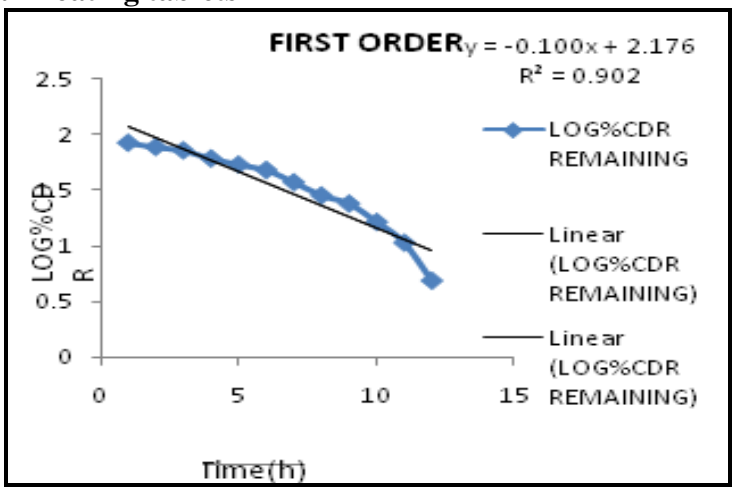

Figure No.3: First order release kinetics of Sumatriptan F4

CONCLUSION

From the compatibility studies, it is concluded that HPMCE15LV, HPMCK15M, Carbopo l940 were compatible with drug Sumatriptan and thus suitable for the formulation of Sumatriptan floating tablets. Sumatriptan tablets were fabricated by direct compression method. *In-vitro* buoyancy studies were performed for all the formulations, F1 to F12 by using 0.1NHCL solution sat 37^0C. Tablet containing HPMC (F4) showed good buoyancy with very short lag time and long floatation time of more than 12hrs in 0.1NHCL. *In-Vitro* release study is performed for 12hrs. Optimized formula containing HPMC E15LV (F4) showed better release compare too ther formulations and it followed zero order kinetics. The non-Fickian diffusion was confirmed as the drug release mechanism from this formulation.

From this study, it was concluded that HPMCE15LV can be used in formulation of Sumatriptan sustained release gastro retentive floating drug delivery system. Overall, this study concludes that viscosity of the polymer is a major factor affecting the drug release and floating properties of FDDS.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Department of Pharmaceutics, Faculty of Pharmacy, Anurag Group of Institutions, School of Pharmacy, Ghatkesar, Medchal, Hyderabad, India for providing necessary facilities to carry out this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Chandra Sekhar. Pabbathi *et al.* Design and characterization of gastro retentive floating tablets of sumatriptan succinate, *International Journal* of *Research in Pharmaceutical and Nano Sciences,* 6(6), 2017, 287-293.