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FORMULATION AND *IN VITRO* EVALUATION OF NIFEDIPINE FLOATING MATRIX TABLETS BY USING NATURAL POLYMERS

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Abstract:

In the present research work gastro retentive floating matrix formulation of Nifedipine by using Natural polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimised. Then the formulation was developed by using different concentrations of polymers Xanthan gum, guar gum and Karaya Gum as polymeric substances. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations Karaya Gum as polymer were retarded the drug release more than12 hours. whereas in low concentrations the polymer was unable to produce the desired action. The formulations prepared with guar gum were also retarded the drug release up to 12 hours (F6=96.32%). The optimised formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed zero order mechanism of drug release.

Keywords: *Nifedipine, Xanthan gum, guar gum and Karaya Gum, Floating Tablets*

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INTRODUCTION:

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process [1]. Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the Css values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs [2].

Advantages of GFDDS: Floating drug delivery offers several applications for drugs having poor Bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage forms at the site of absorption and thus enhances the Bioavailability. These are summarized as follows.

1. Sustained Drug Delivery: Sustained drug absorption from oral controlled release dosage form is often limited due to short gastric retention time. However, GFDDS remain in the stomach for several hours to increase GRT.

2. Site Specific Drug Delivery: Drugs having absorption sites in the upper small intestine like furosemide and riboflavin are typically formulated in the floating dosage forms. It has been reported that absorption of furosemide takes place mainly through stomach followed by duodenum. This characteristics of furosemide prompted scientists to develop a monolithic floating system, which could prolong the GRT and thereby increase the bioavailability

3. Absorption or Bioavailability Enhancement: Drugs that have poor Bioavailability because of site-specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.

4. Fewer Doses: Creating once daily formulations for improved patient compliance.

5. Improved plasma levels: Both extends plasma concentration levels and provides a more linear release profile.

6. Better Bioavailability: Delivers the drug in the upper G.I. tract for optimal absorption.

7. Less Irritation: the polymer matrix acts as a buffer between harsh drug crystals and the stomach lining.

8. Fewer side effects: keeps drugs out of the lower GI tract which can be harmful to intestinal flora. Lower peak concentrations can also reduce adverse pharmacological effects.

9. Low risk inactive ingredients: Tablets are composed of well understood polymers from the FDA.s inactive ingredients list. This keeps the regulatory risks and hurdles of the formulation to an absolute minimum.

10. Manufacturing ease: Tablets are made in standard high-speed tableting equipment. No special tooling or engineering is required. This enables high quality, consistency, rapid scale-up and technology transfer to the development and marketing partners.

11. Low cost: The ingredients used in these systems are commodity items produced in extremely large quantity and at very low cost [4].

Limitations:

1. The major disadvantage of floating systems is requirement of a sufficiently high level of fluids in the stomach for the drug delivery i.e. up to 400ml of gastric fluids should be present for optimum buoyancy. However, this limitation can be overcome by coating the dosage form with bioadhesive polymers, which easily adhere to the mucosal lining of the stomach and retain. The dosage form can be administered with a glass full of water (200-250 ml) to provide the initial fluid for buoyancy.
2. Floating system is not feasible for those drugs that have solubility or stability problems in gastric fluids.
3. Drugs that are not stable at gastric pH are not suitable candidates to be as GFDDS.
4. Drugs that irritate the mucosa are not suitable candidates and should be avoided to be formulated as GFDDS [5,6].

Nifedipine Is Used For the management of vasospastic angina, chronic stable angina, hypertension, and Raynaud's phenomenon. May be used as a first line agent for left ventricular hypertrophy and isolated systolic hypertension (long-acting agents).

MATERIALS AND METHODS:

Materials

Nifedipine was a gift sample Provided by Sura Labs, Dilsukhnagar. Xanthan Gum, Guar Gum, Karaya Gum, Sodium bicarbonate, Citric Acid, PVP K 30, Magnesium stearate, Micro crystalline cellulose, Talc were obtained from Merck Specialities Pvt Ltd, Mumbai, India.

Methods

Preparation of Floating Matrix Tablets

Table 1: Formulation composition for Floating tablets

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nifedipine	30	30	30	30	30	30	30	30	30
Xanthan Gum	30	60	90	-	-	-	-	-	-
Guar Gum	-	-	-	30	60	90	-	-	-
Karaya Gum	-	-	-	-	-		30	60	90
PVP K30	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
$NaHCO_3$	15	15	15	15	15	15	15	15	15
Citric Acid	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mg. Stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
MCC PH 102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Post-Compressional Studies:

Weight variation test:

According USP twenty tablets were selected randomly from each batch and weighed individually by using analytical weighing balance. The average and standard deviation were calculated.

Thickness:

The tablets thickness is important for uniformity of tablet size. Thickness was measured using Vernier Caliper. The average of three tablets was taken. The tablet thickness should be controlled within ± 5 variations of a standard value.

Hardness test:

The hardness of the tablet indicates the ability of a tablet to withstand mechanical shocks while handling. It is measured by using Monsanto hardness tester. It is expressed in kg/cm^2. The average of six tablets was taken according to USP guidelines from each formulation.

Friability test:

It indicates the loss in weight of tablets in containers during transportation. Roche friabilator was used. 20 tablets were weighed and initial weight was recorded and place in Roche friabilator and rotates at 25 rpm for 4 minutes. The tablets were removed and again weighed, final weight was recorded. It is calculated by using the equation.

$$\% \text{ Friability} = \frac{\text{Initial weight of the tablets} - \text{Final weight of the tablets}}{\text{Initial weight of the tablets}} \times 100$$

Determination of drug content:

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of clopidogrel were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* Buoyancy studies:**

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described by Rosa et al) The tablets were placed in a 100ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float

was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

***In vitro* drug release studies**

Dissolution parameters:

Apparatus -- USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCL
RPM -- 50
Samplingintervals(hrs)--0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature --37°c + 0.5°c

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

RESULT AND DISCUSSION:

Analytical Method

a. Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 237 nm.

b. calibration curve :Graphs of Nifedipine was taken in 0.1N HCL (pH 1.2)

Table 2: Observations for graph of Nifedipine in 0.1N HCL

Conc [µg/mL]	Abs
0	0
5	0.139
10	0.284
15	0.44
20	0.578
25	0.702

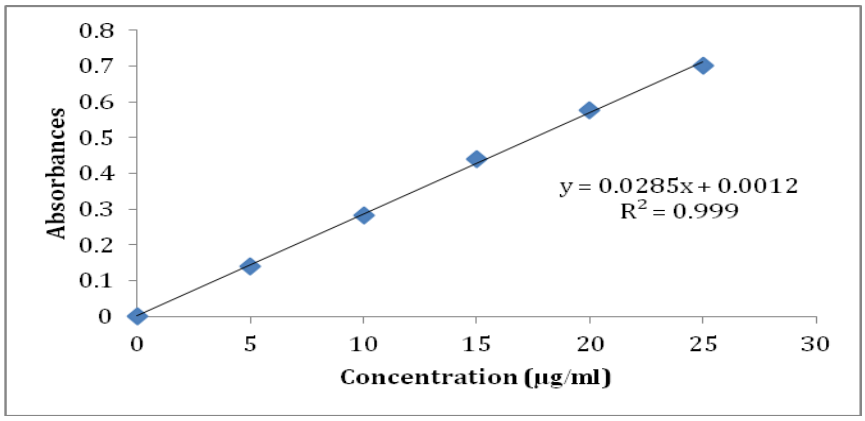

Fig1 : Standard graph of Nifedipine in 0.1N HCL

Standard graph of Nifedipine was plotted as per the procedure in experimental method and its linearity is shown in Table and Fig. The standard graph of Nifedipine showed good linearity with R2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Drug – Excipient compatability studies

Fourier Transform-Infrared Spectroscopy:

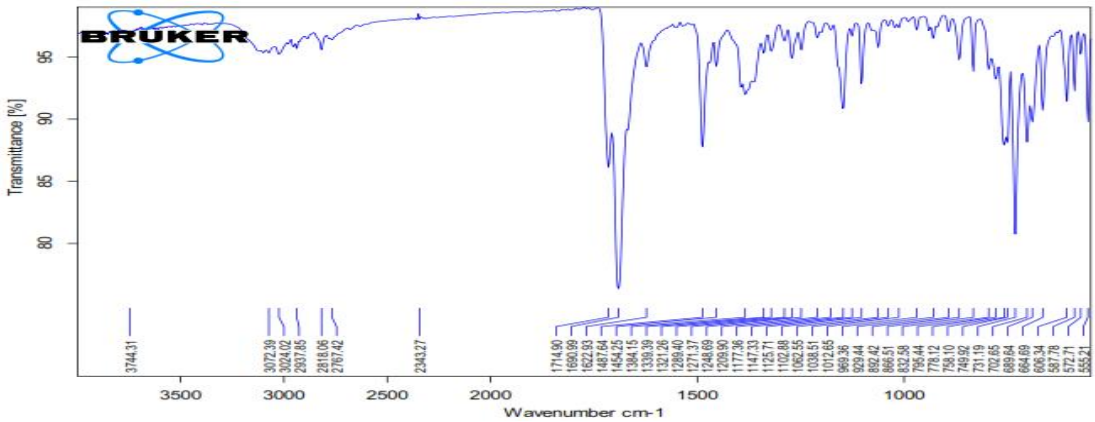

Fig.2: FTIR Spectrum of pure drug

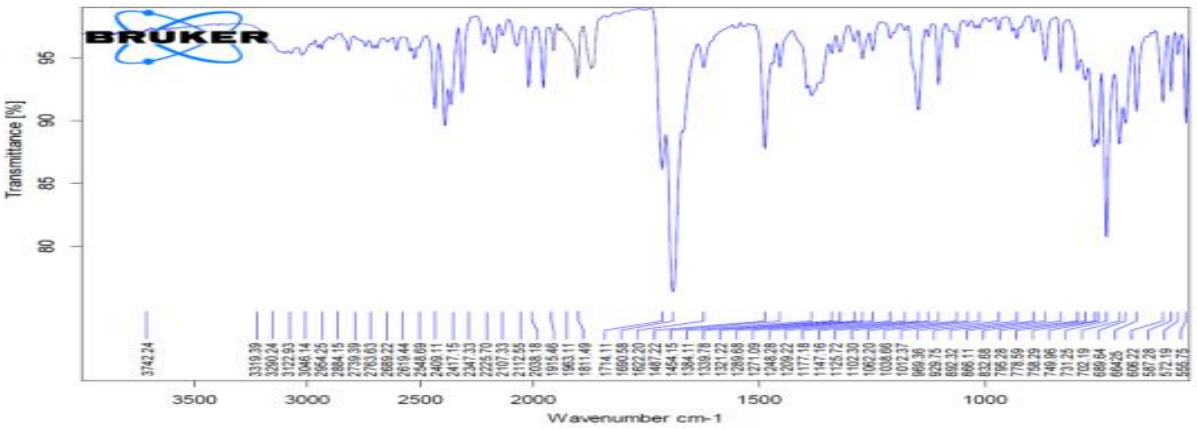

Fig.3: FTIR Spectrum of optimised formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Nifedipine are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

Preformulation parameters of powder blend:

Table 3: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
F1	25.12	0.59	0.66	11.86	1.11
F2	26.8	0.48	0.54	12.5	1.12
F3	23.74	0.56	0.66	17.85	1.17
F4	26.33	0.44	0.55	18.18	1.18
F5	25.21	0.48	0.57	16.66	1.16
F6	27.18	0.51	0.59	15.68	1.15
F7	24.29	0.46	0.56	17.85	1.21
F8	26.01	0.50	0.59	15.25	1.18
F9	26.12	0.52	0.63	17.46	1.21

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.48 to 0.59 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.54 to 0.66 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 18 which shows that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Optimization of sodium bicarbonate concentration:

Three formulations were prepared with varying concentrations of sodium bicarbonate by direct compression method and three more formulations were prepared by wet granulation method to compare the floating buoyancy in between direct and wet granulation methods. The formulation containing sodium bicarbonate in 15mg concentration showed less floating lag time in wet granulation method and the tablet was in floating condition for more than 12 hours.

Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

***Table 4 : In vitro* quality control parameters**

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)	Total Floating Time(Hrs)
F1	148.4	5.1	0.61	3.3	98.42	5.5	4
F2	149.2	5.2	0.58	3.2	99.65	4.2	6
F3	151.3	5.5	0.45	3.4	99.12	5.0	12
F4	146.3	5.1	0.61	3.3	98.42	5.1	6
F5	148.6	5.3	0.59	3.5	99.65	4.0	8
F6	152.4	5.5	0.65	3.4	99.12	3.2	12
F7	150.6	5.3	0.62	3.6	98.16	4.5	5
F8	151.2	5.2	0.59	3.4	98.11	3.6	12
F9	147.5	5.4	0.60	3.3	98.25	4.7	12

All the parameters for SR layer such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

***In Vitro* Drug Release Studies**

Table 5: Dissolution data of Floating Tablets

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	35.32	30.04	24.63	19.17	14.90	10.49	23.56	16.76	10.15
1	54.53	47.56	30.63	24.12	20.45	17.63	46.45	21.89	15.41
2	69.90	54.35	42.52	38.64	32.02	26.55	51.23	28.24	20.98
3	74.96	63.52	50.31	50.20	39.31	32.84	70.54	33.32	25.09
4	86.14	74.75	58.25	69.56	47.82	39.39	79.73	37.75	29.54
5	92.85	82.54	65.78	75.43	53.47	44.71	86.46	42.09	33.36
6		89.26	70.17	83.01	59.74	53.05	98.12	49.16	39.67
7		95.95	75.79	95.57	64.05	60.87		53.36	44.36
8			82.27		79.93	67.02		59.12	50.77
9			89.64		84.26	74.15		63.78	56.42
10			94.87		95.45	79.24		67.79	60.02
11						87.54		76.31	64.46
12						96.32		84.45	69.39

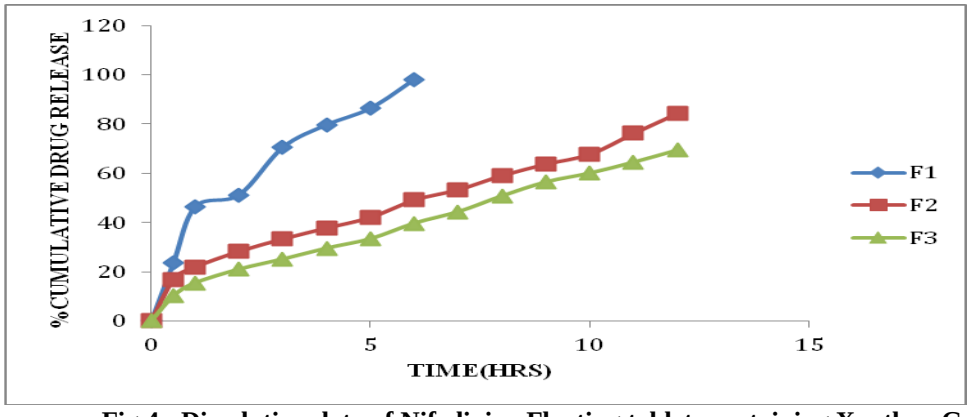

Fig.4 : Dissolution data of Nifedipine Floating tablets containing Xanthan Gum

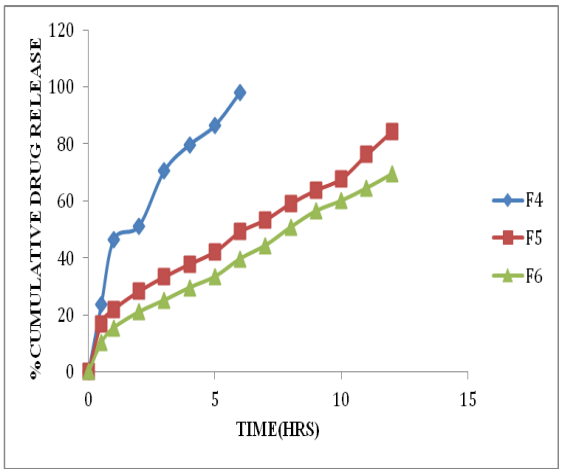

Fig. 5: Dissolution data of Nifedipine Floating tablets containing Guar Gum

From the dissolution data it was evident that the formulations prepared with Karaya Gum as polymer were retarded the drug release more than 12 hours.

Whereas the formulations prepared with higher concentration of guar gum retarded the drug release up to 12 hours in the concentration 90 mg. In lower concentrations the polymer was unable to retard the drug release.

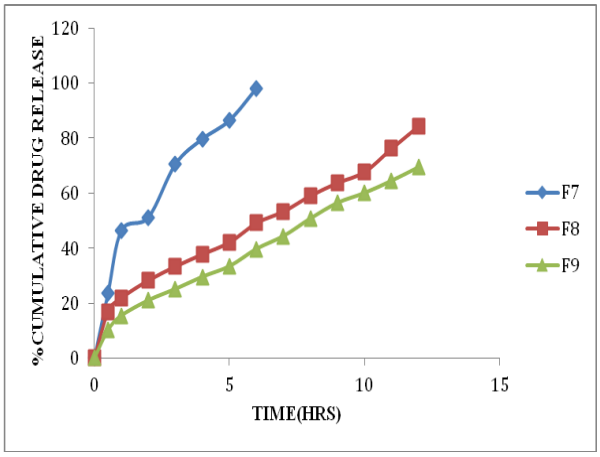

Fig.6: Dissolution data of Nifedipine Floating tablets containing Karaya Gum

The formulations prepared with xanthan gum showed very less retardation capacity hence they were not considered.

Hence from the above dissolution data it was concluded that F6 formulation was considered as optimised formulation because good drug release (96.32%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation:

Table 6: Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3 -Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
10.49	**0.5**	0.707	1.021	-0.301	1.952	20.980	0.0953	-0.979	89.51	4.642	4.473	0.168
17.63	**1**	1.000	1.246	0.000	1.916	17.630	0.0567	-0.754	82.37	4.642	4.351	0.291
26.55	**2**	1.414	1.424	0.301	1.866	13.275	0.0377	-0.576	73.45	4.642	4.188	0.454
32.84	**3**	1.732	1.516	0.477	1.827	10.947	0.0305	-0.484	67.16	4.642	4.065	0.577
39.39	**4**	2.000	1.595	0.602	1.783	9.848	0.0254	-0.405	60.61	4.642	3.928	0.713
44.71	**5**	2.236	1.650	0.699	1.743	8.942	0.0224	-0.350	55.29	4.642	3.810	0.832
53.05	**6**	2.449	1.725	0.778	1.672	8.842	0.0189	-0.275	46.95	4.642	3.608	1.034
60.87	**7**	2.646	1.784	0.845	1.593	8.696	0.0164	-0.216	39.13	4.642	3.395	1.247
67.02	**8**	2.828	1.826	0.903	1.518	8.378	0.0149	-0.174	32.98	4.642	3.207	1.435
74.15	**9**	3.000	1.870	0.954	1.412	8.239	0.0135	-0.130	25.85	4.642	2.957	1.685
79.24	**10**	3.162	1.899	1.000	1.317	7.924	0.0126	-0.101	20.76	4.642	2.748	1.893
87.54	**11**	3.317	1.942	1.041	1.096	7.958	0.0114	-0.058	12.46	4.642	2.318	2.323
96.32	**12**	3.464	1.984	1.000	0.566	8.027	0.0104	-0.016	3.68	4.642	1.544	3.098

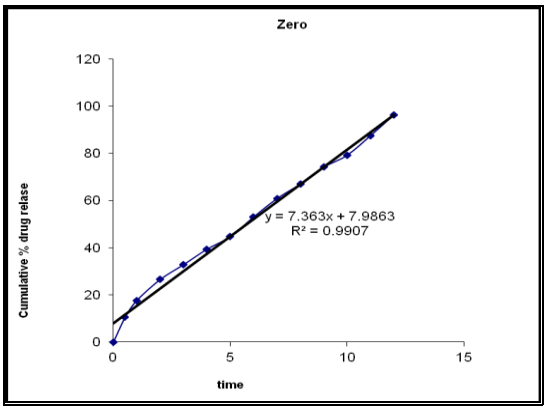

Fig.7 : Zero order release kinetics

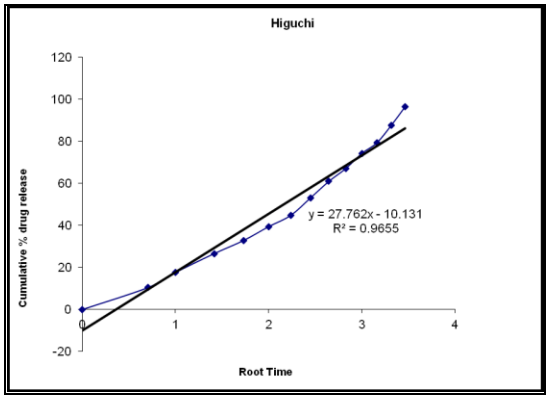

Fig.8 : Higuchi release kinetics

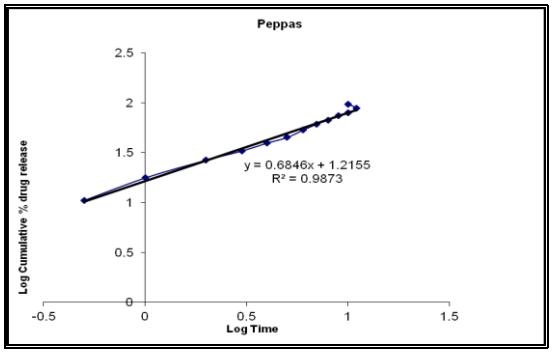

Fig.9 : Kors mayer peppas release kinetics

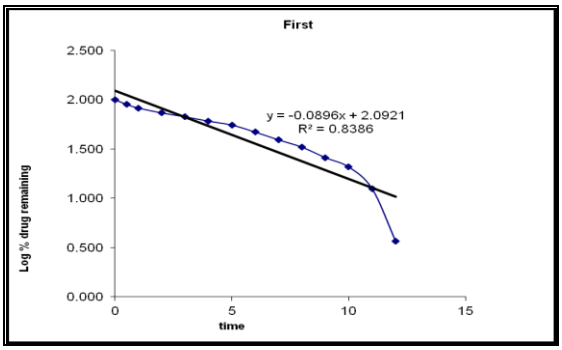

Fig.10: First order release kinetics

Optimised formulation F6 was kept for release kinetic studies. From the above graphs it was evident that the formulation F6 was followed Zero order release mechanism.

CONCLUSION:

Development of Gastro retentive floating drug delivery of Nifedipine tablets is to provide the drug action up to 12 hours.

Gastro retentive floating tablets were prepared by direct compression method using various Natural polymers like Xanthan gum, guar gum and Karaya Gum.

The formulated gastro retentive floating tablets were evaluated for different parameters such as drug excipient compatability studies, weight variation, thickness, hardness, content uniformity, In vitro Buoyancy studies, In-vitro drug release studies performed in 0.1N HCL for 12 hrs and the data was subjected to zero order, first order, Higuchi release kinetics and karsmayer peppas graph.

The following conclusions could be drawn from the results of various experiments

1. FTIR studies concluded that there was no interaction between drug and excipients.
2. The physico-chemical properties of all the formulations prepared with different polymers Xanthan gum, guar gum and Karaya Gum were shown to be within limits.
3. Quality control parameters for tablets such as weight variation, Hardness, Friability, thickness, drug content and floating lag time were found to be within limits.
4. In-vitro drug release studies were carried out for all prepared formulation and from that concluded F6 formulation has shown good results.
5. Finally concluded release kinetics to optimised formulation (F6) has followed Zero order kinetics.
6. Present study concludes that gastro retentive floating system may be a suitable method for Nifedipine administration.

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REFERENCES:

1.Leon lachman, herbert a. Liberman, the theory and practice of industrial pharmacy: p.293-302.

2.Robinson jr, lee v.h.l, controlled drug delivery: fundamentals and applications, 2nd edn. Marcel dekker, new york: (1978) p.24-36.

3.Roop k. Khar, controlled drug delivery,

gastroretentive system 4th edn. P. 202-203.
4.Mendhan j, denney r.c, barnes d.j, thomas m. Vogel's textbook of quantitative chemical analysis, 6th ed. Pearson education ltd: new delhi: (2000); p.367-384.
5.M. Sravanthi, dr. K. Abbulu and aastha saxena "formulation and evaluation of bilayer floating tablets of amlodipine besylate and metoprolol succinate" ipp, (2014):2 (1); 328-339,
6.Martindale: thirty first edition, the complete drug reference. P.102.1
7.S. Sathiyaraj, Ramya D. Devi, Vedha B. N. Hari . Lornoxicam gastro retentive floating matrix tablets:Design and in vitro evaluation. Journal of Advanced Pharmaceutical Technology & Research. Vol 2 () . 2016 , 156-162 .
8.S. T. Prajapati , L. D. Patel and D. M. Patel . Studies on Formulation and In Vitro Evaluation of Floating Matrix Tablets of Domperidone. Indian Journal of Pharmaceutical Sciences. 2016 , 19-23.
9.C. Loh, Zhiao; A. Elkordy, Amal . Formulation and Evaluation of Different Floating Tablets Containing Metronidazole to Target Stomach. Current Drug Delivery, Volume 12,(4), 2015, 425-443.
10.Safwan Abdel Rahim , Paul ACarter , Amal Ali Elkordy . Design and evaluation of effervescent floating tablets based on hydroxyethyl cellulose and sodium alginate using pentoxifylline as a model drug . Drug Design, Development and Therapy . 2015 , 1843-1859 .
11.Lakshmaiah, a. S., akki, r., & reddy, d. N. Formulation and evaluation of hydrodynamically balanced floating tablets of antidiabetic agent.acta chim. Pharm. Indica.(2014);4(1): 7-19.
12.Alam, p., mk anwer, and ma ghanie. "Development and evaluation of gastroretentive floating tablets of ginger extract: antiulcer activity". (2014); 3(11): 2455-2465.
13.Rao, M. S., Madhuri, K. S. N., & Kumar, G. V. Formulation and evaluation of controlled release floating tablets of lamivudine employing HPMC K4M and sodium alginate. Int. J. Pharm. Sci. & Res. (2014); 4(1):396-400.
14.Chavan Bhagyashri, and Abha Doshi. "Formulation and evaluation of floating tablets of losartan potassium." (2013): 048-059.
15.CH Swarna Kamala, K. Srinivas Reddy Kota, M. Hadassah, E. Hepsibha Metilda, and S. Sridevi. "Formulation and evaluation of gastroretentive floating tablets of gabapentin using effervescent technology."Int J Pharm .(2012);3(4): 202-208.
16.MargretChandira, R., Arafath, A. M. Y., Bhowmik, D., Jayakar, B., & Kumar, K. S. Formulation and Evaluation of Bilayered Floating Tablets of Metformin Hydrochloride.(2012);1(5):23-34.
17.Sivabalan, M., Vani, T., Phaneendhar Reddy, V., & Anup Jose, N. G. Formulation and evaluation of gastroretentive Glipizide floating tablets.International Journal of Comprehensive Pharmacy. (2011);2(1): 1-4.
18.Kumar M. Vinoth, D. Krishnarajan, R. Manivannan, and K. G. Parthiban. "Formulation and evaluation of bi-layer domperidone floating tablets."International journal of Pharmaceutical sciences and Research. (2011); 2: 2217-2225.