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FORMULATION AND INVITRO EVALUATION OF NIFEDIPINE EFFERVESCENT FLOATING MATRIX TABLETS BY USING HYDROPHILIC POLYMERS

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ABSTRACT

In the present work, an attempt has been made to develop gatroretentive effervescent floating matrix tablets of nifedipine by using hydrophilic polymers such as Gum Cyamopsis, Xanthan gum and Sodium alginate as retarding polymers. The polymers are used in different ratios, all the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters such as hardness, thickness, friability, percent drug content, weight variation tests and they passed all the quality control evaluation parameters as per I.P limits. Sodium bi carbonate concentration is optimized by trails, we found 20% is optimum to obtain required floating lag time (22.9 seconds) and total floating time (≥12 hours). Among all the formulations F3 formulation showed maximum percent drug release i.e., 99.86% in 12 hours. Hence it is considered as optimized formulation with the optimum concentration of polymer. It was observed that the 1:30 ratio of gum cyamopsis has distinct effect on in vitro drug release profiles up to 12 hours, when compared to all the other ratios of polymers. Drug release kinetics followed Zero order.

KEYWORDS: nifedipine, floating matrix tablets, Gum Cyamopsis, Xanthan gum, Sodium, floating lag time, total floating time.

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.[1,2]

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, drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{ss} values fall or rise beyond the therapeutic range. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs. In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.

Controlled drug delivery systems

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue.[13]

Nifedipine under goes hepatic metabolism, therefore it has very low bioavailability (40-56%) and short half-life (2hr) due to which the drug is administered in multiple doses. So to enhance the bioavailability and reduce the dosage of Nifedipine is best formulated as intra gastric floating tablets.

METHODOLOGY

Formulation development of tablets

All the formulations were prepared by direct compression. The formulae of different formulations are given in Table 1. Total weight of the tablet was considered as 200mg.

Table 1: The formulae of different formulations F1-F9 (mg/tablet).

F Code	Drug	Gum Cyamopsis	Xanthan gum	Sodium alginate	$NaHCO_3$ (20%)	Mag. Stearate (2%)	Talc (2%)	MCC pH102	Total weight
F1	20	20	-----	-----	40	4	4	112	200
F2	20	40	-----	-----	40	4	4	92	200
F3	20	60	-----	-----	40	4	4	72	200
F4	20	-----	20	-----	40	4	4	112	200
F5	20	-----	40	-----	40	4	4	92	200
F6	20	-----	60	-----	40	4	4	72	200
F7	20	-----	-----	20	40	4	4	112	200
F8	20	-----	-----	40	40	4	4	92	200
F9	20	-----	-----	60	40	4	4	72	200

RESULTS

Analytical method

Standard calibration curve of Nifedipine was taken in Simulated Gastric fluid (pH 1.2) at 237 nm (table 2 and figure 1).

Table 2: Observations for graph of Nifedipine in 0.1N HCl (237 nm).

Conc (µg/ml)	Absorbance
0	0
2	0.12
4	0.243
6	0.373
8	0.503
10	0.612

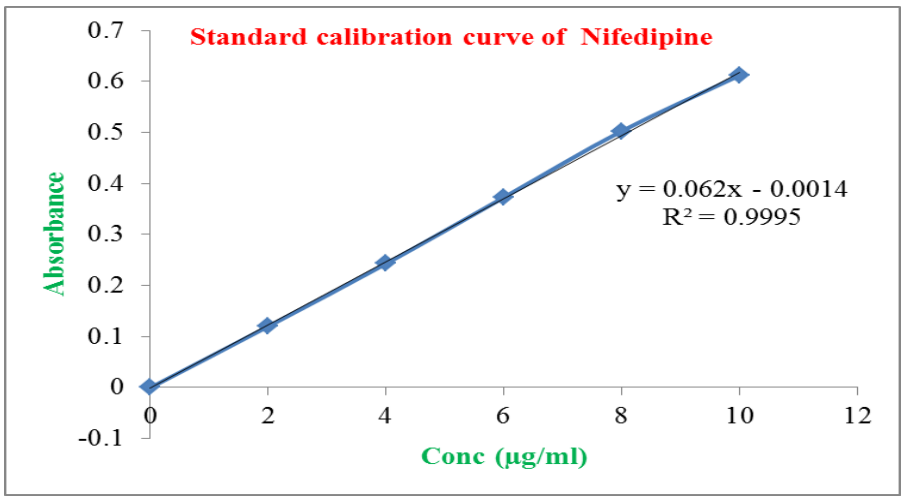

Figure 1: Standard graph of nifedipine in 0.1N HCl.

Drug – excipient compatability studies

Fourier transform-infrared spectroscopy

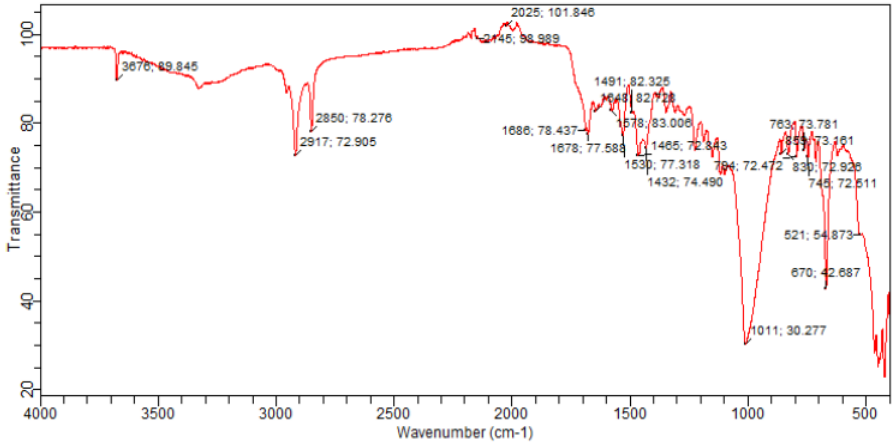

Figure 2: FT-IR Spectrum of Nifedipine pure drug.

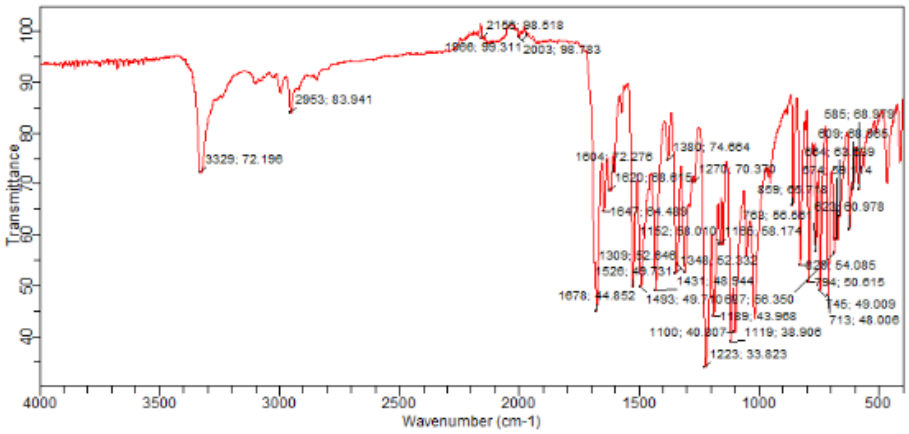

Figure 3: FT-IR Spectrum of Optimised Formulation.

From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible (figure 2 and 3).

Table 3: Preformulation parameters of powder blend.

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	25.19 ± 0.12	0.35 ± 0.08	0.41 ± 0.14	14.63 ± 0.53	1.17 ± 0.02
F2	27.32 ± 0.25	0.37 ± 0.12	0.45 ± 0.35	17.77 ± 0.44	1.21 ±0.03
F3	25.43 ± 0.31	0.40 ± 0.34	0.48 ± 0.43	16.66 ± 0.37	1.2 ± 0.04
F4	28.17 ± 0.43	0.46 ± 0.53	0.53 ± 0.51	13.02 ± 0.25	1.15 ± 0.04
F5	26.43 ± 0.25	0.40 ± 0.41	0.48 ± 0.35	16.66 ± 0.37	1.2 ± 0.06
F6	29.32 ± 0.18	0.47 ± 0.53	0.55 ± 0.43	14.54 ± 0.25	1.17 ± 0.03
F7	29.34 ± 0.43	0.40 ± 0.36	0.49 ± 0.22	18.36 ± 0.34	1.22 ± 0.05
F8	27.68 ± 0.51	0.41 ± 0.43	0.48 ± 0.43	14.5 ± 0.43	1.17 ± 0.04
F9	27.86 ± 0.35	0.38 ± 0.33	0.46 ± 0.52	17.39 ± 0.18	1.21 ± 0.08

The bulk density of all the formulations was found to be in the range of 0.35 ± 0.08 to 0.47 ± 0.53 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.41 ± 0.14 to 0.53 ± 0.51 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 14.5 ± 0.43 to 18.36 ± 0.34 which show that the powder has good flow properties. All the formulations has shown the hausner's ratio ranging between 0 to 1.25 indicating the powder has good flow properties (table 3).

Post compression parameters for tablets

Tablet quality control tests such as weight variation, hardness and friability, thickness and drug release studies in different media were performed on the tablets.

Table 4: Post compression parameters for tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (seconds)
F1	202.5±3.25	4.1±0.17	0.58±0.05	3.8±0.29	95.67	24.5
F2	200.4±3.20	4.0±0.17	0.61±0.05	3.9±0.29	98.54	25.1
F3	199.6±3.42	4.1±0.16	0.56±0.05	4.5±0.30	101.43	22.9
F4	201.6±3.66	4.3±0.17	0.59±0.05	4.0±0.25	100.78	25.6
F5	201.4±3.92	4.5±0.18	0.64±0.06	4.2±0.27	96.41	24.9
F6	200.7±2.35	4.1±0.14	0.50±0.05	3.5±0.27	98.65	25.4
F7	201.3±2.55	4.4±0.16	0.63±0.05	4.0±0.20	108.24	25.2
F8	196.2±2.45	4.0±0.11	0.50±0.03	3.7±0.25	102.56	24.6
F9	197.3±2.53	4.2±0.007	0.55±0.01	4.2±0.15	99.21	25.4

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits (table 4).

In-vitro drug release studies

Table 5: Dissolution data of Nifedipine Tablets.

Time (hrs)	Cumulative percent drug released (n=3±SD)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	23.57	14.09	10.98	45.56	26.77	20.45	46.23	15.14	10.77
1	32.12	25.45	18.67	62.54	37.89	29.45	58.42	29.81	23.91
2	42.45	37.28	24.35	80.32	46.24	39.98	65.9	35.34	35.23
3	53.1	44.31	29.34	98.36	55.23	47.99	73.56	40.52	39.13
4	69.66	52.67	36.68		63.25	54.91		48.53	41.1
5	76.33	66.78	40.31		78.9	65.46		53.64	47.97
6	84.01	75.32	47.76		89.56	71.47		59.54	52.57
7	96.77	81.04	54.72		97.66	77.32		63.53	59.49

8		90.73	65.33			85.49		69.46	63.67
9		98.76	69.92			91.12		72.53	67.82
10			77.24			99.55		78.23	70.32
11			86.22					81.56	76.39
12			99.86					88.78	80.21

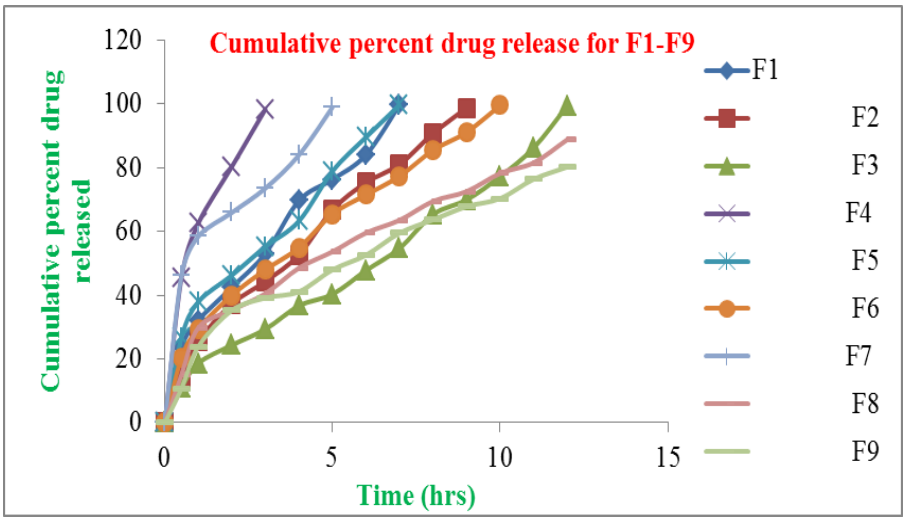

Figure 4: Dissolution data of Nifedipine Tablets.

Table 6: Release kinetics data for optimised formulation.

Cumulative (%) release Q	Time (T)	Root (T)	Log (%) release	Log (T)	Log (%) remained
10.98	0.5	0.707	1.041	-0.301	1.949
18.67	1	1.000	1.271	0.000	1.910
24.35	2	1.414	1.386	0.301	1.879
29.34	3	1.732	1.467	0.477	1.849
36.68	4	2.000	1.564	0.602	1.802
40.31	5	2.236	1.605	0.699	1.776
47.76	6	2.449	1.679	0.778	1.718
54.72	7	2.646	1.738	0.845	1.656
65.33	8	2.828	1.815	0.903	1.540
69.9	9	3.000	1.844	0.954	1.479
77.2	10	3.162	1.888	1.000	1.358
86.22	11	3.317	1.936	1.041	1.139
99.36	12	3.464	1.997	1.079	-0.194

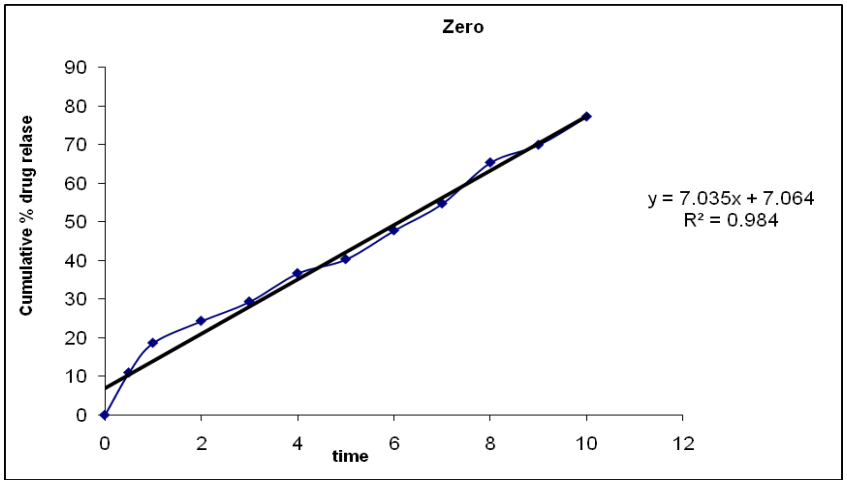

Figure 5 : Zero order release kinetics graph.

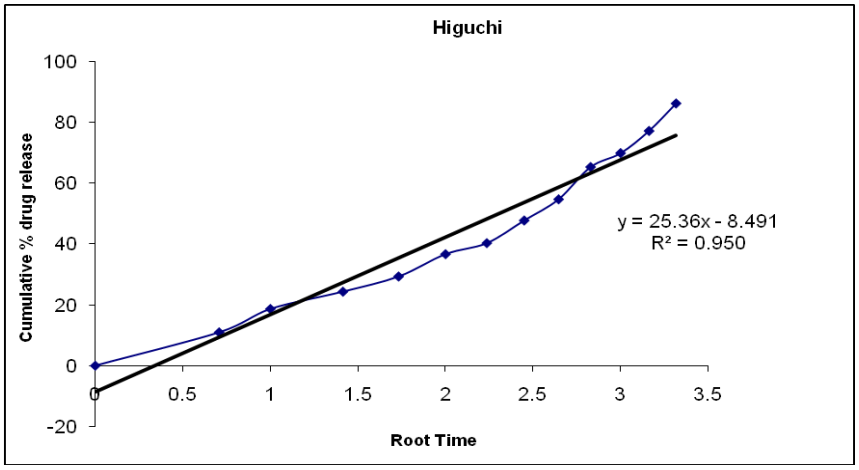

Figure 6 : Higuchi release kinetics graph.

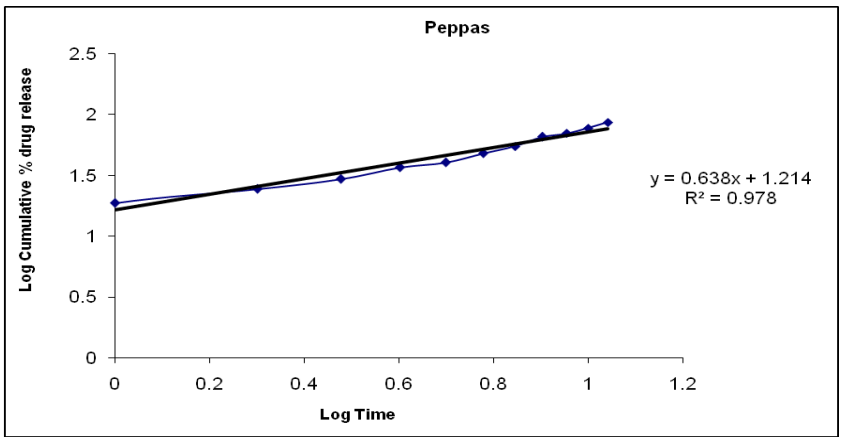

Figure 7: Kars mayer peppas graph.

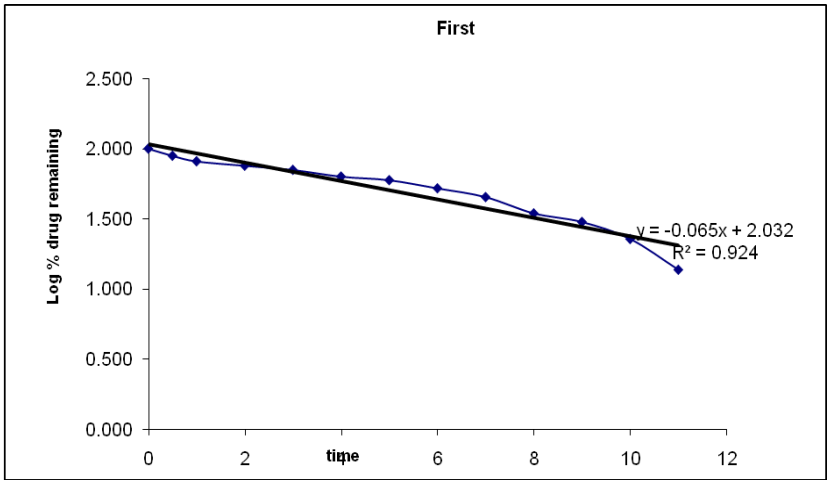

Figure 8: First order release kinetics graph.

From the above graphs it was evident that the formulation F3 was followed Zero order drug release mechanism.

CONCLUSION

Among all the prepared formulations, F3 was better formulation based on the in vitro drug release studies. FTIR studies concluded that there was no interaction between drug and excipients. The physico-chemical properties of all the formulations prepared with different polymers Gum cyamposis, Xanthan gum and sodium alginate were shown to be within limits. Quality control parameters for tablets such as weight variation, Hardness, Friability, thickness, drug content and floating lag time were found to be within limits. The drug release kinetics of optimised formulation F3 followed Zero order release kinetics. Gastroretentive drug delivery is most suitable for drugs which are active in stomach such as nifedipine.

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