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Design and evaluation of bilayer Floating tablets of Metronidazole and Rantidine

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ABSTRACT

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the GIT. It retains the dosage form at the site of absorption and thus enhances the bioavailability. The aim of the present study was to design and evaluate bilayer Floating tablets of Metronidazole and Rantidine. An attempt was made to develop bi-layer tablet suitable for delivering different drugs with different release pattern like one layer of drug as immediate release to get quick relief and second drug as sustained release of drug which gives effect of drug for sufficient long time and reduce frequency of dose. The Bilayered tablets containing Rantidine and metronidazole were successfully prepared by direct compression method respectively.

Keywords: Bi-layered floating tablets, Bioavailability, Metronidazole and Rantidine.

INTRODUCTION

A solid dosage form is drug delivery system that incorporates tablets, capsules, sachets and pills and in addition a mass or unit-measurement powders and granules [1]. Among the different dosage forms oral solid dosage forms have more prominent significance and involve a prime part in the pharmaceutical market. Oral course of drug organization is broadly satisfactory and drugs managed orally as solid dosage form speaks to the favored class of items [2]. More than 90% of drugs formulated to create systemic impacts are delivered as solid dosage forms. In light of these reason at whatever point New chemical entity (NCE) has found, which demonstrates an adequate pharmacological activity, first the pharmaceutical organization asks whether the drug is effectively regulated by oral route of administration. The oral route of administration still continues to be the most preferred route due to its manifold advantages including:

Tablets and capsules represent unit dosage forms in which the accurate dose of drug to show sufficient pharmacological action can be administered [3]. In case of liquid oral dosage forms such as Syrups, Suspensions, Emulsions, Solutions and Elixirs the patient is asked to administer the medication of 5-30 ml. Such dosage measurements are typically error by factor ranging from 20-50 %, when the drug is self

administered by patient. Solid dosage forms are less expensive to shipping and less prone for the degradation when compared to liquid dosage forms[1].

MATERIALS & METHODS

Formulation development

The pharmaceutical development studies have to be carried out with the purpose of selecting right dosage form and a stable formulation [7]. These studies give detailed description of all the steps involved in the process of formulation development [4]. Such details are intended towards identifying critical parameters involved in the process, which have to be controlled in order to give reliable and reproducible quality product.

Formulation of bilayer tablet (floating layer)

The Floating tablets were set up by direct compression strategy. As appeared in Table powder blends of Rantidine microcrystalline cellulose, polymers and sodium bicarbonate were dry mixed for 20 min took after by expansion of Magnesium Stearate and Powder [5]. The blends were then additionally mixed for 10 min., 350mg of resultant powder mix was physically compressed utilizing KBr water powered press at a pressure of 1 ton, with a 9mm punch and bite the dust to get the tablet..

Composition of floating layer

Table no. 1 formulation table for floating layer

Ingredients(mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7
Rantidine	150	150	150	150	150	150	150
NaHCO3	52.5	52.5	52.5	52.5	52.5	52.5	52.5
HPMC K100	122.5	-	-	70	-	-	70
Xanthum Gum	-	122.5	-	-	87.5	87.5	-
Guar gum	-	-	122.5	-	-	-	-
EC	-	-	-	52.5	35	17.5	52.5
Talc	7	7	7	7	7	7	7
Magnesium stearate	7	7	7	7	7	7	7
MCC(mg)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	350	350	350	350	350	350	350

Direct compression for immediate layer

Every one of the ingredients were gone through sifter and blended in an mortar and pestle for 30min for uniform blending [6]. The incorporation of ingredients was done in a geometrical way. At that point the Metronidazole layer was compressed utilizing 8mm round punch.

Composition of immediate release layer

Table no. 2 formulation table for immediate release layer

Ingredients (mg)	F_1	F_2	F_3	F_4	F_5	F_6
Metronidazole	200	200	200	200	200	200
Starch	10	10	-	-	-	-
CCS	20	-	20	-	14	30
SSG	-	20	-	20	-	-
PVP K30	-	-	20	20	20	20
Magnesium stearate	10	10	10	10	10	10
MCC	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	400	400	400	400	400	400

EVALUATION OF PRECOMPRESSION BLEND

Angle of Repose

The flow property was controlled by estimating the Angle of Repose. With a specific end goal to decide the flow property, the Angle of Repose was resolved. It is the greatest angle that can be gotten between the free standing surface of a powder heap and the horizontal [10].

Angle of repose= $\tan^{-1}$ (h/r)

Where,

h = height of a pile (2 cm)

r = radius of pile base.

Procedure:

- 20gms of the sample was taken

Evaluation of tablets

The quantitative evaluation and appraisal of a tablets compound, physical and bioavailability properties are imperative in the plan of tablets and to screen item quality [11]. There are different standards that have been set in the different pharmacopeias in regards to the nature of pharmaceutical tablets. These incorporate the measurement, estimate, shape, thickness, weight, hardness, Friability and invitro-disintegration characters.

EVALUATION OF PRE COMPRESSION PARAMETERS FOR FLOATING LAYER OF RANTIDINE

Table no.3 Pre compression parameters

Formulations	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index(%)	Hausner'sratio
F1	29.36	0.35	0.41	14.63	1.17
F2	32.35	0.33	0.4	17.50	1.21
F3	25.21	0.31	0.36	13.89	1.16
F4	27.08	0.34	0.39	12.82	1.15
F5	26.32	0.36	0.42	14.29	1.17
F6	29.51	0.3	0.37	18.92	1.23
F7	27.43	0.35	0.42	16.67	1.20

Tablet No. 4 -Post Compression Parameters for Sustained Release Tablet

Formulations	Weight variation	Hardness	Thickness (mm)	Friability (%)
F1	350	7.5	2.3	0.45
F2	352	7.3	2.5	0.48
F3	349	6.5	2.7	0.50
F4	351	7.6	2.3	0.52
F5	350	7.5	2.1	0.40
F6	348	7.5	2.4	0.49
F7	352	7.3	2.3	0.41

INVITRO DISSOLUTION STUDIES FOR FLOATING TABLETS -

Dissolution study (floating tablets)

In-Vitro Drug Release Studies for Floating tablets

Table No.5. Cumulative drug release of Floating layer

Time(hrs)	F1	F2	F3	F4	F5	F6	F7
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**
0.5	59	36	25	91.42	11.05	25.8	39.5
1	66.8	51.63	37.6	100.2	22.57	37.2	55.9

2	85.1	63.63	49.8	101.6	30.31	43.6	77.3
3	98.7	72.94	66.3		34.73	55.8	86.4
4		86.3	79.8		38.68	63.7	91.5
6		97.5	83.9		50.05	74.9	100.28
8			94		67.1	89.5	
10					84.15	100.34	
12					95.52		

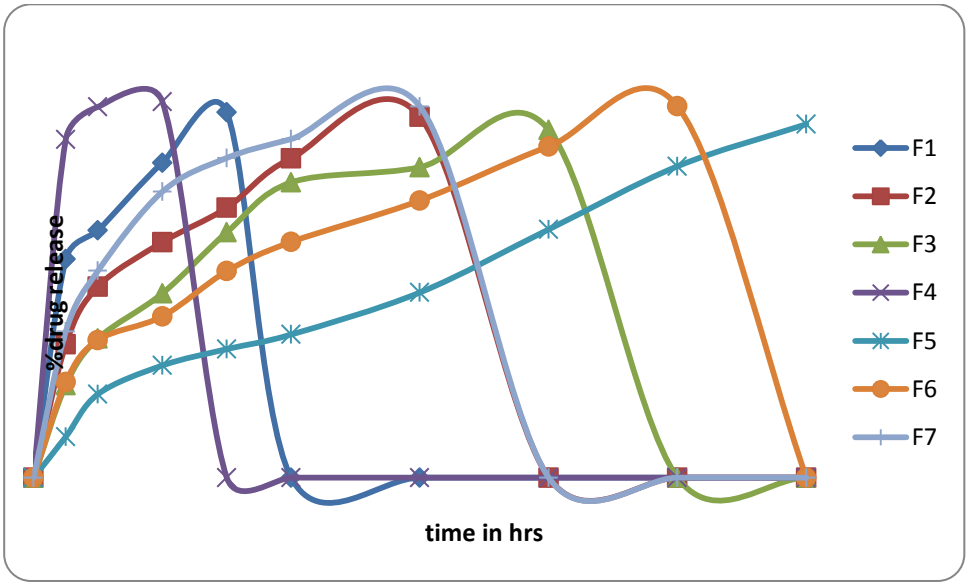

Fig No. 1Dissolution graph for Floating Tablets

Kinetic release models

Table no. 6 Release kinetics for F5 formulation for Floating layer

	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	**Log % Remain Vs T**	**%CDR Vs √T**	**Log C Vs Log T**
Slope	7.300243632	-0.09328534	27.02261421	0.927791717
Intercept	9.46986711	2.068834844	-7.27212068	0.994780181
Correlation	0.988676295	-0.93585635	0.979283304	0.758374413
R 2	0.977480817	0.875827116	0.95899579	0.57513175

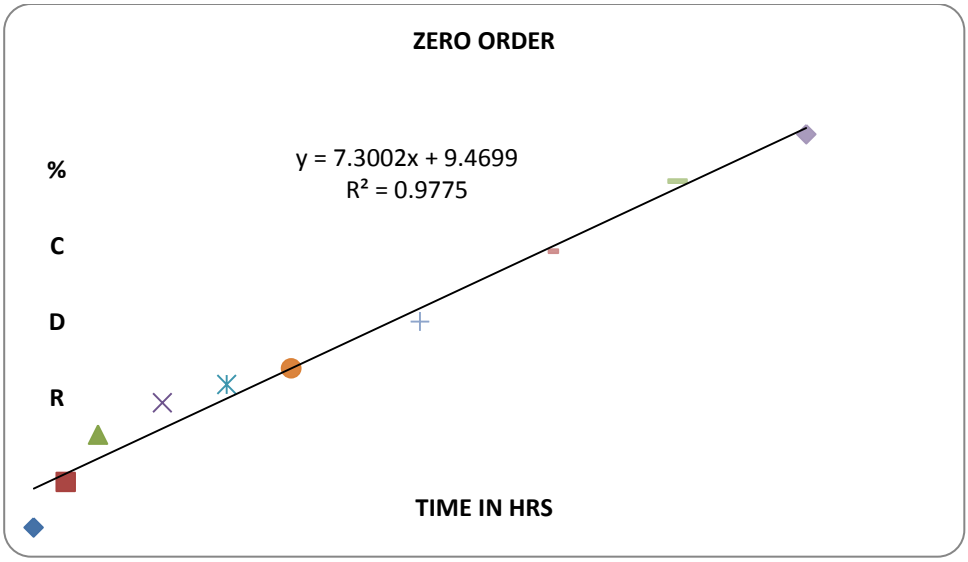

Fig no. 2 Zero order release graph for F5 sustained release formulation

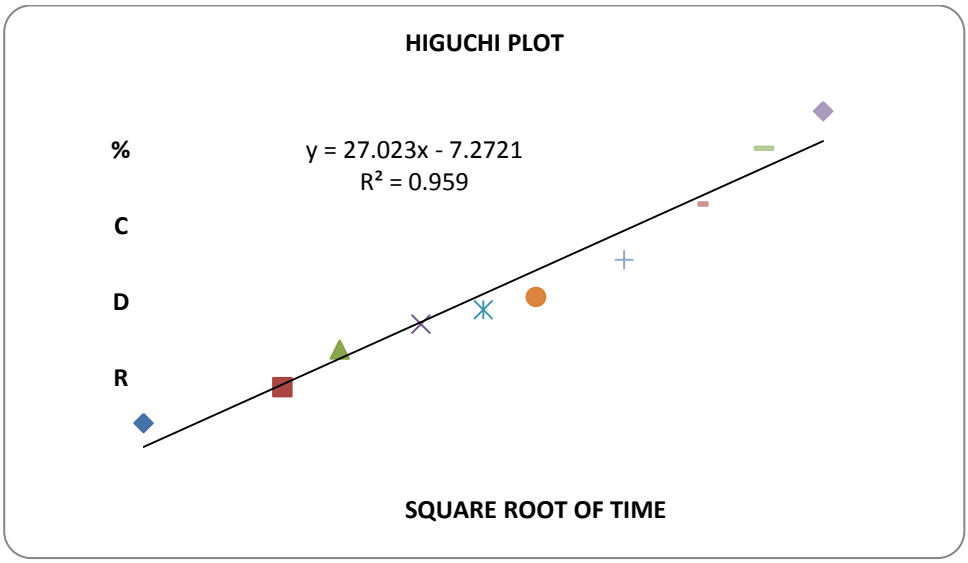

Fig no. 3 Higuchi model graph for F5 sustained release formulation

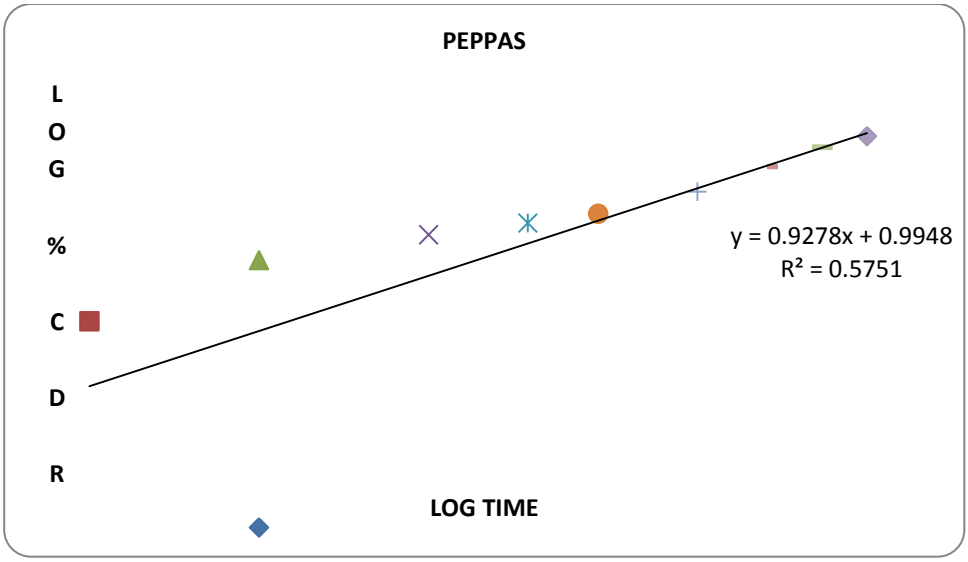

Fig no. 4 Peppas model for F5 sustained release formulation

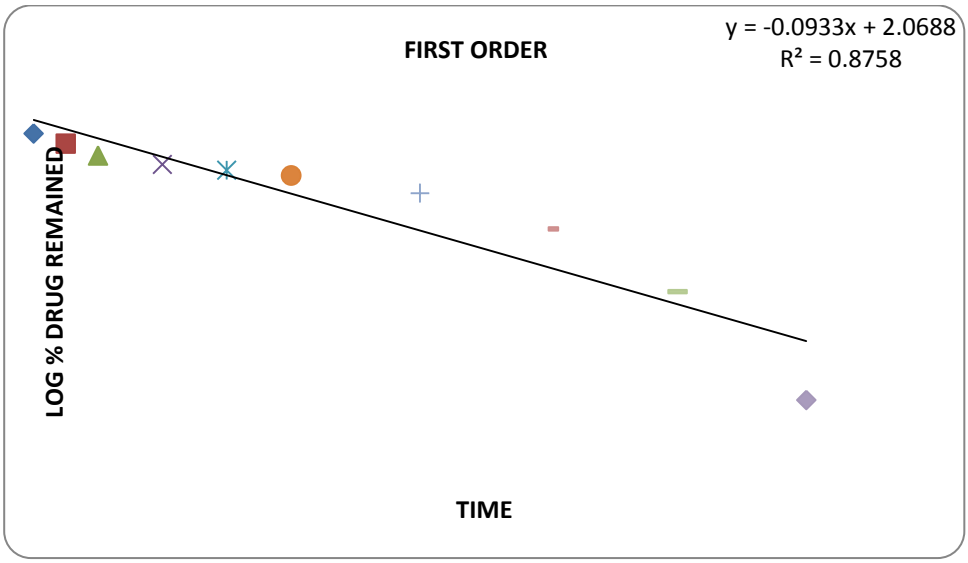

Fig no. 5 First order release graph for F5 sustained release formulation

Discussion for *in-vitro* release of rantidine layer

From the table, it was confirmed that the F1, F2, F3, F4, F6, F7 of floating layer does not fulfill the sustained release theory up to 12 hrs. And also from the table, it was also confirmed that the formulation made with combination of Xanthum and EC (F5) showed maximum drug release up to 12hrs.

EVALUATION CONSTRAINTS FOR INSTANT RELEASE LAYER OF METRONIDAZOLE

Pre compression parameters

Table No. 7 precompression parameters of Metronidazole

Formulations	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density(g/mL)	Carr's Index (%)	Hausner's ratio
F1	25.64	0.33	0.38	13.16	1.15
F2	27.13	0.35	0.41	14.63	1.17
F3	26.34	0.29	0.33	12.12	1.14
F4	27.5	0.32	0.37	13.51	1.16
F5	28.4	0.31	0.37	16.22	1.19
F6	27.9	0.37	0.43	13.95	1.16

Post compression evaluation parameters for immediate release formulation

The results of the uniformity of weight, hardness, thickness and friability of the tablets are given in Table. All the tablets of different batches complied with the official necessities of weight as their weights diverse amid 398 to 402mg. The hardness of the tablets ran from 3.1 to 3.6kg/cm2 and the friability values were under 0.5% showing that the matrix tablets were minimized and hard. The thickness of the tablets extended from to 2.1 to 2.5mm. Accordingly all the physical qualities of the readied tablets were found be for all intents and purposes inside control.

Table No. 8 Post compression parameters for immediate release tablets

Formulations	Average weight (mg)	*Hardness* Kg/cm^2	Thickness (mm)	Friability (%)
F1	400	3.4	2.1	0.29
F2	399	3.5	2.3	0.25
F3	400	3.1	2.5	0.30
F4	402	3.3	2.2	0.41
F5	401	3.6	2.4	0.52
F6	398	3.2	2.2	0.49

Table No. 9 Dissolution for immediate release tablet of Metronidazole

Time	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
5	12.45	11.77	32.77	16.2	11	25.9
10	24.75	20.77	49.2	28.57	21	38.7
15	33.75	30.15	60.75	32.85	40	49
30	46.20	40.2	87.3	49.8	49	54.8
45	60.07	56.77	92.25	72.15	61	76.5
60	66.75	60.15	99	81.75	73	98.3

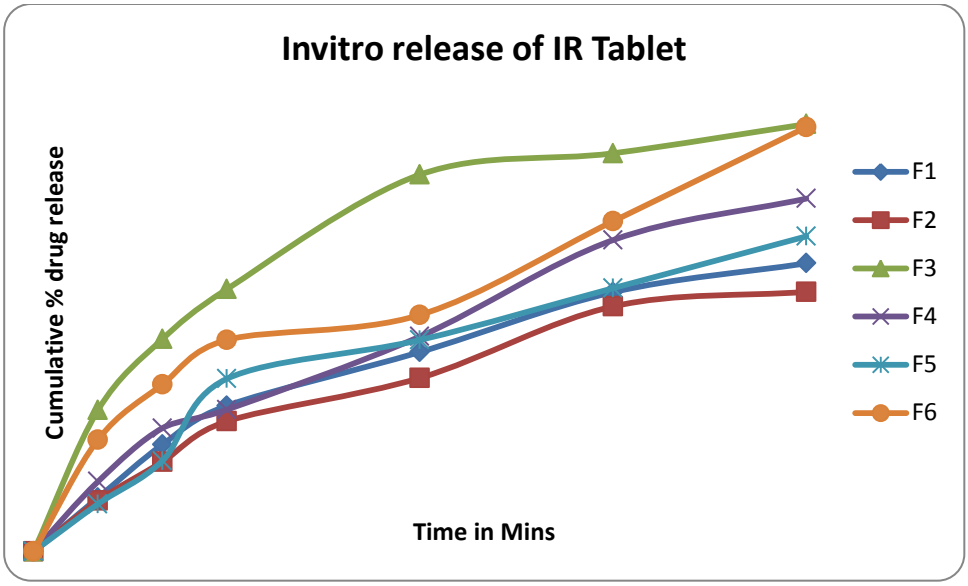

Figure No. 6 Dissolution graph for formulations F1-F6

Bilayered tablet compression

After the batch was optimized in both immediate release layer (F3) and Floating layer (F5).The optimized batch in both was compressed by using same ingredients.

Dissolution study (bilayered tablets)

Dissolution Medium for bilayered tablets

Table No. 10 Dissolution data for bilayered tablet

Time	Bilayered tablet (IR + SR)
0.1N Hcl as dissolution medium for instant release tablets (dose 200mg)	
60min	99.05
0.1N Hcl as dissolution medium for floating tablets (dose 150mg)	
1hr	22.10
2hr	30.60
3hr	33.39
4hr	39.50
6hr	50.31
8hr	66.89
10hr	85.04
12 hr	95.24

CONCLUSION

In this context, of all the formulation the optimized of formulation F5 contains the average thickness of 2.1 average hardness of 7.5, friability of 0.40. The F5 formulation which releases the Rantidine in sustained way in up to twelve hours and Metronidazole immediate release F3 formulation showed 99% release with in 60min. Hence it might be abridged that the tablets arranged by direct compression method for sustained release layer and immediate release layer may be a flawless and viable definition to treat the disorder.

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