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DESIGN AND EVALUATION OF GASTRORETENTIVE NIFEDIPINE FLOATING TABLETS IN THE TREATMENT OF HYPERTENSION

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Abstract

Gastro retentive floating tablets of Nifedipine were prepared using various grades of HPMC as a release retarding agent. Nifedipine is a dihydropyridine derivative effectively used in the management of various cardiovascular diseases in long term therapy, the biological half life is only 2 hours. The main aim of the present study is to prolong the drug release upto 24 hours. The tablets were prepared by direct compression method and the formulations were evaluated different physic chemical and dissolution studies. The formulations from each polymer F6, F10 and F20 gave better controlled drug release and floating properties in comparison to the other formulations. HPMC K 250 PH PRM, HPMC K 750 PH PRM and HPMC K 1500 PH PRM were used in different ratios to check the release retarding mechanism and duration. Among all the formulation F10 was selected as optimized formulation because it showed maximum drug release FTIR studies results revealed that there was no incompatibility between drug and excipients. The optimized formulation was best fitted in Zero Order and Korsmeyer-Peppas. Nifedipine floating tablets can be an innovative and promising approach for the delivery of Nifedipine for the treatment of hypertension (high blood pressure) and angina (chest pain) for prolonged period of time.

Keywords: *Nifedipine, Floating tablets, Hypertension, HPMC, Floating lag time.*

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INTRODUCTION:

Nifedipine is a calcium channel blocker mainlyused for treatment of hypertension. It reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Nifedipine is a good candidate for incorporation in a gastro-retentive dosage form due to its high solubility in the stomach pH compared to its solubility in the small intestine pH[1]. As its solubility decreases with increase in pH, it would be more beneficial to retain the drug in stomach (acidic environment) for prolonged duration so as to achieve maximum absorption and bioavailability. So gastro-retentive floating drug delivery system is desirable to prolong the residence time of the dosage form in the stomach or upper gastrointestinal tract until the drug is completely released from the system. The primary goal of a Gastro-retentive floating system is to permit reductions in the frequency of Nifedipine administration, preferably to once daily, and thus improve patient compliance. Sustained release Nifedipine formulations are generally better tolerated than their conventionally formulated counterparts, particularly with regard to reflex tachycardia. Adverse effects seem to be dose related, are mainly associated with the drug's potent vasodilatory action, and include headache, flushing and dizziness. Sustained release Nifedipine formulations are useful and established cardiovascular therapeutic agents which have demonstrable efficacy in various forms of angina, mild to moderate hypertension and Reynaud's phenomenon [2].

Gastric emptying is unpredictable if there are physiological problems and other factors like the presence of food. Drugs having a short half-life are eliminated quickly from the blood circulation. Various oral controlled delivery systems have been designed which can overcome these problems and release the drug to maintain its plasma concentration for a longer period of time, thus leading to the development of oral gastro-retentive dosage forms. Gastro-retention is essential for drugs that are absorbed from the stomach, drugs that are poorly soluble or degraded by the higher pH of intestine, and drugs with an absorption which can be modified by changes in gastric emptying time. They are also useful for local as well as sustained drug delivery for certain conditions, like H. pylori infection which is the cause of peptic ulcers. Gastro-retentive floating dosage form improves therapeutic efficacy, bioavailability and reduction in the dose because of steady therapeutic levels of drug [3]. Nifedipine is a dihydropyridine derivative effectively used in the management of various cardiovascular diseases in long term therapy [4].

MATERIALS AND METHODS:

Materials

Nifedipine was gifted by was procured from Aurobindo Pharma Ltd, Hyderabad. HPMC K 250 PRM, HPMC K 750 PRM, HPMC K 1500 PRM, and Polyox WSR 301 were obtained from Granules India Ltd, Hyderabad. Sodium bicarbonate, Avicel pH 102, Citric acid, PVP K 30, Talc and Magnesium Stearate were procured from Sd Fine Ltd, Mumbai and all other chemicals used were of analytical grade.

Methods

Drug-Excipient Compatibility Studies

Fourier Transform Infrared (FTIR) Spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR spectrophotometer (Perkin Elmer). Pure drug, individual polymers and optimised formulations were subjected to FTIR study. About 2–3 mg of sample was mixed with dried potassium bromide of equal weight and compressed to form a KBr disk[5]. The samples were scanned from 400 to 4000 cm^{-1}.

Evaluation of final blend

The Final blend of all formulations was evaluated for Bulk density, Tapped density, Compressibility Index (CI), Hausner ratio and Angle of repose[6].

Formulation method

Accurately weighed quantities of HPMC polymer and MCC were taken in a mortar and mixed geometrically, to this required quantity of Nifedipine was added and mixed slightly with pestle. Accurately weighed quantity of Sodium bicarbonate was taken separately in a mortar and powdered with pestle. The powder is passed through sieve no 40 and mixed with the drug blend which is also passed through sieve no 40. The whole mixture was collected in a plastic bag and mixed for 3 minutes. To this Magnesium stearate was added and mixed for 5 minutes, later Talc was added and mixed for 2 minutes[7]. The mixture equivalent to 200 mg was compressed into tablets with 10 mm round concave punches at a hardness of 6 kg/cm^2. The compositions of different formulations were shown in Table 1, 2 &3.

Table 1: Composition of floating matrix tablets of Nifedipine by using HPMC K 250 PH PRM

Ingredients (weight in mg)	Formulations						
	F1	F2	F3	F4	F5	F6	F7
Nifedipine	60	60	60	60	60	60	60
HPMC K 250 PH PRM	56	60	64	68	72	76	80
Sodium Bicarbonate	16	18	20	22	24	26	28
Citric acid	10	10	10	10	10	10	10
Avicel pH 102	46	40	34	28	22	16	10
PVP K 30	8	8	8	8	8	8	8
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	200	200	200	200	200	200	200

Table 2: Composition of floating matrix tablets of Nifedipine by using HPMC K 750 PH PRM

Ingredients (weight in mg)	Formulations						
	F8	F9	F10	F11	F12	F13	F14
Nifedipine	60	60	60	60	60	60	60
HPMC K 750 PH PRM	54	56	60	64	68	72	76
Sodium Bicarbonate	16	18	20	22	24	26	28
Citric acid	10	10	10	10	10	10	10
Avicel pH 102	50	44	38	32	26	20	14
PVP K 30	8	8	8	8	8	8	8
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	200	200	200	200	200	200	200

Table 3: Composition of floating matrix tablets of Nifedipine by using HPMC K 1500 PH PRM

Ingredients (weight in mg)	Formulations						
	F15	F16	F17	F18	F19	F20	F21
Nifedipine	60	60	60	60	60	60	60
HPMC K 750 PH PRM	50	54	56	60	64	68	72
Sodium Bicarbonate	16	18	20	22	24	26	28
Citric acid	10	10	10	10	10	10	10
Avicel pH 102	54	50	44	36	30	24	18
PVP K 30	8	8	8	8	8	8	8
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	200	200	200	200	200	200	200

Evaluation of floating tablets of Nifedipine

Weight variation test

Twenty tablets from each batch were individually weighed in grams on an analytical balance. The average weight and standard deviation were calculated, individual weight of each tablet was also calculated using the same and compared with average weight.

Thickness test

The thickness in millimetres (mm) was measured individually for 10 pre weighed tablets by using Vernier Calipers and their mean value was considered.

Hardness test

Tablet hardness was measured using a Monsanto hardness tester. The crushing strength of the 10 tablets with known weight and thickness of each was recorded in kg/cm^2 and the average hardness, and the standard deviation was reported [8].

Friability test

Twenty (20) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25 rpm for 4 minutes (100 rotations) in the Roche Friabilator. The tablets were then dusted and re-weighed to determine the loss in weight. Friability was then calculated as per weight loss from the original tablets [9].

In vitro buoyancy studies

The in vitro buoyancy was determined by floating lag time, as per the method described by Rosa et al. The tablets were placed in a 100 ml beaker containing 0.1N hydrochloric acid. The time

required for the tablet to rise to the surface and float was determined as floating lag time. The duration of time for which the dosage form constantly remained on the surface of medium was determined as the total floating time [10].

Drug Content

Twenty tablets were taken, powdered and the powder equivalent to one dose each was transferred to a 100 ml volumetric flask and 0.1N HCl was added. The volume was then made up to the mark with 0.1N HCl. The solution was filtered and diluted suitably and drug content in the samples was estimated using UV-spectrophotometer at 238 nm[11].

***In vitro* drug release studies**

The in vitro drug release study was performed for the single- & multiple-unit tablets using USP Type II dissolution apparatus. 900 ml of 01.N HCl was used as the dissolution medium. The rotation speed was 50 rpm and temperature was maintained at 37±0.5ºC. At predetermined time intervals samples (5 ml) were collected and replenished with same volume of fresh media. The samples were collected at 0, 1, 2, 4, 6, 8, 12, 16, 20, 24 hours and the drug content in the samples was estimated using UV-spectrophotometer at 238 nm [12].

Release order kinetics

The *in vitro* release data from several formulations containing Nifedipine was determined kinetically using different mathematical models like Zero order, First order, Higuchi, and Korsmeyer–Peppas model [13].

Drug-excipient compatibility studies

Fourier transform infrared spectroscopy (FTIR)

The spectral analysis can be used to identify the functional groups in the pure drug and drug-excipient compatibility. Pure Nifedipine FTIR spectra, physical mixtures and optimized formulation were recorded by using FTIR (SHIMADZU). Weighed quantity of KBr and drug-excipients were taken in the ratio 100: 1 and mixed by mortar. The samples were made into pellet by the application of pressure [14]. Then the FTIR spectra were recorded in the wavelength region between 4000 and 400 cm^{-1}.

Stability studies

Stability testing was conducted at 40˚C ± 2˚C/75% RH ± 5% RH for 3 months using stability chamber (Thermo Lab, Mumbai). Samples were withdrawn at predetermined intervals 0, 30, 90 and 180 days period according to ICH guidelines [15]. Various *in vitro* parameters like % yield, entrapment efficiency and *in vitro* release studies were evaluated.

RESULTS AND DISCUSSION:

Table 4: Physical properties of prepared powder blends of Nifedipine

Formulation Code	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (θ)	Carr's index (%)	Hausner ratio
F1	0.59±0.19	0.61±0.15	24.34±0.44	12.23±1.12	1.13±0.24
F2	0.57±0.16	0.60±0.17	22.67±0.31	11.23±1.42	1.12±0.10
F3	0.57±0.17	0.64±0.21	25.54±0.41	10.12±0.8	1.13±0.20
F4	0.59±0.25	0.68±0.25	25.89±0.55	11.34±0.6	1.14±0.24
F5	0.57±0.18	0.69±0.18	23.56±0.0.57	12.23±0.12	1.12±0.32
F6	0.52±0.20	0.54±0.20	21.30±0.30	10.23±0.25	1.11±0.30
F7	0.54±0.14	0.60±0.16	22.56±0.57	10.34±0.31	1.14±0.20
F8	0.60±0.16	0.68±0.17	23.67±0.60	11.11±0.24	1.12±0.25
F9	0.59±0.18	0.67±0.19	25.56±0.44	12.45±1.15	1.13±0.70
F10	0.50±0.25	0.53±0.18	21.66±0.31	09.45±1.3	1.09±0.20
F11	0.58±0.17	0.64±0.16	24.34±0.37	14.23±1.5	1.13±0.16
F12	0.59±0.16	0.65±0.20	25.99±0.70	13.34±1.25	1.12±0.12
F13	0.58±0.19	0.66±0.18	23.14±0.50	12.67±1.55	1.12±0.14
F14	0.57±0.13	0.66±0.17	24.09±0.57	13.23±1.55	1.14±0.15
F15	0.56±0.18	0.63±0.16	24.78±0.77	11.45±1.5	1.15±0.15
F16	0.56±0.13	0.61±0.15	23.45±0.80	12.68±1.3	1.16±0.18
F17	0.58±0.13	0.68±0.19	23.09±0.86	12.47±1.09	1.12±0.15
F18	0.56±0.16	0.67±0.20	23.05±0.75	14.99±1.20	1.14±0.15
F19	0.54±0.18	0.61±0.16	26.06±0.67	12.45±1.45	1.13±0.15
F20	0.52±0.17	0.54±0.17	23.78±0.57	10.12±1.45	1.11±0.17
F21	0.59±0.13	0.63±0.18	25.34±0.70	11.09±1.07	1.16±0.20

Above parameters are communicated as Average ± Standard Deviation; (n=3)

The results of bulk densities formulations bearing F1 to F21 were in the range of 0.50g/cc to 0.60g/cc. The findings of tapped density formulations F1 to F21 were in the range of 0.54g/cc to 0.68g/cc. The angle of repose of all the formulations was found to be satisfactory. The formulation F10 was found to have a value of 21.66 which indicates good flow property. The compressibility index values were found to be in the range of 9 to 12 %. These findings indicated that the all the batches of formulations exhibited good flow properties. The Hausner's ratio values in the space of 1.09 to 1.16 %. These findings designated that the all the batches of formulations advertised good flow criterions (Table 4).

Physicochemical properties of Nifedipine tablets

Fig 1: Nifedipine floating tablets

Table 5: Physico-chemical parameters of Nifedipine floating tablets

F.No	*Weight variation (mg)	#Thickness (mm)	#Hardness (Kg/Cm^2)	#Friability (%)	#Content uniformity (%)	Floating Lag time (sec)	Total floating time (hrs)
F1	201.12±0.20	4.1±104	5.1±0.13	0.57±0.08	97.23±1.23	57	>24
F2	199.23±0.24	4.01.16	5.0±0.33	0.54±0.09	98.04±1.03	54	>24
F3	198.08±0.15	4.1±1.05	5.3±0.13	0.63±0.07	96.56±0.94	50	>24
F4	201.09±0.70	4.2±1.09	5.2±0.10	0.56±0.05	97.11±0.63	49	>24
F5	201.89±0.50	4.1±1.37	5.1±0.10	0.61±0.07	95.23±0.81	43	>24
F6	200.34±0.20	4.2±1.11	5.2±0.10	0.51±0.09	99.45±0.32	36	>24
F7	203.23±0.60	4.0±1.61	5.3±0.15	0.54±0.02	95.11±1.17	43	>24
F8	199.12±0.50	4.2±0.3	5.2±0.15	0.67±0.02	97.23±0.45	46	>24
F9	200.23±0.48	4.2±0.45	5.2±0.19	0.56±0.02	97.13±1.17	44	>24
F10	200.24±0.20	4.1±0.25	5.1±0.21	0.50±0.07	99.93±0.49	32	>24
F11	201.45±0.97	4.1±0.70	5.4±0.10	0.76±0.05	96.97±0.95	39	>24
F12	202.03±0.54	4.4±0.25	5.6±0.15	0.73±0.08	97.45±0.35	41	>24
F13	201.04±0.30	4.5±0.60	5.9±0.18	0.52±0.09	96.85±0.24	45	>24
F14	198.23±0.35	4.1±0.56	5.5±0.10	0.72±0.02	96.18±0.13	49	>24
F15	199.34±0.25	4.5±0.70	5.6±0.08	0.71±0.20	97.25±1.21	48	>24
F16	201.12±0.55	4.1±0.40	5.2±0.21	0.78±0.9	97.45±1.30	46	>24
F17	202.23±0.50	4.5±0.17	5.7±0.04	0.79±0.04	96.94±1.31	43	>24
F18	201.67±0.30	4.5±0.40	5.6±0.14	0.82±0.03	98.56±1.36	41	>24
F19	199.13±0.45	4.0±0.17	5.5±0.12	0.51±0.01	97.29±1.31	37	>24
F20	200.45±0.55	4.3±0.96	5.0±0.10	0.63±0.03	99.38±1.36	34	>24
F21	198.12±0.70	4.9±0.50	5.3±0.12	0.66±0.03	96.27±1.30	39	>24

#Values are expressed in mean± SD :(n=3)

The Weight variation of all formulations witnessed to be in the limit allowed that is ± 5% of total tablet weight.

The suitable hardness for compressed tablets is considered as a vital function for the end user. The deliberated crushing strength of fabricated tablets of formulations F1-F21 trended between 5.0-6.0kg/cm^2. The thickness of all the formulations ranges between the ranges 4-4.9 mm. The friability of all prepared formulation ranges between 0.52-0.84. The friability properties limits are in between 0-1%. The drug content of all formulation is in between 95.11-99.93%, drug content depends on the angle of repose since the angle of repose indicates uniform flow nature of powder blend which makes the drug to evenly distribute in all the formulation and to maintain content uniformity in all batches. Tablets of all batches had floating lag time below 3 minutes regardless of viscosity and content of HPMC because of evolution of CO_2 resulting from the interaction between sodium bi carbonate and dissolution medium; entrapment of gas inside the hydrated polymeric matrices enables the dosage form to float by lowering the density of the matrices. Total Floating time for the HPMC formulations were above 24 hrs (Table 5).

In vitro dissolution studies:

Table 6: *In vitro* Drug Release Profile of Nifedipine floating tablets F1-F7

Time(h)	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	04.18±2.09	05.24±1.16	07.58±1.25	08.33±1.37	7.46±1.25	07.47±1.18	06.55±2.33
2	12.22±1.23	13.01±1.15	15.12±1.29	18.90±2.22	20.15±0.88	23.41±0.29	18.71±2.25
4	18.04±1.34	21.01±1.15	23.12±1.29	24.77±2.22	27.67±0.88	30.78±0.29	24.71±2.25
6	24.05±1.68	28.49±1.44	33.34±1.82	38.55±1.78	39.56±0.78	40.09±1.29	36.24±1.75
8	35.28±1.71	38.32±1.58	41.12±1.29	44.34±1.28	45.87±1.75	51.49±1.16	43.34±2.52
12	43.78±1.89	47.83±2.24	52.72±1.27	56.20±1.32	58.45±2.28	62.22±0.29	54.18±1.52
16	55.13±1.45	64.49±1.78	67.45±1.19	70.32±2.26	70.27±0.19	73.81±0.27	69.56±1.86
20	69.26±1.33	72.28±1.59	77.56±1.27	79.55±2.29	81.51±0.32	84.67±0.27	77.29±1.67
24	77.12±1.12	80.21±1.52	87.29±1.22	89.53±1.17	92.31±0.25	93.78±0.29	87.23±1.45

Above parameters are communicated as Average ± Standard Deviation; (n=3)

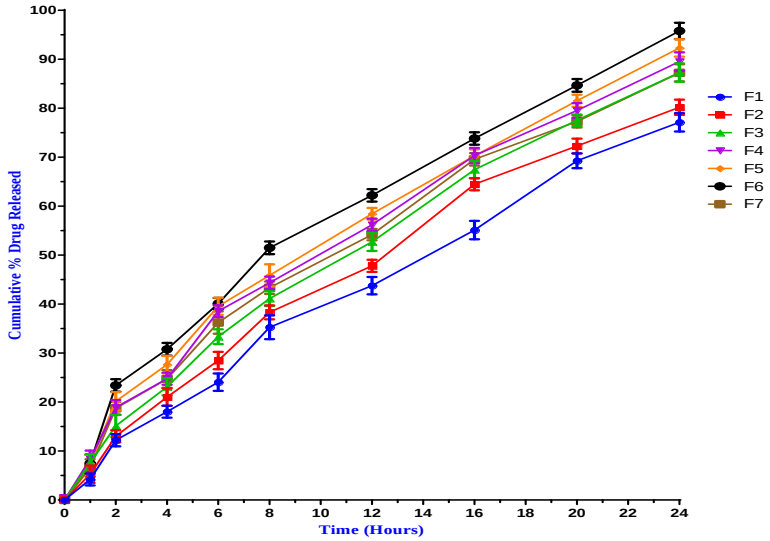

Fig 2: *In vitro* Drug Release Profile of Nifedipine floating tablets F1-F7

Table 7: *In vitro* Drug Release Profile of Nifedipine floating tablets F8-F14

Time (h)	F8	F9	F10	F11	F12	F13	F14
0	0	0	0	0	0	0	0
1	03.45±1.23	05.47±1.26	11.18±2.09	10.26±1.56	08.36±1.48	06.29±1.16	06.82±1.8=25
2	13.95±1.96	15.01±0.21	28.77±0.52	26.15±0.26	22.08±1.28	19.77±2.29	17.89±1.46
4	22.09±1.44	26.58±0.45	33.54±1.18	31.18±0.52	30.89±2.28	28.79±1.11	27.35±1.74
6	30.72±174	32.38±1.78	53.58±2.22	50.81±0.58	49.87±2.23	40.58±0.75	35.67±1.78
8	37.15±1.23	40.44±1.78	59.36±1.29	54.19±1.68	52.66±1.45	48.19±1.21	39.78±1.27
12	44.77±1.75	46.87±1.89	66.28±2.29	63.49±1.89	60.97±1.16	58.70±0.56	49.97±1.18
16	50.36±1.86	53.89±1.16	79.54±2.85	74.57±1.75	69.76±1.78	64.09±1.86	56.89±1.85
20	61.23±1.22	63.28±1.89	87.78±1.86	87.21±1.24	78.69±0.18	75.79±2.22	65.78±2.18
24	80.86±1.86	86.49±0.88	98.88±1.74	94.23±1.66	91.68±0.89	88.79±0.85	83.73±2.21

Above parameters are communicated as Average ± Standard Deviation; (n=3)

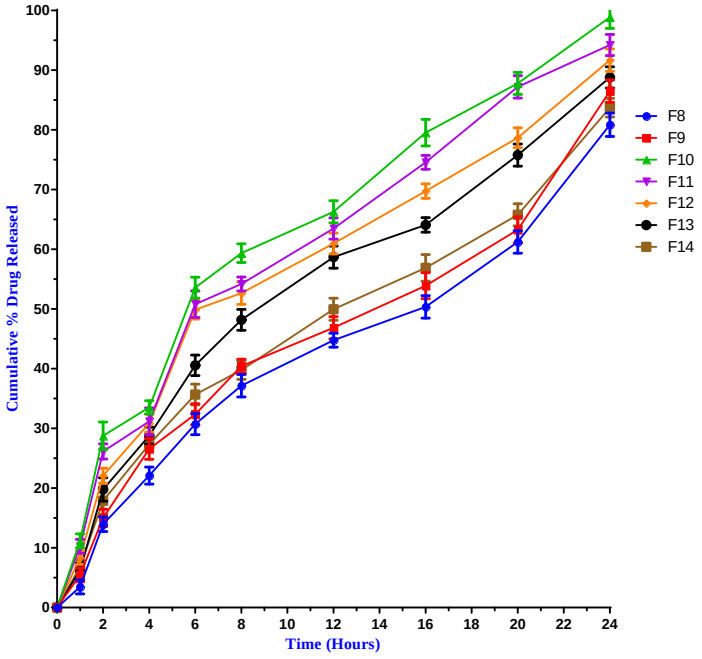

Fig 3: *In vitro* drug release profile of Nifedipine floating tablets F8-F14

Table 8: *In vitro* Drug Release Profile of Nifedipine floating tablets F15-F21

Time(h)	**F15**	**F16**	**F17**	**F18**	**F19**	**F20**	**F21**
0	0	0	0	0	0	0	0
1	04.18±2.09	05.24±1.16	07.58±1.25	08.47±1.18	14.33±1.37	10.46±1.25	09.55±2.33
2	12.37±1.52	15.27±1.78	17.35±1.14	19.65±1.14	20.46±2.24	23.34±1.78	16.12±1.21
4	19.28±1.22	22.46±1.15	25.79±1.33	27.64±1.31	28.78±2.38	30.58±1.69	25.67±1.29
6	32.54±1.18	40.05±1.17	44.64±1.86	46.30±1.98	40.97±2.22	48.78±1.28	38.34±2.89
8	40.25±1.20	47.35±1.78	52.56±1.89	54.40±1.82	56.67±1.75	59.78±1.24	47.12±2.41
12	53.28±2.29	59.94±1.96	62.78±1.75	63.50±1.78	64.89±1.96	67.66±1.75	59.72±2.11
16	61.54±2.85	64.88±1.48	66.69±1.44	68.76±1.44	69.67±1.18	73.56±1.22	65.45±2.75
20	73.78±1.86	75.74±1.47	79.89±2.45	80.27±1.47	81.66±2.15	84.65±1.16	80.56±1.78
24	82.23±1.16	85.78±1.24	89.69±1.27	91.67±1.39	93.18±1.23	95.65±1.17	91.45±1.19

Above parameters are communicated as Average ± Standard Deviation; (n=3)

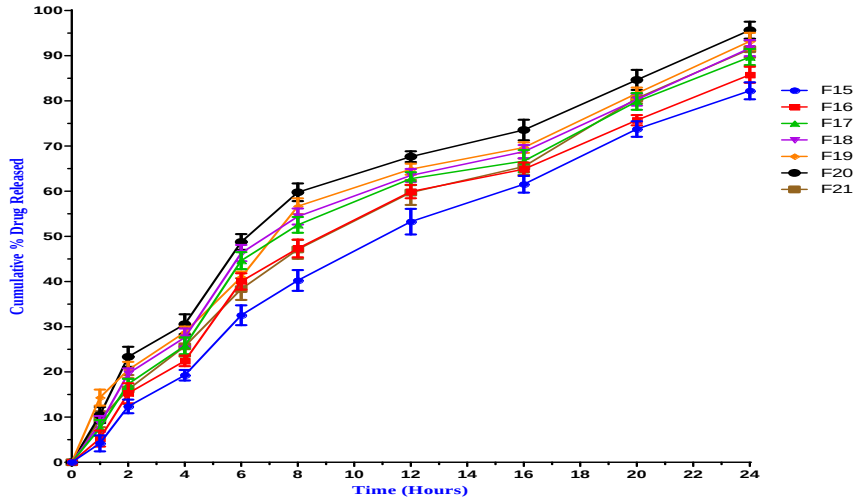

Fig 4: *In vitro* Drug Release Profile of Nifedipine floating tablets F15-F21

From the above Tables (Table 6, 7 and 8) and figures (Figure 2, 3 and 4), it can be observed that the polymer HPMC K 250 PH PRM has more controlling effect on Nifedipine when compared to HPMC K 750 PH PRM and HPMC K 1500 PH PRM. The difference in the drug release from various formulations was due to the presence of different concentrations of polymer. The concentrations of polymers was added in acsending order to check its drug retarding and release ability and F10 was considered as best formulation among all as it showed good buoyancy properties and controlled the drug release for desired period of time (24 hrs), where as marketed product drug release was found to be 97.33±1.21 within 1 hour.

Mathematical modeling of optimized formula (F10) of Nifedipine floating tablets

***In vitro* drug release order kinetics for optimized (F10) Formulation**

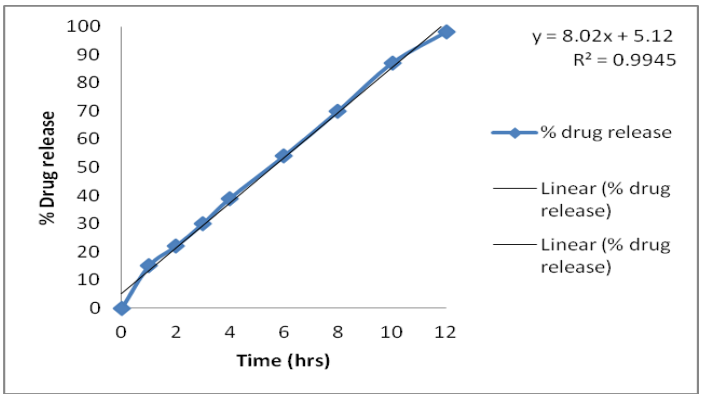

Fig 5: Zero order plots for the optimized formulation (F10) of Nifedipine floating tablets

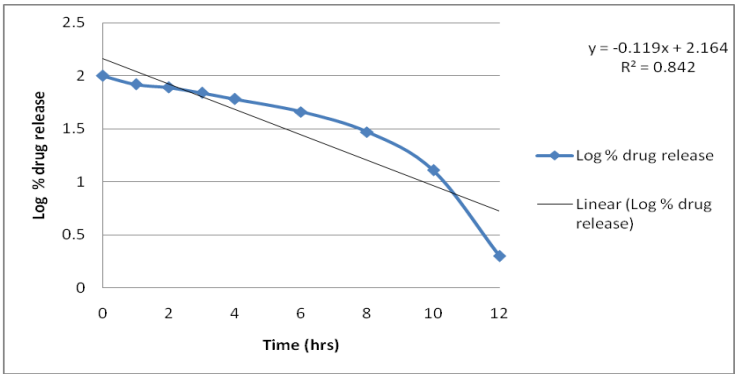

Fig 6: First order plots for the optimized formulation (F10) of Nifedipine floating tablets

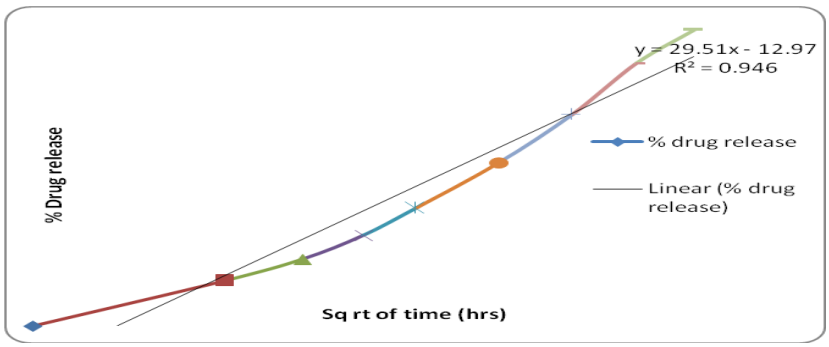

Fig 7: Higuchi plots for the optimized formulation (F10) of Nifedipine floating tablets

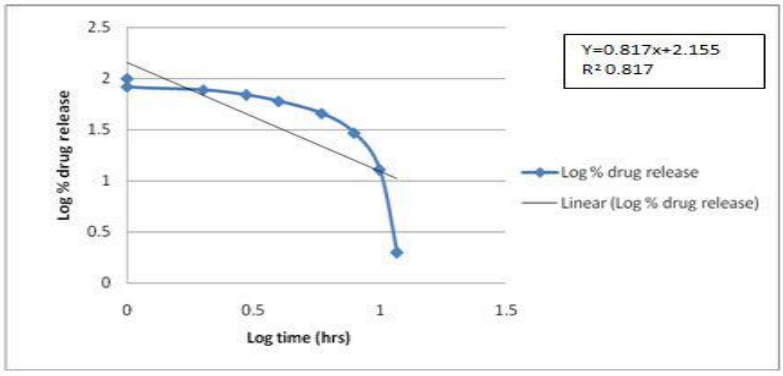

Fig 8: Korsmeyer-Peppas plots for the optimized formulation (F10) of Nifedipine floating tablets

***In vitro* drug release order kinetics for Marketed product**

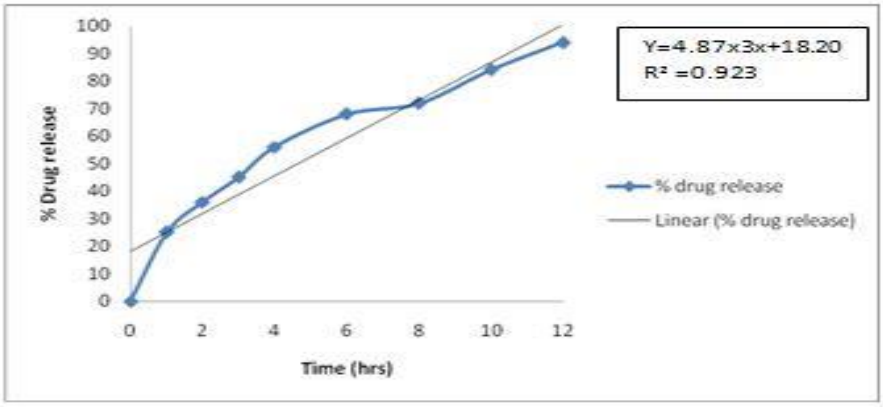

Fig 9: Zero order plots for the Marketed product

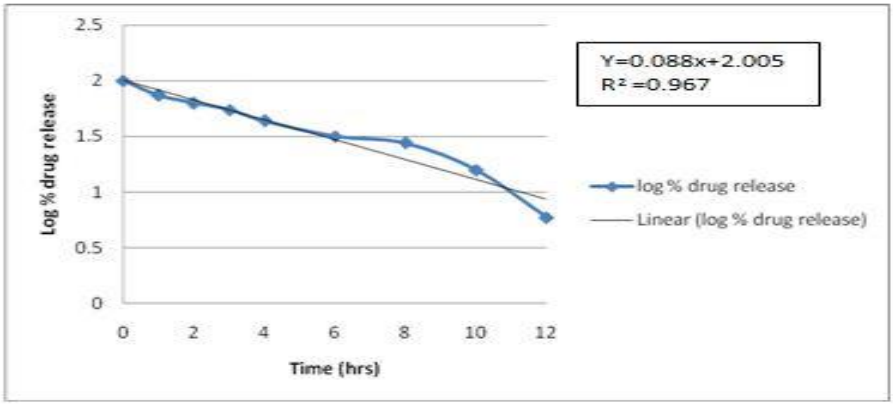

Fig 10: First order plot for the Marketed product

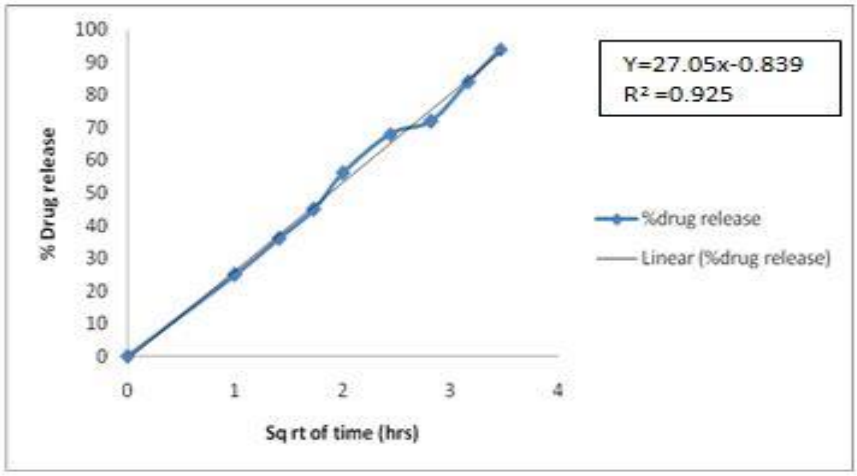

Fig 11: Higuchi plot for the Marketed product

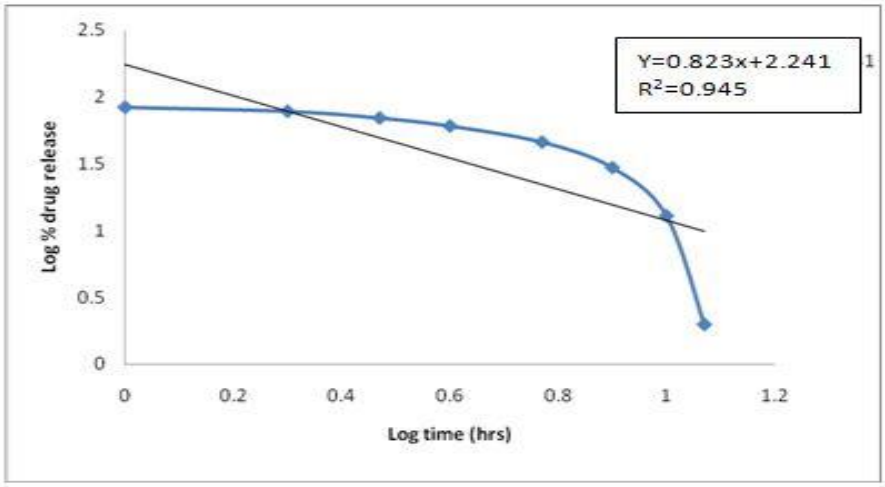

Fig 12 :Korsmeyer-Peppas plot for the Marketed product

Mathematical modeling of optimized formula (F10) of Nifedipine floating tablets

The in vitro drug release profiles were fitted to several kinetic models and release data followed by their R2. The optimized formulation was best fitted in Zero Order and Korsmeyer-Peppas. The optimized formulation n value was 0.817 indicating non Fickian (anomalous) transport thus it projected that delivered its active ingredient by coupled diffusion and erosion. The marketed conventional formulation followed the first order kinetics indicating drug release is directly proportional to the concentration of drug. The results are summarized in Table 9, and Figure 5-12.

Table 9: Regression coefficient (R^2) & n values for F10 and Marketed Product

Formulation Code	Zero Order		First Order		Higuchi		Korsmeyer-Peppas	
	R^2	n	R^2	n	R^2	n	R^2	n
F10	0.994	8.02	0.842	0.119	0.946	29.41	0.988	0.817
Marketed Formulation	0.923	4.87	0.967	0.088	0.925	27.05	0.945	0.823

FTIR STUDIES:

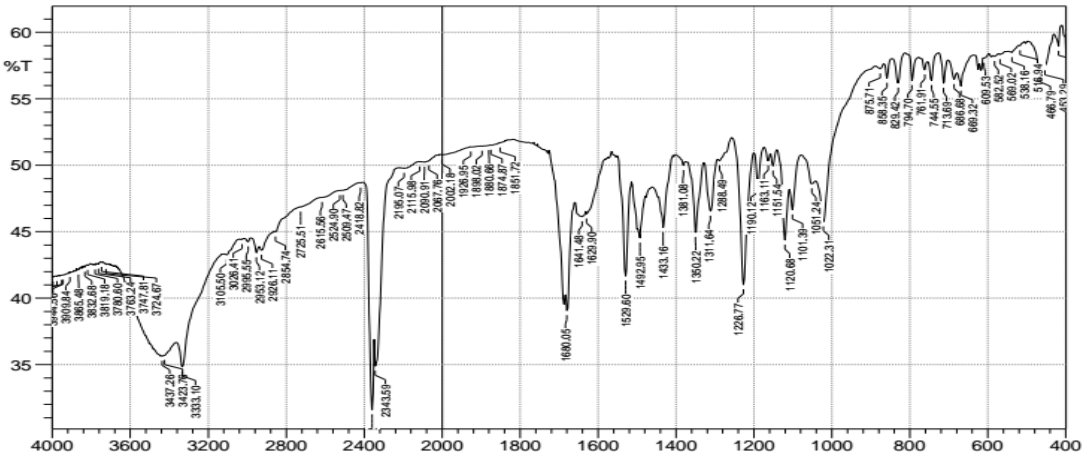

Fig 13: FTIR spectrum of Nifedipine pure drug

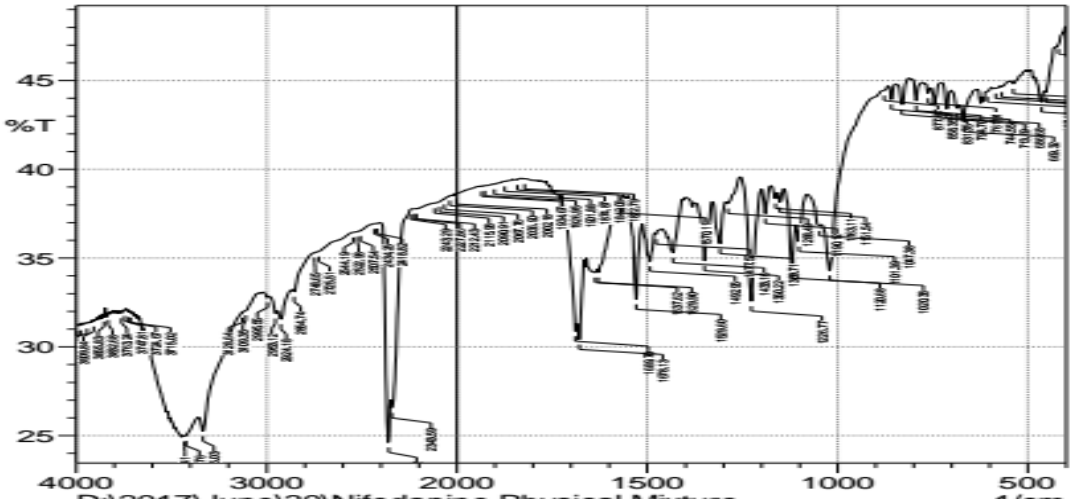

Fig 14: FTIR spectrum of Nifedipine physical mixture of optimized formulation

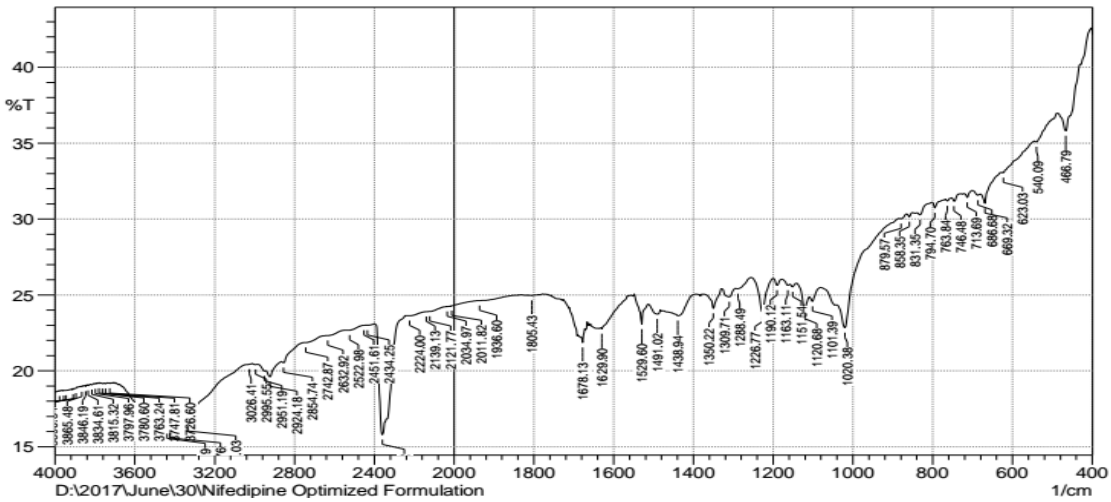

Fig 15: FTIR spectrum of optimized formulation of Nifedipine F10

The FTIR Spectrum of Nifedipine pure drug, physical mixture and optimized formulation are shown in Figure 13, 14 and 15. The FTIR spectrum of Nifedipine optimized formulation F10 exhibited characteristic bands consistent with the molecular structure of Nifedipine which indicated that no chemical interaction occurred between the drug and excipients used in the formulation.

Stability studies

Table 10: Parameters after accelerated stability study of optimized formulation F10

Parameters	Temperature Maintained at 40±2^{0}C ; Relative Humidity (RH) Maintained at 75%±5%RH			
	Initial	After 1 month	After 3 months	After 6 months
Drug Content (%)	99.93±1.21	99.91±1.47	99.88±1.36	99.82±1.29
In Vitro Drug Release (%)	98.88±1.62	98.86±1.58	98.85±1.42	98.80±1.35
Floating lag time	32	33	33	33

There were no physical changes in appearance and flexibility.After subjecting the optimized formulation (F10) to the Accelerated Stability Studies, the results showed that there were no major changes in Drug Content, *In Vitro* Drug Release, and floating lag time. Hence the formulation was found to be stable (Table 10).

CONCLUSION:

In the present work Nifedipine sustained release tablet was successfully formulated by using different novel polymers by wet granulation method. The drug-excipient interaction study was carried out using FTIR. In the drug-excipient interaction study, it was found that Nifedipine was having compatibility with all the excipients used in the formulation. Among all the formulation F10 was selected as optimized formulation because it showed maximum drug drug compared with other formulations. Nifedipine floating tablets can be an innovative and promising approach for the delivery of Nifedipine for the treatment of hypertension (high blood pressure) and angina (chest pain) for prolonged period of time.

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