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FORMULATION AND EVALUATION OF EFFERVESCENT FLOATING TABLET OF FELODIPINE

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ABSTRACT
Felodipine effervescent floating tablets were developed in nine different formulations (T1 to T9) by employing different grades of polymers and effervescent agents such as sodium bicarbonate and citric acid. The formulations were evaluated for various physical parameters, buoyancy studies, dissolution parameters. T9 formulation showed maximum floating time of 13 hours and gave slow and maximum drug release of Felodipine spread over 13 hours.so the composition of the batch 9 should be optimized,to achieve the goal of formulation and evaluation of effervescent floating tablet of felodipine.

Key words: Felodipine, Effervescent floating tablet.

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INTRODUCTION

Effervescent floating drug delivery systems generate gas (CO2), thus reduce the density of the system and remain buoyant in the stomach for a prolonged period of time and released the drug slowly at a desired rate.[1,2,3] Felodipine is long acting calcium channel blocker and used in the treatment of hypertension, and chronic stable angina. In hypertension or angina, initially 5 mg. one daily and adjusted to maximum dose 10 mg one daily dose of Felodipine is given orally.[4] Felodipine has maximum solubility in acidic pH. Felodipine has some adverse effect such as nausea, abdominal pain. Effervescent floating tablet of Felodipine retain in stomach improves solubility, bioavailability, reduces drug waste and decrease side effect such as gastric irritation and nausea.[5]

In present work, effervescent floating tablets of different formulation were developed with an objective of achieving 13 hrs floating and drug release time[6].

EXPERIMENTAL

MATERIALS

Felodipine was procured from Signa Pharma Pvt. Ltd. Kanpur. HPMC K15 M. Carbapol 934p, Sodium

biacarbonate, Citric acid, poly vinyl pyrrolidine and Talc were obtained from Colorcon Asia Pvt. Ltd and Loba chemicals.

METHODS

Effervescent Floating tablets containing Felodipine were prepared by direct compression technique using varying concentrations of different grades of polymers with Sodium bicarbonate and citric acid. All the ingredients were accurately weighed and passed through different mesh sieves accordingly. Then, except Magnesium stearate all other ingredients were blended uniformly in glass mortar After sufficient mixing of drug as well as other components, Magnesium stearate was added, as post lubricant, and further mixed for additional 2-3 minutes. The tablets were compressed using rotary tablet machine. The weights of the tablets were kept constant for all formulation[6]

Evaluation of effervescent floating tablet formulation

Hardness of the tablets was tested using a Monosanto hardness tester. Friability of tablets was determined in Roche friabilator. Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. The results are given in table no. 2

The buoyancy lag time (BLT) and total floating time (TFT)

On immersion of tablets of different formulations in 0.1N HCl solution at 37±5°C, the tablets floated, and remained buoyant without disintegration, the results of the buoyancy lag time (BLT) and total floating time (TFT) were shown in Table 3[7].

Estimation of Amlodipine besylate

Amlodipine besylate content in the tablets was estimated by using UV spectrophotometric method based on the measurement of absorbance at λ max 239 nm in phosphate buffer 7.4. Amlodipine besylate content of the tablets are given in Table 4[8].

Drug release study

In vitro release studies of T1 to T9 formulations and one brand of were carried out in the dissolution test apparatus (USP Type II). The tests were carried out in 900 ml of dissolution media 7.4 pH buffers for 13 hrs at 50 rpm at 37±0.5°C 10 ml of the aliquot were withdrawn at different predetermined time intervals (1,2

Table 1: Composition of all the Formulations (T1 to T9):

Ingradient	T1	T2	T3	T4	T5	T6	T7	T8	T9
Felodipine	10	10	10	10	10	10	10	10	10
HPMC K15M	90	90	------	90	85	20	40	40	30
Carbopol 934P	------	------	90	------	40	40	------	40	40
MCC	35	35	35	35	------	65	85	45	55
Sodium Bicarbonate	50	50	50	50	50	50	50	50	50
Citric acid	40	40	40	40	40	40	40	40	40
Polyvinyl pyrrolidine K30	10	10	10	10	10	10	10	10	10
Magesium Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Aerosil	5	5	5	5	5	5	5	5	5
Total Weight	250	250	250	250	250	250	250	250	250

Table 2:Hardness,friability,weight variation of tablets of different formulation T1 to T9:

Formulation	Hardness (kg/cm²)	Friability (%)	Weight Variation(mg)	Drug content uniformity
T1	4.7±0.47	0.80	234±5%	98.01
T2	4.5±0.54	0.76	244±5%	97.55
T3	4.4±0.44	0.74	247±5%	97.42
T4	4.3±0.50	0.68	242±5%	97.61
T5	4.4±0.48	0.69	248±5%	96.24
T6	4.6±0.49	0.62	244±5%	98.03
T7	4.5±0.51	0.69	239±5%	94.33
T8	4.4±0.54	0.77	241±5%	95.49
T9	4.6±0.53	0.64	249±5%	97.62

3, 4, 5, 6, 7, 8, 9, 10,11,12,13 hr) and filtered. TheEffervescence production, decrease the several local required dilutions were made with and the solutionGIT side effect, such as gastric irritation, nausea and was analyzed for the drug content by using UVgastritis. The effervescent floating tablets of felodipine detector detecting at λ max 239 nm 10 ml of samplewere formulated in ten different batches T1 to T9 by was replaced in the vessel after each withdrawal tousing hydrophilic polymers HPMC K15M and maintain sink condition. From this percentage drughydrophobic polymer carbopol
release was calculated and this was plotted against934P along with effervescing agent sodium function of time to study the pattern of drug release.bicarbonate and citric acid. It was found that carbopol The in-vitro drug release profiles of tablet from eachhas a negative effect on floating behavior but it was batch (T1 to T9) were shown in Table 5[9]. used only for the drug release retardant

RESULTS AND DISCUSSION:

characteristics. All the formulations were prepared by Felodipine is a potent drug for the treatment of angina,direct compression method. The prepared tablets of all hypertension and also suitable in the treatmentthe formulations were evaluated for physical diabetic hypertension. Felodipine had maximumcharacters like tablet hardness, friability, weight solubility in acidic pH. Felodipine has some adversevariation buoyancy lag time, in-vitro drug release. The effect such as headache, nausea, abdominal pain.main aim was to optimize the formulation for 12 to13 Prolonged gastric retention improves bioavailability,hours in-vitro release and total floating time to more reduces drug waste and improves solubility for drugsthan 12 hours.
that are less soluble in high pH environment.

Table 3: Buoyancy Lag Time, Total Floating Time of formulations (T1toT9)

lation	ncy Lag Time	loating time

The measured hardness of tablets of each formulation ranged between 4.1 to 4.5 kg/cm2. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable. All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of ±5% of the weight. Buoyancy lag time (BLT) and total floating time (TFT) of different formulation were noted, where T1 BLT of 46 sec and TFT of >11 hours, T2 BLT of 40 sec and TFT of >10 hours, T3 fails to buoyancy because of absence of HPMC polymers, T4 BLT of 55 sec and TFT of >12 hours, T5 BLT of 35 sec and TFT of >11 hours, T6 BLT of 30 sec and TFT of >12 hours, T7 BLT of 34 sec and TFT of >10 hours, T8 BLT of 43 sec and TFT of >11 hours, T9 BLT of 47 sec and TFT of >13 hours, With reference to buoyancy studies results it can be concluded that the batch containing HPMC polymers showed good buoyancy lag time (BLT) and total floating time (TFT). Formulation T9 containing HPMC K15M, and carbopol 934P showed good BLT of 47 sec and TFT of more than 13 hrs. Felodipine release from the effervescent floating tablets was studied in phosphate buffer pH 7.4. The release profile of various formulations are shown in table no.5 and Figure no.1.Formulation. T1 released 86.44% of the drug in 10 hours. Formulation T2 released 89.88 % of the drug in 11 hours. Formulation T3 released 87.75% of the drug in 11 hours. Formulation T4 released 89.53% of the drug in 12 hours Formulation T5 released 88.27% of the drug in 12 hours. Formulation T6 released 88.28% of the drug in 13 hours.Formulation T7 released 92.53% of the drug in 13 hours. Formulation T8 released 96.25% of the drug in 13 hours. Formulation. T9 released 94.04% of drug in 24 hours. Thus F9 formulation was said to be optimized formulation

Table 4: Drug Content Uniformity of Tablets of Batch T1 to T9

Batches	Drug content uniformity (%)
T1	97.01
T2	99.51
T3	98.01
T4	97.42
T5	98.41
T6	99.05
T7	99.05
T8	98.46
T9	99.82

The optimized formulation T9 released the drug 94.04% in 13hrs. And the optimized formulation T9 remained floatable in the stomach for 13 hours .and give the maximum released 94.04 at 13th hours. It is, thus concluded that effervescent floating tablet containing Felodipine (F9formulation) gave slow and complete drug release spread over 13 hours [10,11].

Table 5: In-vitro drug release profile of tablets of T1 to T10

Sr. No	Time (hrs)	% Cumulative release ± SD								
		T1	T2	T3	T4	T5	T6	T7	T8	T9
1	0	0	0	0	0	0	0	0	0	0
2	1	30.11 ±0.9	28.63 ±1.3	25.79 ±1.4	27.81 ±1	25.36 ±0.8	22.63 ±1.3	23.40 ±1.2	19.52±0.7	18.25 ±0.8
3	2	43.08	39.72	37.53	40.44	35.67	33.82	33.37	31.51±0.	26.54

		±1.1	±1	±1.2	±0.8	±0.7	±0.8	±1.5	6	±0.7
4	3	50.55 ±1.3	45.53 ±0.9	44.33 ±1.3	47.68 ±0.7	41.73 ±0.7	39±1	38.70 ±0.9	36.50±1	31.57 ±0.8
5	4	60.08 ±0.8	55.65 ±0.8	50.33 ±0.7	55.61 ±0.9	51.86 ±1.8	46.41 ±1.4	46.24 ±0.8	45.42±0.6	38.64 ±0.7
6	5	70.22 ±1	69.71 ±1.1	62.67 ±2.1	62.63 ±0.7	61.96 ±0.9	54.65 ±1	51.68 ±1	51.22±0.8	46.68 ±1
7	6	78.83 ±0.9	76.14 ±1.5	70.8± 2	73.25 ±1	71.80 ±1.4	60.68 ±1.2	59.40 ±0.7	56.79±0.9	50.57 ±0.6
8	7	90.48 ±1.6	82.35 ±1.2	82.65 ±1.5	80.17 ±0.8	77.94 ±1.1	68.03 ±1	65.35 ±0.9	62.03±0.8	58.01 ±0.4
9	8	98.78 ±0.7	89.67 ±0.9	90.75 ±0.8	89.45 ±0.9	86.05 ±1.3	76.26 ±1.1	70.39 ±0.7	67.45±0.7	64.88 ±0.8
10	9	94.53 ±1	97.76 ±0.4	97.62 ±0.7	94.87 ±0.5	92.42 ±1.6	85.17 ±1.7	76.56 ±0.9	72.41±1.2	70.63 ±0.8
11	10	86.44 ±2.1	94.29 ±0.7	93.44 ±0.8	98.73 ±0.4	98.10 ±0.7	92.02 ±1.1	82.59 ±1.5	78.27±0.8	77.81 ±0.7
12	11	-	89.88 ±0.7	87.75 ±1.8	94.92 ±0.8	93.89 ±0.3	97.65 ±1	89.68 ±1.1	83.40±0.8	82.35 ±1
13	12	-	-	-	89.53 ±1	88.27 ±1.1	92.52 ±1.7	97.50 ±0.8	88.75±0.8	88.61 ±0.8
14	13	-	-	-	-	-	88.28 ±1.4	92.53 ±0.8	96.25±0.8	94.04 ±0.3

CONCLUSION

In present work, a floating gastroretentive system for Felodipine was developed. Felodipine was selected for this investigation because less biological half life, to improve bioavailability by retaining the drug in acidic environment as its solubility decreases with increasing pH and to reduce wastage. Step by step studies were carried out to develop and optimize oral floating tablet for felodipine using low density polymers. The floating tablets were prepared by direct compression technique using effervescent system for floating. *In- vitro* drug release profile from all formulations (T1-T9) showed sustained release of Felodipine over a period of 13 hours. Among all the formulation, F9 showed drug release upto 94.04% at the end of 13 hours. The present study was carried out to develop the floating drug delivery with sustained release of Felodipine using HPMC K-15M,Carbopol 934p, Aerosil and MCC polymers. *In-vitro* dissolution studies showed good percent yield, good buoyancy and release upto 13hrs, Felodipine floating system as an alternative to the conventional dosage form. At the end, from the experiments carried out and results obtained, it can be concluded that the developed formulations achieved the objective of the investigation.

FUTURE SCOPE

In vitro-In vivo correlation studies can be done.Instead of HPMC, other natural polymers like Guar gum, Xanthan gum, Chitosan can be used.Useful tool for delivering multiple drugs in same dosage form.

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