



# FORMULATION AND EVALUATION OF CINNARAZINE NON EFFERVESCENT FLOATING TABLETS

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## ABSTRACT

*The objective of the present work is preparing non effervescent floating tablets. Different grades of HPMC polymers HPMC K4M, K15M & K100M were 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-F12 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 F10 was found to be best with maximum % drug release of 97.13% and lag time of 12 hours.*

**KEYWORDS:** *Cinnarizine, HPMCK4M, HPMCK15M, HPMCK100M & Floating tablets.*

## INTRODUCTION

Out of all route of drug administration, oral route is the most convenient and commonly used route. [1] But this route has many problems such as an unpredictable gastric emptying rate, gastrointestinal transit time, and the existence of an absorption window in the upper small intestine for several drugs that way very difficult to prepare such a doses form which stay in the stomach for long period of time. For the solution of such problem, many approaches have been developed such as swelling system, bioadhesive system, floating system, high density approach. [2] Among from all approaches, name of floating system itself suggest its work like it will remain float or buoyant on stomach fluid providing desire retention and drug release.

Cinnarizine is the most widely used drug for management of motion sickness. [3] Chemically, cinnarizine is piperazine derivative which has short half-life (4 to 6 hrs) as well as small dose. [4] Related to pharmacokinetics of cinnarizine which provide anti-histaminic activity and calcium channel blocking

activity by higher affinity towards H1 and calcium channel receptor. But it suffers from incomplete and variable oral absorption which occurs mainly in the proximal small intestine thus it is a good candidate to be formulated as a floating dosage form. [5] Cinnarizine is weakly basic in nature and has a lower pka value that's why it remains in ionized form at stomach pH and thereby it provides higher solubility in stomach and it remains in un-ionized form at intestinal pH so it has lower solubility in intestine. [6]

The main objective of this research work is to formulate cinnarizine floating tablet as floating tablet remains for longer period of time in stomach which provides larger acidic environment and thereby it increases the solubility of cinnarizine and hence absorption of cinnarizine in small intestine increases.

## MATERIALS AND METHODS

### Materials

Cinnarizine, HPMC K4M, K15 K100, Magnesium stearate, Talc were gifted from Balaji Drugs, Surat.

**Methods****1. Preparation of Cinnarizine Floating Tablets**

The cinnarizine floating tablets were prepared by direct compression method using HPMC as matrix forming agent. The compositions of different formulations are given in Table 1. Cinnarizine, HPMC K4M K15M and HPMC K100 were mixed homogeneously using a pestle and mortar then mixed talc and magnesium stearate added as lubricant and glidant respectively. The granules were compressed to form a tablet using tablets compression machine.

**2. Evaluation Parameters****a. Hardness Test**

The hardness of floating tablet was measured by Monsanto hardness tester. Hardness of tablet was measured in kg/cm<sup>2</sup> and it provides information about withstand ability during handling. [7]

**b. Friability**

The friability test was performed for all the formulated tablets using Roche Friabilator. Ten tablets were taken and their weight was determined (W<sub>0</sub>) and then they were placed in a rotating drum. Then they were subjected to 100 revolutions. After completion of 100 revolutions or 4 min of time at 25 rpm, the tablets were again weighed (W). The percentage friability (f) was calculated by the formula:

$$F = \frac{W_0 - W}{W_0} \times 100$$

Where, W<sub>0</sub> = weight of the tablets before the test and W = weight of the tablet after the test.

Acceptance criteria: the friability value should be less than 1.0 %. [8]

**c. Buoyancy/Floating Studies**

Buoyancy lag time means time interval between introduction of tablet into the dissolution medium and its floatation on top of the dissolution medium. Floating time means it is the duration of time up to which tablets floats on the dissolution medium. Both floating lag time and floating time were carried out in 0.1N HCL in dissolution apparatus at 37±1°C. [9]

**d. Drug Content**

Drug content of floating tablet was done by random selection of five tablets from each formulation and then fine powder of five tablets was made. From this powder, equivalent to 50 mg of cinnarizine powder was weighed and make desire concentration in 0.1N HCL then samples were analysed in spectrophotometrically at 254 nm. [10]

**e. In-vitro Dissolution Studies**

Release of cinnarizine was determined using USP (XXI) six stage dissolution rate test apparatus I (Electrolab, Mumbai) at 75 rpm. The dissolution rate was studied using 900 ml of 0.1N HCL. The temperature was maintained at 37±0.5°C. Samples of 5 ml each were withdrawn at different time intervals for 12 hrs and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and samples were suitably diluted and analyzed for cinnarizine content using double beam UV/Visible spectrophotometer (UV-1800 Shimadzu, Japan) at 254 nm. [11]

**Table 1: Composition of Floating Tablets of Cinnarizine by Using Different Concentrations of Polymers**

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Cinnarizine (mg)	10	10	10	10	10	10	10	10	10	10	10	10
HPMC K4M (mg)	5	10	15	20	-	-	-	-	-	-	-	-
HPMC K15M (mg)	-	-	-	-	5	10	15	20	-	-	-	-
HPMCK100M (mg)	-	-	-	-	-	-	-	-	5	10	15	20
Accural (mg)	10	10	10	10	10	10	10	10	10	10	10	10
Magnesium Stearate (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
MCC pH 102 (mg)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	100	100	100	100	100	100	100	100	100	100	100	100



## RESULT AND DISCUSSION

### Compatibility Studies

The principal peaks for cinnarizine were observed at wave numbers 3180, 3017, 2960, 2880 cm<sup>-1</sup>. Principal peaks of drug were also present in drug and HPMC K4M physical mixture, The study indicated that there was no interaction between drug and polymers or excipients, which were shown in Figure 1 and 2.

### Evaluation of Floating Tablet

#### 1. Hardness Test

The measured hardness of tablets of each batch ranged between 4.44 to 4.56 kg/cm<sup>2</sup> as reported in Table 2. This ensures good handling characteristics of all batches.

#### 2. Friability Test

The % friability was found to be in the range of 0.54% to 0.49% ensuring that the tablets are mechanically stable. The values of friability test are tabulated in Table 2.

#### 3. Weight Variation Test

Twenty tablets were selected randomly from each batch and weighed individually using

electronic balance to check for weight variation. The values of weight variation are shown in Table 2.

#### 4. In-vitro Buoyancy Studies

The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid pH 1.2. The time taken for the tablet to rise to the surface and float was taken as floating lag time. The overall floating time was calculated during the dissolution studies which were given in Table 2.

#### 5. In-vitro Drug Release Study

The values of dissolution profile were shown in Table 3. The In-vitro drug release profile of cinnarizine floating tablet is shown in Figure 3. Amongst all the formulations, formulation F10 showed 97.32% drug release at 10 hours.

#### 6. Drug Release Kinetic Studies

The drug release data of cinnarizine were fitted to Zero order, First order, and Higuchi model kinetics. The results were given in Table 4.

**Table no 2: EVALUATIONS OF PHYSICAL PARAMETERS OF TABLETS:**

Formulation Code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm <sup>2</sup> )	Friability (%)	Drug content (%)	Floating lag time (sec)	Floating buoyancy time (hrs)
F1	95	2.5	3.4	0.48	100.8	89	2
F2	101	3.3	3.25	0.38	97.8	112	3
F3	99	3.1	3.5		99.99	134	4
F4	106	2.5	3.1	0.40	101.33	104	5
F5	101	3.9	3.4	0.60	100.07	114	7
F6	103	2.2	3.5	0.43	95.6	145	>24
F7	106	3.1	3.2	0.45	98.9	87	>24
F8	105	3.19	2.9	0.52	100.2	134	>24
F9	103	3.2	3.2	0.45	99.8	176	>24
F10	101	3.1	3.5	0.40	101.33	104	10
F11	102	3.6	3.4	0.60	100.07	114	7
F12	98	3.2	3.5	0.43	95.6	145	>24

**Table no: 3 Drug release data of Cinnarizine floating matrix tablets:**

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	6.87	9.09	4.87	8.48	6.98	8.03	5.41	5.09	3.36	4.92	4.04	5.97
1	11.98	15.65	9.82	11.32	12.37	14.37	9.83	11.12	6.89	8.54	9.37	11.87
2	18.8	28.94	16.1	16.47	22.42	26.56	16.14	19.87	11.52	16.18	13.74	19.84
3	24.87	34.52	29.74	24.89	32.05	34.92	27.35	33.45	29.36	38.27	21.71	25.1
4	36.12	48.21	30.56	32.11	44.51	44.52	30.73	45.62	35.2	44.96	28.27	32.26
5	45.35	56.45	48.29	41.82	51.25	54.85	45.24	58.73	49.65	51.02	39.16	38.58
6	51.21	67.43	57.1	56.01	63.33	67.21	51.27	62.64	61.1	68.63	46.18	43.83
7	57.31	70.32	65.25	67.35	69.24	70.05	57.83	70.43	68.99	72.65	57.98	54.39
8	62.19	76.52	70.32	76.25	70.01	74.16	62.19	76.21	72.58	79.45	62.39	65.25
9	68.55	82.46	76.25	80.24	76.45	79.61	67.02	81.26	79.56	83.85	69.87	71.29
10	71.24	85.27	79.23	85.16	84.29	82.83	72.01	84.75	82.95	87.52	75.96	75.41
11	76.21	91.75	84.56	92.98	87.25	84.21	79.58	87.89	83.25	91.89	78.33	79.64
12	81.27	93.28	86.74	94.38	90.03	89.74	82.41	92.38	89.36	97.13	82.76	82.33



CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
4.92	0.5	0.000	0.692	0.000	1.978
8.54	1	1.000	0.931	0.000	1.961
16.18	2	1.414	1.209	0.301	1.923
38.27	3	1.732	1.583	0.477	1.790
44.96	4	2.000	1.653	0.602	1.741
51.02	5	2.236	1.708	0.699	1.690
68.63	6	2.449	1.837	0.778	1.497
72.65	7	2.646	1.861	0.845	1.437
79.45	8	2.828	1.900	0.903	1.313
83.85	9	3.000	1.924	0.954	1.208
87.52	10	3.162	1.942	1.000	1.096
91.89	11	3.317	1.963	1.041	0.909
97.13	12	3.464	1.987	1.079	0.458

Table 4.: Release kinetics data for optimised formulation

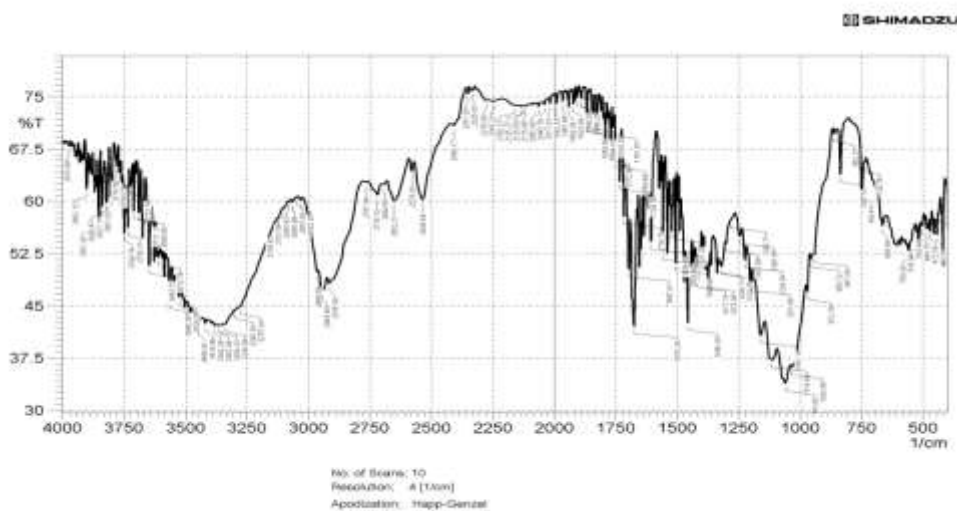


Fig 1 : FTIR spectrum of pure drug

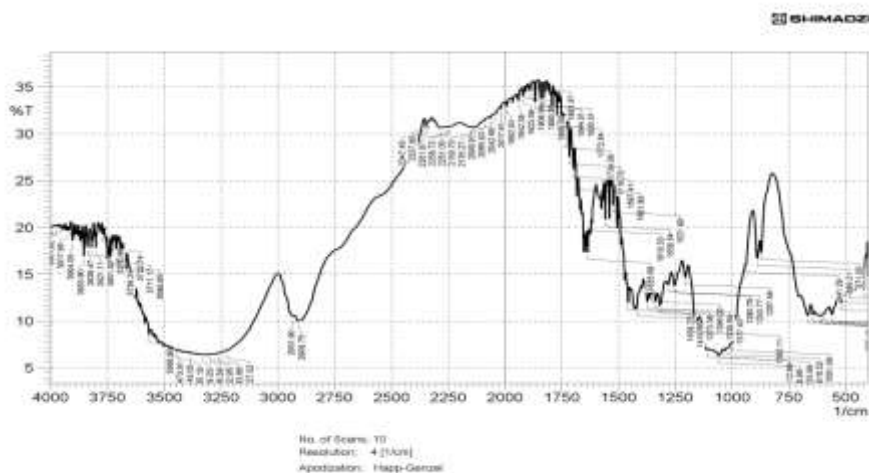


Fig 2 : FTIR spectrum of optimized formulation.



## CONCLUSION

The object of the present work is preparing non effervescent floating tablets in controlled fashion. The gas generating agent Accural was added in different concentrations with varying amount of retardation polymers. Different grades of HPMC polymers HPMC K4M, K15M & K100M were 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-F12 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 **F10** was found to be best with maximum % drug release of **97.13%** and floating time of 10 hours.

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