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RESEARCH ARTICLE

Formulation and *In-vitro* Evaluation of Terfenadine Non-Effervescent Floating Tablets

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ABSTRACT

The objective of the present work is preparing non effervescent floating tablets. The gas generating agent accrual was added in different concentrations with varying amount of retardation polymers. Chitosan xanthan gum karaya gum was used as retarding polymers. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F9 were formulated and evaluated for various quality control parameters. All the formulations were passed the tests and the results were within limits. From the dissolution data it was evident that formulation F8 was found to be best with maximum % drug release of 98.41% and lag time of 12 hours.

Keywords: Terfenadine, Chitosan, xanthan gum karaya gum & Floating tablets.

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CONTENTS

1. Introduction

The purpose of writing this review on floating drug delivery systems (FDDS) was to compile the recent literature with special focus on the principal mechanism of floatation to achieve gastric retention. The recent developments of FDDS including the physiological and formulation variables affecting gastric retention, approaches to design single-unit and multiple-unit floating systems, and their

classification and formulation aspects are covered in detail. This review also summarizes the in vitro techniques, in vivo studies to evaluate the performance and application of floating systems, and applications of these systems. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

2. Materials and Methods

Chemicals:

Terfenadine, Xanthan gum, Chitosan, Gum karaya, Accural, Micro crystalline cellulose, Magnesium stearate, Talc all the chemicals used were laboratory grade.

Formulation (Or) Preparation Of Floating Tablets Of Terfenadine

Optimization of Accural concentration:

Accural was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of Accural were employed; floating lag time and floating duration were observed. Based on that the concentration of Accural was finalised and preceded for further formulations.

Table 1: Optimized accrual concentration

S.No	Excipient Name	EF1	EF2	EF3
1	Terfenadine	60	60	60
2	Karaya gum	60	60	60
4	Accural	30	60	90
5	Mg.Stearate	4	4	4
6	Talc	4	4	4
7	MCC pH 102	Q.S	Q.S	Q.S

Accural Optimization:

The floating lag time of the EF1 is 65sec, EF2 is 35sec and EF3 is 85sec. Since EF2 has shown less time to float compared to EF1 & EF3. It is considered as the optimised concentration.

Method of Preparation: In this work, direct compression method has been employed to prepare floating matrix tablets of Terfenadine with Chitosan, Karaya gum, Xanthan gum .All the ingredients were accurately weighed and passed through mesh # 60. In order to mix the ingredients thoroughly drug and polymer were blended geometrically in a mortar and pestle for 15 minutes then, Micro crystalline cellulose, Accural, talc and magnesium stearate were mixed one by one. After thoroughly mixing these ingredients, the powder blend was passed through # 40mesh. Tablets were compressed by direct compression method on a multi punch 8 station Rotary tablet compression machine (Cemach, machineries ltd, lab press 8 station, India) using 9mm flat round punches.

Evaluation of post compression parameters for prepared Tablets: The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

3. Results and Discussion

Calibration curve of Terfenadine:

The standard curve of Terfenadine was obtained and good correlation was obtained with R^2 value of 0.998.

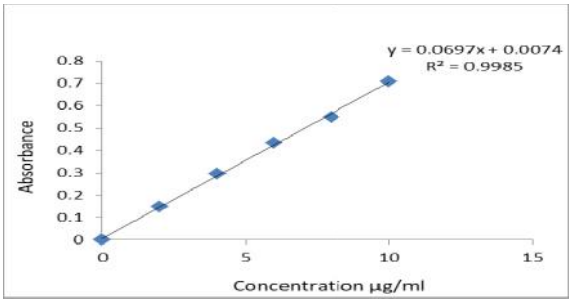

Fig 1: Standard curve of Terfenadine

Pre compression Evaluation Parameters of Terfenadine Floating Formulation Blend:

The powder blends were prepared by mixing of various ingredients mentioned and used for characterization of various flow properties of powder.

Bulk density:

The bulk density of all the formulations was found to be in the range of 0.49 to 0.58(gm/cm3) showing that the powder has good flow properties.

Tapped density:

The tapped density of all the formulations was found to be in the range of 0.57 to 0.69 showing the powder has good flow properties.

Compressibility index:

The compressibility index of all the formulations was found to be ranging between 16 to 18 which shows that the powder has good flow properties.

Hausner ratio: All the formulations has shown the hausner ratio ranging between 0.6 to 1.2 indicating the powder has good flow properties.

Post Compression Evaluation Parameters of Terfenadinefloating Tablets:

Appearance:

The tablets were observed visually and did not show any effect such as capping, chipping and lamination.

Physical characteristics:

The physical characteristics of Terfenadine floating tablets (F1 to F9) such as weight variation, thickness, hardness, friability and drug content were determined and results of the formulations (F1 to F9) found to be within the limits specified in official books.

Thickness:

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness can result in problems with packaging as well as consumer acceptance. There no marked variation in the thickness of tablets within each formulation indicating uniform behaviour of powders throughout the compression process. The thickness of the tablets of all formulations was found to be within the range of 2.5 to 4.0 mm.

Hardness: A difference in tablet hardness reflects difference in tablet density and porosity. The hardness of tablets was found to be in the range of 2.9 Kg/cm2 to 3.5 Kg/cm2.

Percentage friability: Percentage friability of all formulations was found to be in the range of 0.38% to 0.60%.This indicates good handling property of the prepared tablets.

Weight variation:

The average weight of the tablet is 300mg. The pharmacopoeial limit for percentage deviation is ±5%. The weights of all tablets were ranged from 295mg to 306mg.

Drug content:

All the floating tablet formulations shown good uniformity in drug content and they contain 97.2 to 101.33% of Terfenadine which is within the specified limit.

***In-vitro* buoyancy studies:**

To provide in vitro buoyancy, an effervescent approach was selected. Sodium bicarbonate was added as a gas-generating agent. As the dissolution medium (0.1N HCl) imbibed into the tablet matrix, the interaction of acidic fluid with sodium bicarbonate resulted in the generation of CO_2. The generated gas was entrapped and protected within the polymer and thus decreasing density of the tablet. As the density of the tablet falls below 1, the tablet became buoyant. The system should float in a few minutes after contact with gastric fluid to prevent the dosage form from transiting into the small intestine together with food. All the formulations (F1to F9) showed the floating lag time of <146 sec. The results were shown in the table no: 6

***In-vitro* Drug Release Studies:**

The in-vitro dissolution studies of floating tablets of Terfenadine were conducted in simulated gastric fluid 0.1N HCl for 12 hours and The In-vitro drug release data of all formulations shown in table.7. The formulations prepared with Chitosan with the concentrations of 30, 60 , 90 were undergone dissolution.

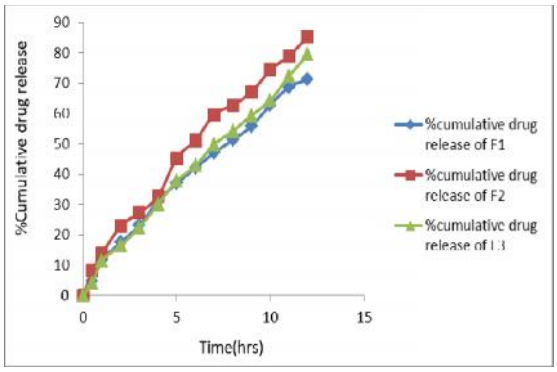

Fig 2:% drug release of formulation (F1-F3)

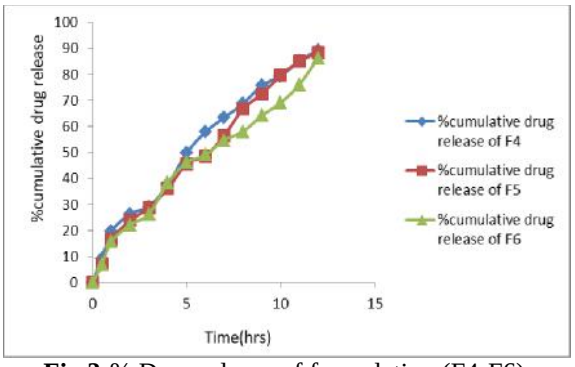

Fig 3:% Drug release of formulation (F4-F6)

The formulations prepared with Karaya gum in with the concentrations of 30, 60, 90 mg were undergone dissolution.

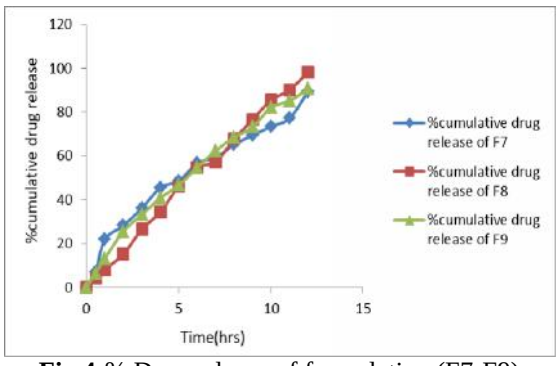

Fig 4:% Drug release of formulation (F7-F9)

The formulations prepared with Xanthan gum in with the concentrations of 30, 60 90 mg were undergone dissolution. Formulation F8 obtained the desired drug release profile with 98.41% and floated with Lag time of 104 sec, for the reasons it was considered as the best formulation. The results were shown in the table no: 7 and figure no: 2,3 4 respectively.

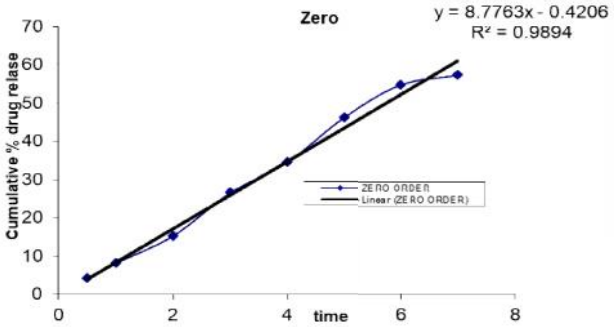

Fig 5: Zero order release kinetics graph

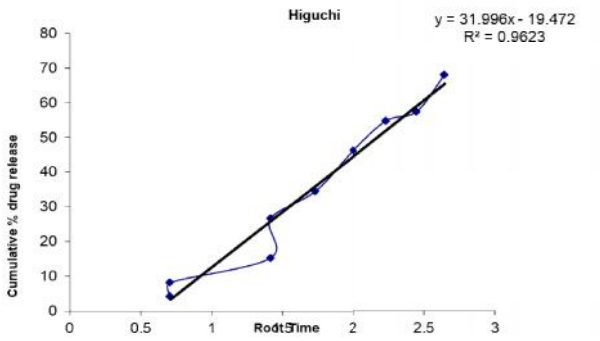

Fig 6: Higuchi release kinetics graph

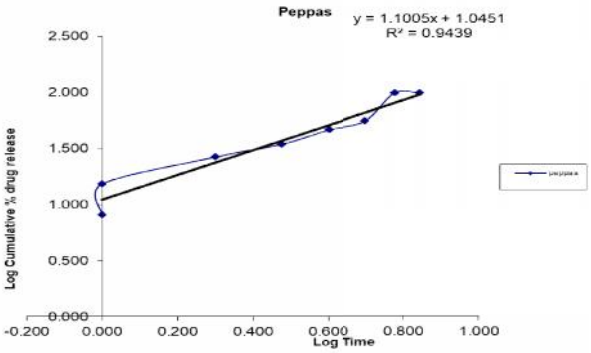

Fig 7: Kars Mayer peppas graph

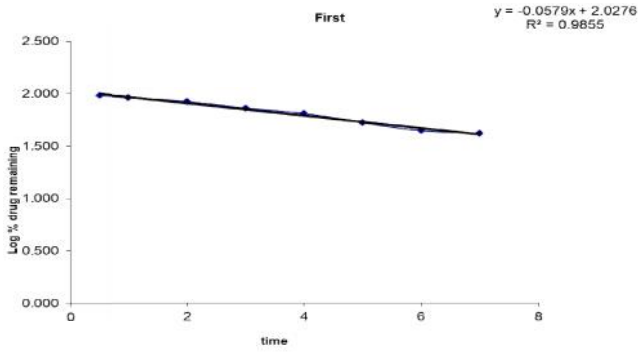

Fig 8: First order release kinetics graph

Table 2: Composition of Floating Tablets of Terfenadine by Using Different Concentrations of Polymers

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Terfenadine (mg)	60	60	60	60	60	60	60	60	60
Chitosan (mg)	30	60	90	-	-	-	-	-	-
Karaya gum (mg)	-	-	-	30	60	90	-	-	-
Xanthan gum (mg)	-	-	-	-	-	-	30	60	90
Accural(mg)	60	60	60	60	60	60	60	60	60
Magnesium Stearate (mg)	4	4	4	4	4	4	4	4	4
Talc (mg)	4	4	4	4	4	4	4	4	4
MCC pH 102 (mg)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	300	300	300	300	300	300	300	300	300

Table 3: Standard Graph values of Terfenadinein 0.1N HCl at 225nm

Concentration (µg/ml)	bsorbance
2	0.149
4	0.295
6	0.435
8	0.549
10	0.708

Table 4: Micromeritic properties of powder blend

ormulation Code	Bulk density	Tapped density	Compressibility Index	ausner's ratio
F1	0.52	0.58	16.01	0.89
F2	0.51	0.69	16.34	0.78
F3	0.49	0.66	16.78	0.69
F4	0.53	0.67	17.06	1.19
F5	0.56	0.57	16.54	1.20
F6	0.55	0.68	17.09	1.04
F7	0.51	0.59	16.33	0.98
F8	0.49	0.57	17.89	1.11
F9	0.52	0.69	18.00	1.19

Table 5: Evaluations of Physical Parameters of Tablets

Formulation Code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Floating lag time (sec)	Floating buoyancy time (hrs)
F1	296	2.7	3.5	0.38	98.81	98	>24
F2	301	3.1	3.6	0.46	98.68	103	>24
F3	298	3.2	3.7	0.57	99.87	105	5
F4	305	2.9	3.5	0.46	96.31	106	7
F5	302	3.2	3.6	0.51	98.01	134	8

F6	304	2.9	3.4	0.49	97.62	105	7
F7	305	3.2	3.5	0.48	98.91	89	5
F8	304	3.1	3.5	0.60	98.21	109	>24
F9	301	3.2	3.6	0.58	98.82	108	>24

Table 6: Drug release data of Terfenadine floating matrix tablets

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	4.73	8.16	4.15	9.27	7.18	7.18	7.23	4.14	6.54
1	11.52	13.72	11.47	19.59	16.59	15.81	21.89	8.13	13.17
2	17.45	22.75	16.49	26.45	23.85	22.27	28.23	15.22	25.58
3	23.11	27.41	22.43	29.19	28.88	26.43	36.16	26.51	33.19
4	31.15	32.67	30.16	37.68	36.16	38.51	45.48	34.46	40.79
5	36.98	45.31	37.72	49.79	45.67	46.14	48.66	46.23	46.69
6	41.95	51.16	42.79	57.89	48.69	49.15	56.59	54.76	54.75
7	47.11	59.71	49.81	63.46	56.61	54.79	59.32	57.31	62.38
8	51.32	62.75	54.25	68.79	66.76	58.14	65.19	67.72	68.54
9	55.91	67.14	59.41	75.77	72.56	64.18	69.47	76.64	73.28
10	62.85	74.39	64.35	79.42	79.56	69.14	73.43	85.53	82.19
11	68.71	79.11	72.41	85.18	85.17	76.19	77.29	90.16	85.14
12	71.21	85.29	79.48	89.49	88.37	86.45	89.54	98.41	90.68

Table 7: Release kinetics data for optimized formulation

Cumulative (%) release Q	Time (T)	Root (T)	Log(%) release	Log (T)	Cumulative (%) release Q
0	0	0.707106781			0
4.14	0.5	0.707	0.910	0.000	4.14
8.13	1	1.414	1.182	0.000	8.13
15.22	2	1.414	1.423	0.301	15.22
26.51	3	1.732	1.537	0.477	26.51
34.46	4	2.000	1.665	0.602	34.46
46.23	5	2.236	1.738	0.699	46.23
54.76	6	2.449	1.989	0.778	54.76
57.31	7	2.646	1.989	0.845	57.31
67.72	8	2.828	1.989	0.903	67.72
76.64	9	3.000	1.989	0.954	76.64
85.53	10	3.162	1.989	1.000	85.53
90.16	11	3.317	1.989	1.041	90.16
98.41	12	3.464	1.989	1.079	98.41

4. Conclusion

The objective of the present work is preparing non effervescent floating tablets. The gas generating agent accrual was added in different concentrations with varying amount of retardation polymers. Chitosan xanthan gum karaya gum was used as retarding polymers. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F9 were formulated and evaluated for various quality control parameters. All the formulations were passed the tests and the results were within limits. From the dissolution data it was evident that formulation F8 was found to be best with maximum % drug release of 98.41% and lag time of 12 hours.

5. Reference

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