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Phenhylephrine Hydrocloride Gastro Retentive Floating Matrix Tablets: Design and *in Vitro* Evaluation

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ABSTRACT

The objective of this research is to obtain sustained release of Phenylephrine hydrochloride. In this research work combination of natural and synthetic gums were used in different ratio to get sustain release; different gas generating agents were used to float the tablet. Prepared powder blend is subjected to pre-formulation studies. Then prepared tablet were evaluated for different evaluation tests. Finally dissolution data was subjected to various release kinetic models to understand release mechanism of drug.

KEYWORDS: *HPMC (hydroxyl propyl methyl cellulose) K15M, MCC(microcrystalline cellulose), Buoyancy, Swelling Index*

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INTRODUCTION

Floating drug delivery system (FDDS) exerts buoyancy in stomach for extended time period thereby offering extended gastric residence time for the dosage form ensuring optimal bioavailability [1] . The ideal drug candidate for FDDS are drugs that are acting locally in upper gastro intestinal tract (GIT) or drugs that are degrading in lower GIT or drugs that show poor intestinal absorption or drugs that are absorbed only in the initial part of small intestine (SI). Acid labile drugs and other drugs that are causing gastric lesions are unsuitable for such a formulations. The residence time of the dosage form in the stomach depends upon various factors like pH, size of the dosage form, food intake, and biological factors which include age, body mass index, gender, posture, and diseased states (hepatic failure, diabetes, chrons disease).Other techniques for gastro retentive dosage forms include swelling or expansion, inflation, mucoadhesion, sedimentation, microballoons and low density systems, co-administration with drugs that are delaying gastric emptying. Out of all the available systems, the floating beads, floating tablets, floating granules, and floating microspheres have gained major importance in the formulation development more recently [2,3].

Materials Used

Phenylephrine hydrochloride, HPMC K15M, was obtained as gift sample from (Micro Labs,Hosur, India). Talc, magnesium stearate, microcrystalline cellulose, lactose monohydrate were procured from SD Fine chemicals, Mumbai, India, sodium bicarbonate and citric acid from Paxmy speciality chemicals, Chennai, India. All the materials used were analytical grade, purchased from India.

Evaluation of Granules

- Angle of Repose (θ) [4] :-The angle of repose of powder was determined by the funnel method. The physical mixture was allowed to flow through the funnel that can be rise vertically until a maximum cone height 'h' was obtained.

  $\tan\theta = h / r$

- Bulk Density [5] : An accurately weighed quantity of powder, which was previously passed through sieve # 40 and carefully poured into graduated cylinder. then after pouring the powder into graduated cylinder the powder bed was made uniform without disturbing. Then the volume was measured directly from graduation mark on the cylinder.
- Tapped density [6]:- A quantity of 2 gm of powder from each formula was introduced into a 10 ml measuring cylinder. After initial volume was observed, the cylinder was allow to fall under its own weight on the hard surface from the height of 2.5 cm at two second intervals. The tapping was continued until there is no further change in the volume was noted.

- Hausner'sratio [7] :- Hausner's ratio is an indirect index of ease of power flow. It is calculated by the formula:- Hausner's ratio = Dt/ Db

- Carr's index [8] :- It helps in measuring the force required to break the friction between the particles and the hopper. It is expressed in % and given by,

$$\text{X 100 CI} = \frac{\text{Dt} - \text{Db}}{\text{Dt}}$$

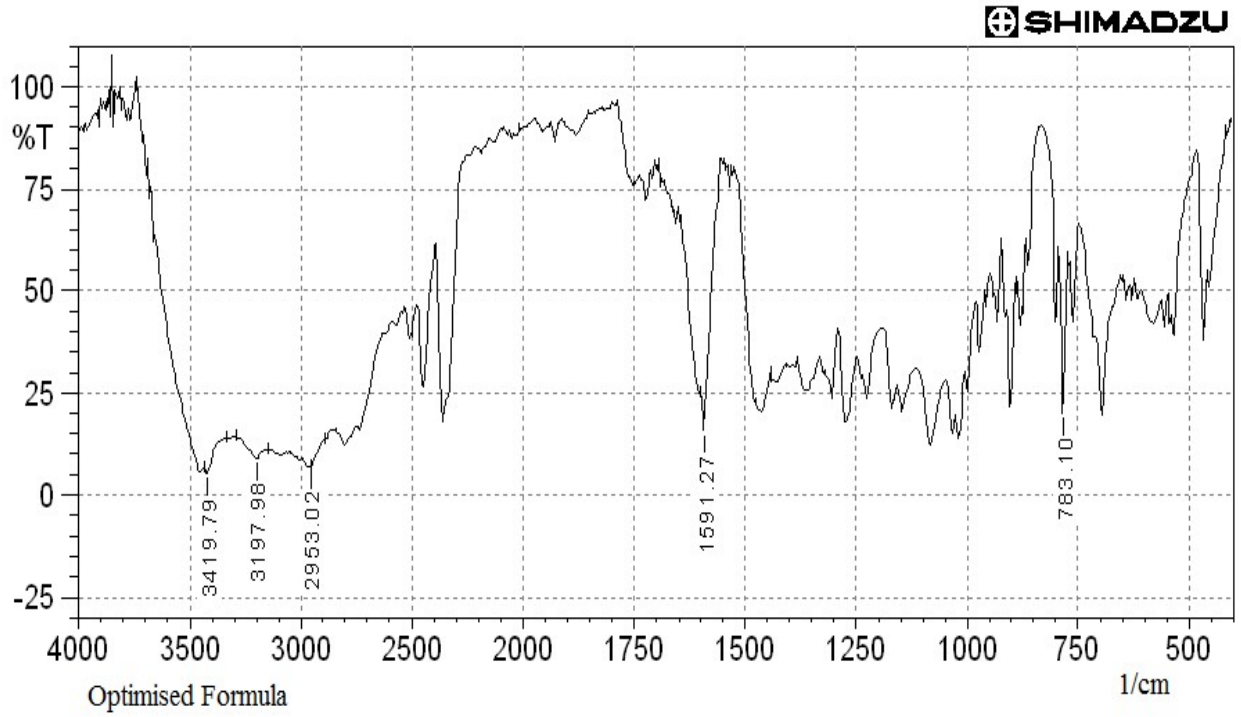
Evaluation of Phenylephrine hydrochloride Floating Tablets.

- Hardness[9]: The resistance of tablets to shipping or breaking under the condition of storage, transportation and handling before the uses depends on its hardness. Hardness of the tablet was determined using a Monsanto Hardness tester. It is expressed in kg / cm^2
- Friability [10]: Friability is the measure of tablet strength. Friability of the tablet was determined using Roche friabilator. It is expressed in percentage (%). 20 tablets were initially weighed ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25 r.p.m for 4 mins. The tablets were weighed again (W_{final}).
- Thickness [11] :- Three tablets were selected randomly from each batch and the thickness was measured using Vernier Caliper and expressed in mm.

- Weight Variation [12] :- Twenty tablets were randomly selected from each batch individually weigh, the average weight and standard deviation of 20 tablet calculated. Not more than two of the individual weights may deviate from the average weight by more than the percent deviation.
- Drug Content[13] :-The drug content in each formulation was determined by triturating 10 tablets and powder equivalent to 100 mg of drug was transferred to 100 ml of 0.1 N HCl in volumetric flask. The solution was analyzed at 272.5 nm using double beam UV/V is spectrophotometer after suitable dilution using 0.1 N HCl as a blank.
- *In-vitro* Buoyancy Studies[14] :-In vitro buoyancy studies were performed for all formulation as per the method described Rosa *et al*. The randomly selected tablets from each formulation were kept in a 100 ml beaker containing 0.1N HCl (pH 1.2). The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). For that duration of time, the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).
- *In Vitro* Dissolution Study[15] :- A sample was withdrawn at predetermined time interval from dissolution medium hourly and the sample was replaced with fresh medium. Diluted to a suitable concentration with 0.1 N HCl. Absorbance of these solutions was analyzed at 272.5nm using double beam UV/Visible spectrophotometer. The content of drug was calculated using calibration curve. The percentage drug release was plotted against time to determine the release profile

Result and Discussion

Infrared Spectroscopy Study:- I.R SPECTRA OF OPTIMIZED BATCH



Differential scanning calorimetry (DSC):- The DSC themogram of Optimized batch featured two sharp melting endotherm, having peak temperature of 142°C and 193°C. It indicates melting thermogram of drug and excipienys. In DSC thermogram of optimized formulation, there is no significant shifting in the endothermic peaks of drug, so it indicates that there is no interaction between drug and excipients.

Pre-compressional Evaluation Parameters

Batch Code	Angle of Repose (θ) (º)	Bulk Density(gm/cm³)	Tapped Density(gm/cm³)	Compressibility Index (%)	Hausner's Ratio
NF1	28.32	0.43	0.47	8.51	1.093
NF2	26.22	0.41	0.45	8.88	1.097
NF3	25.43	0.40	0.44	9.09	1.1
NF4	27.47	0.45	0.48	6.25	1.066
NF5	27.30	0.40	0.44	9.09	1.1
NF6	26.42	0.41	0.45	8.88	1.097
NF7	28.30	0.43	0.45	4.44	1.046
NF8	27.32	0.43	0.47	8.51	1.093
NF9	26.40	0.44	0.48	8.33	1.090

Pre-compressional Evaluation Parameters :-

Batch Code	Angle of Repose (θ) (º)	Bulk Density (gm/cm³)	Tapped Density (gm/cm³)	Compressibility Index (%)	Hausner's Ratio
F1	25.22	0.41	0.47	8.61	1.095
F2	26.42	0.43	0.45	8.58	1.087

Post Compressional Evaluation Parameters :-

Batch Code	Thickness (mm) ± S. D	Hardness (Kg/cm²) ± S. D	Friability (%)	Drug Content (%)	Weight Variation (mg) ± S. D
NF1	3.2 ± 0.25	5.26 ± 0.07	0.38	97.06	296.57 ± 1.93
NF2	3.3 ± 0.17	5.31 ± 0.10	0.57	98.43	292.35 ± 0.65
NF3	3.4 ± 0.15	6.29 ± 0.10	0.31	99.25	299.36 ± 0.40
NF4	3.4 ± 0.23	5.43 ± 0.28	0.42	96.42	298.93 ± 0.53
NF5	3.3 ± 0.15	5.51 ± 0.22	0.61	97.06	298.53 ± 0.60
NF6	3.4 ± 0.25	5.67 ± 0.34	0.66	98.98	299.51 ± 0.36
NF7	3.4 ± 0.3	5.31 ± 0.20	0.33	98.59	299.26 ± 0.60
NF8	3.3 ± 0.11	5.35 ± 0.36	0.52	94.26	299.71 ± 0.32
NF9	3.1 ± 0.20	5.79 ± 0.12	0.47	96.99	299.79 ± 0.13

Post Compressional Evaluation Parameters

Batch Code	Thickness (mm) ± S. D	Hardness (Kg/cm²) ± S. D	Friability (%)	Drug Content (%)	Weight Variation (mg) ± S. D
F1	3.17 ± 0.06	5.36 ± 0.15	0.32	98.06	300 ± 0.11
F2	3.30 ± 0.12	6.66 ± 0.05	0.53	98.43	299.45 ± 0.50

Swelling index for Batch No.F1 and F2 :-

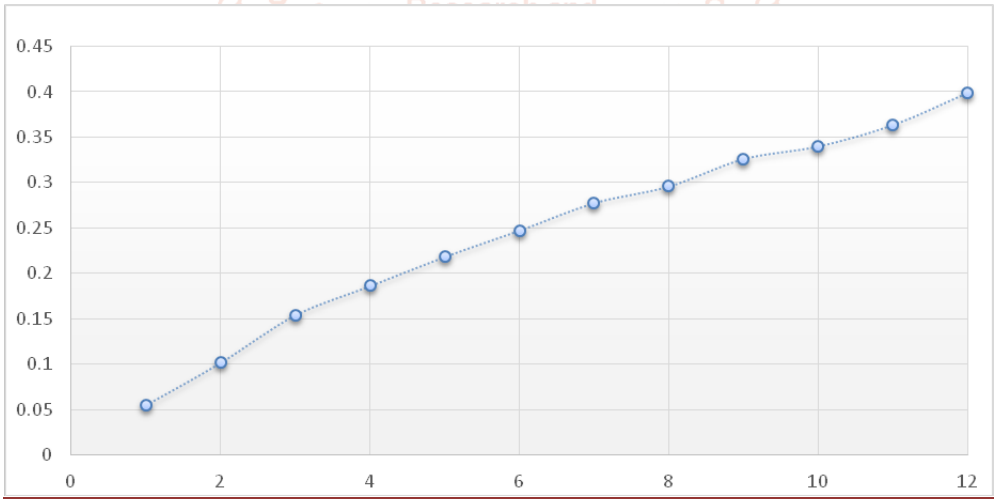
Time (Hrs)	Swelling Index (%)	
	F1	F2
1	27.67	27.97
2	39.49	40.14
3	45.63	46.77
4	53.27	54.68
5	58.36	59.96
6	63.49	64.76
7	69.43	65.32
8	74.34	74.87
9	83.62	83.75
10	87.62	88.89
11	91.68	91.98
12	92.15	92.67

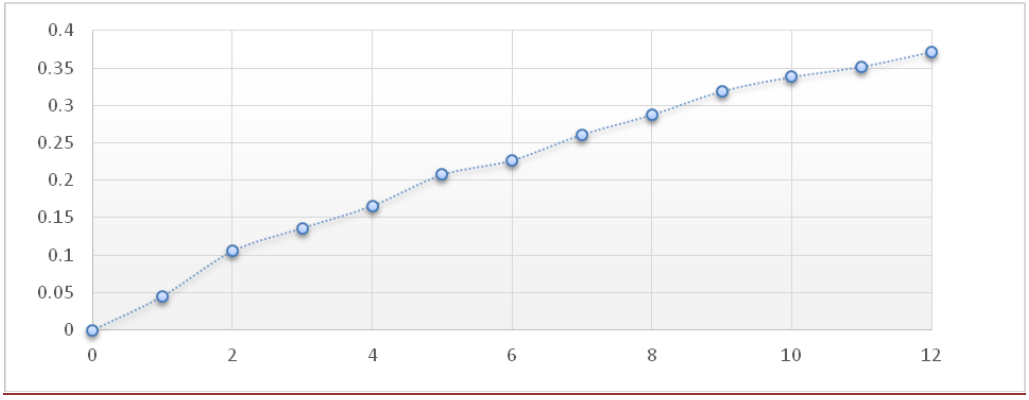
Cumulative% drug release of Batch NF1 to NF9 :-

Time (Hrs)	Cumulative% drug release								
	NF1	NF2	NF3	NF4	NF5	NF6	NF7	NF8	NF9
1	9.03	8.75	8.10	9.17	8.93	8.55	9.92	9.15	8.95
2	13.6	13.7	13.57	15.02	14.85	14.36	15.74	14.15	14.56
3	20.87	19.29	20.66	23.07	22.90	21.98	33.76	29.27	26.37
4	27.73	23.97	22.51	34.22	33.22	31.89	52.62	48.17	40.04
5	36.13	34.02	33.90	55.59	52.17	51.20	63.22	60.90	45.60
6	62.65	52.42	47.19	65.55	63.26	62.53	70.77	69.26	62.87
7	84.85	77.85	56.69	77.08	85.17	84.21	81.37	80.17	80.17
8	100	89.41	69.24	100	100	100	100	84.01	86.38
9	_	100	77.68	_	_	_	_	100	100
10	_	_	82.72	_	_	_	_	_	_
11	_	_	90.28	_	_	_	_	_	_
12	_	_	100	_	_	_	_	_	_

Cumulative% drug release for Batch No.F1 and F2 :-

Time (Hrs)	Cumulative% drug release	
	F1	F2
1	7.83	7.25
2	12.10	11.86
3	19.62	18.75
4	30.91	30.38
5	44.26	42.15
6	53.73	51.18
7	66.14	64.92
8	74.58	72.95
9	79.75	76.52
10	88.18	82.65
11	95.22	93.16
12	100	100





***In Vitro* Drug Release Profile of Batch F1 and F2**

Batch F1-F2 was subjected to various drug release kinetics. In order to find out the order of drug release and mechanism, this was predominantly influence the drug release from tablet.

Conclusion

Phenylephrine HCl floating matrix tablet formulations were prepared and evaluated. Evaluations like thickness, hardness, friability, uniformity of content and weight, floating lag time, buoyancy duration, and dissolution study were performed. Optimized formulation was subjected to dissolution study for 12 hrs. The formulation (F1) containing (HPMC K100 + Xanthun gum) was found to be best among all the formulation batches. It's showed floating lag time (20sec) and prolonged floating duration up to (12 hrs) which was controlled release characteristic. The maximum release observed at 12 hrs was 92.65%.

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