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FORMULATION AND IN – VITRO EVALUATION OF FLOATING HYDROGEL BEADS OF NIMODIPINE

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ABSTRACT

Floating drug delivery systems (FDDS) are those systems which have a bulk density less than gastric fluids and because of these systems remains buoyant (3-4 hours) for a prolonged period of time in the stomach without affecting the gastric emptying rate. Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in the development of FDDS, which are effervescent system and non – effervescent system. Effervescent systems include use of gas generating agents, carbonates (Sodium bicarbonate) and other organic acid (Citric acid and Tartaric acid) to produce carbon dioxide gas, thus reducing the density of the system and making it to float on the gastric fluid.

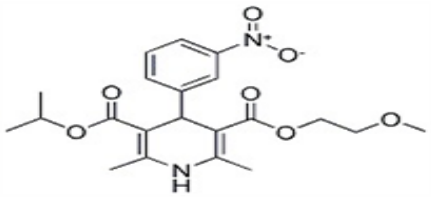
KEYWORDS: Effervescent systems, Floating drug delivery systems (FDDS), buoyancy.

INTRODUCTION

Nimodipine is used to decrease problems due to a certain type of bleeding in the brain (subarachnoid hemorrhage-SAH). **Nimodipine** is called a calcium channel blocker. The body naturally responds to bleeding by narrowing the blood vessel to slow blood flow. However, when the bleeding is in the brain, stopping blood flow causes more brain damage. Nimodipine is thought to work by relaxing narrowed blood vessels in the brain near the area of bleeding so blood can flow more easily. This effect reduces brain damage. Nimodipine (C21H26N2O7) is a second-generation 1,4-dihydropyridine calcium channel blocker. It was originally invented for the management of systemic hypertension.

DRUG PROFILE

Nimodipine

Structure 

CAS number 66085-59-4

Weight Average: 418.4403

Monoisotopic: 418.174001196

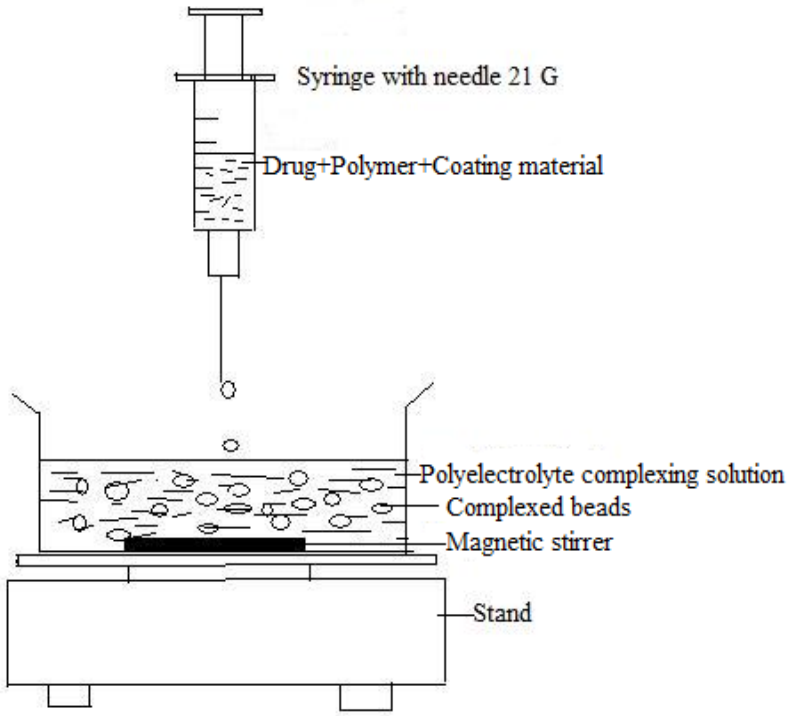
Chemical Formula C21H26N2O7

IUPAC Name: 3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate

Techniques for Preparation of Microbeads

1. Polyelectrolyte complexation technique
2. Emulsion gelation technique [incorporation of oil]
3. Impinging technology

4. Ionotropic gelation technique



Polyelectrolyte solution [alginate (-)/Gellun gum (-)/CMC (-) + Drug]

↓

5% HPMC phthalate as a coating material

Added dropwise under magnetic stirring by 21 G needle

↓

Calcium chloride solution (+) Chitosan solution (+)

↓

Hydrogel beads

MATERIALS AND METHODS

MATERIALS

Table: List of chemicals used with grade and supplier.

Sl. no.	Materials used	Manufacturer
1.	Nimodipine	Micro Labs pvt.Ltd.,Banglore
2.	Sodium alginate	Spectrum Pharma Labs Hyderabad
3.	Xanthan gum	Loba chemie Pvt. Ltd., Mumbai
4.	Guar gum	Loba chemie Pvt. Ltd., Mumbai
5.	Karaya gum	S D fine chemical Ltd, Mumbai
6.	Calcium chloride	Loba chemie Pvt. Ltd. Mumbai
7.	Hydrochloric acid	Loba chemie Pvt. Ltd. Mumbai

Formulation Design

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nimodipine (mg)	500	500	500	500	500	500	500	500	500
Sodium Alginate(mg)	250	500	750	250	500	750	250	500	750
Xanthan gum(mg)	250	500	750	-	-	-	-	-	-
Guar gum (mg)	-	-	-	250	500	750	-	-	-
Karaya gum(mg)	-	-	-	-	-	-	250	500	750
CaCO3(mg)	50	50	50	50	50	50	50	50	50
Calcium chloride(gm)	1	1	1	1	1	1	1	1	1

Preparation of Hydro gel beads of Nimodipine

Method used – Ionotropic gelation method

Accurate quantity of polymer was dissolved in 50ml of distilled water and stirred to form dispersion. Drug was added to the above dispersion and again stirred for uniform distribution. and stirred until a homogenous mixture was obtained. The mixture was extruded through a 23G syringe needle into calcium chloride solution (1% w/v). The beads were allowed to remain in the same solution for 30 min to improve their mechanical strength. The formed beads were separated, washed with water and allowed to dry at room temperature overnight.

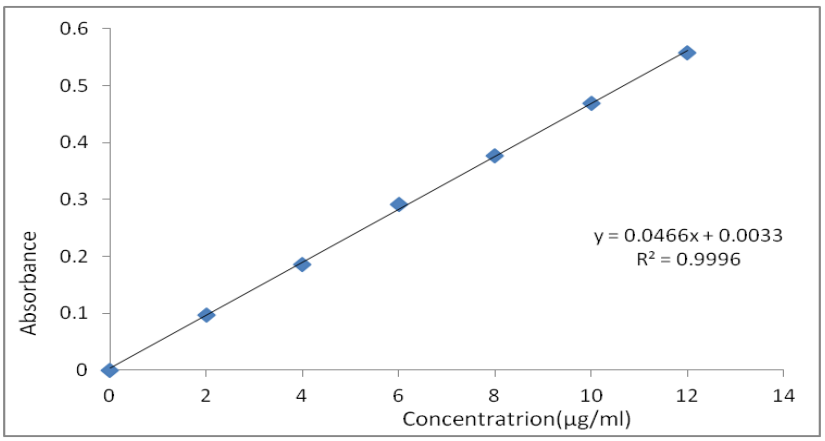
RESULTS AND DISCUSSION

Calibration curve of Nimodipine at λmax of 238nm

Standard calibration data of Nimodipine in 0.1N HCL

Sl. No	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.098
3	4	0.186
4	6	0.291
5	8	0.378
6	10	0.469
7	12	0.559

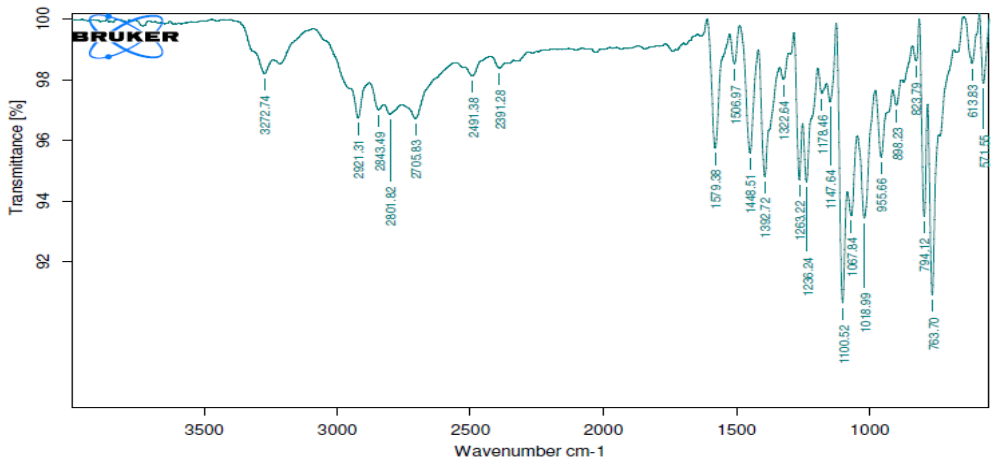
Standard calibration curve of Nimodipine in 0.1N HCL



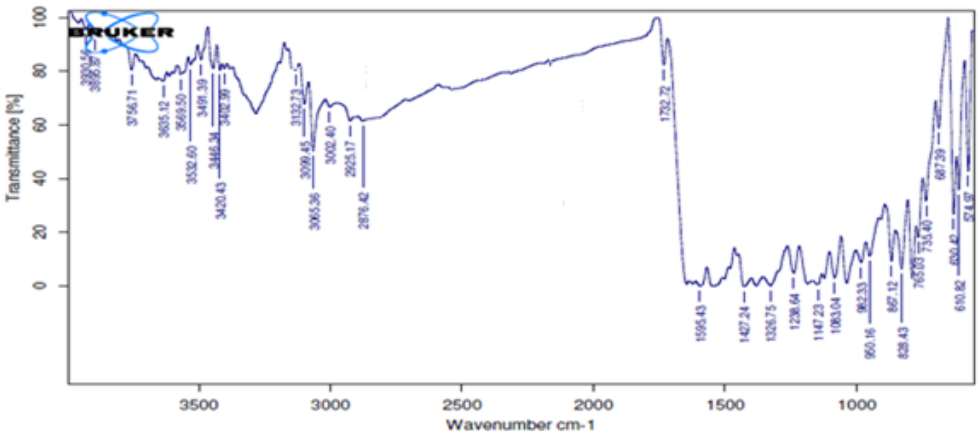
EVALUATION OF NIMODIPINE HYDROGEL BEADS

Drug polymer interaction (FTIR) study

From the spectra of Nimodipine, optimized mixture of Nimodipine and polymer, it was observed that all characteristic peaks of Nimodipine were present in the optimized mixture, thus indicating that no interactions between drug and polymers used in the study.



IR spectra of Nimodipine



IR spectra of optimized formulation

In vitro dissolution studies.

Table: *In vitro* release data of Hydrogel beads of Nimodipine.

In vitro dissolution studies.

Table: *In vitro* release data of Hydrogel beads of Nimodipine

Buoyancy characteristics

Table : Buoyancy characteristics of Nimodipine Hydrogel beads.

Sl. No.	Formulation code	FLT (secss)	Floating duration (hrs)
1	F1	88	6
2	F2	74	10
3	F3	52	12
4	F4	93	8
5	F5	76	10
6	F6	59	11
7	F7	97	8
8	F8	84	10
9	F9	63	11

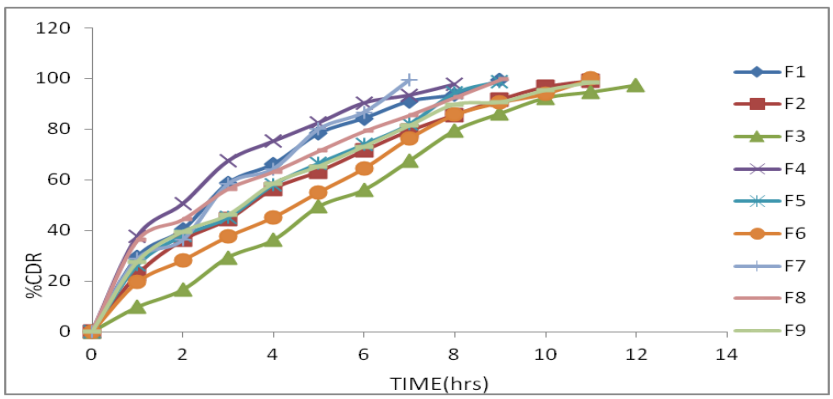
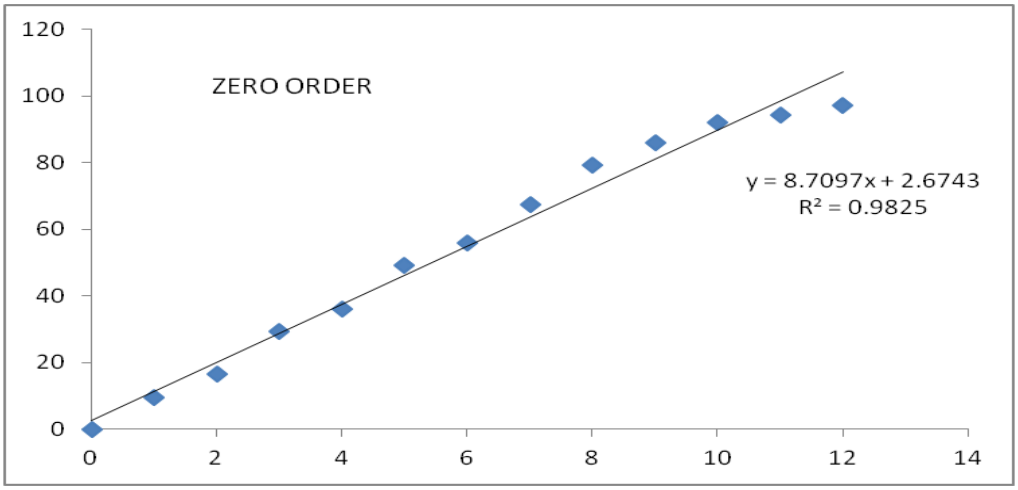
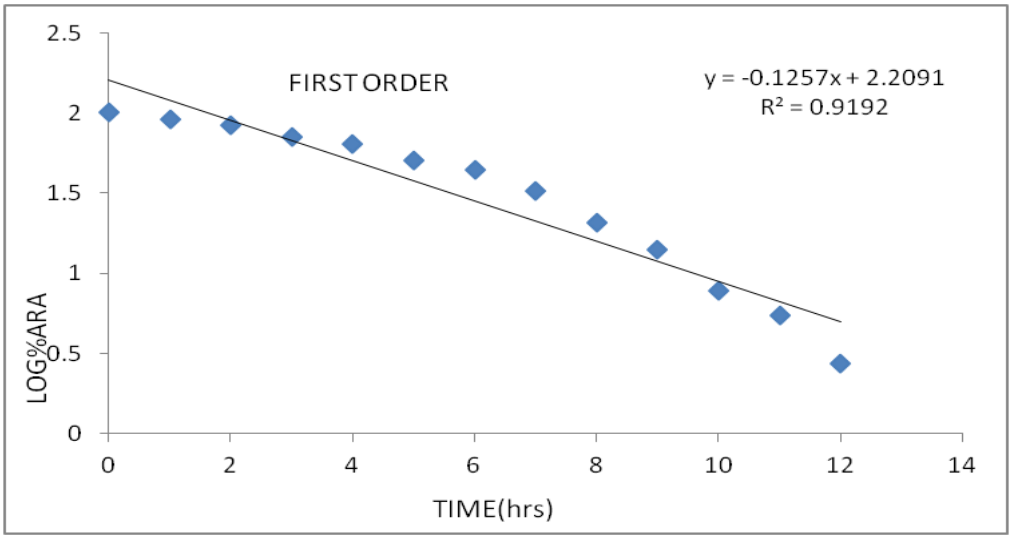


Fig: %CDR of F1-F9.

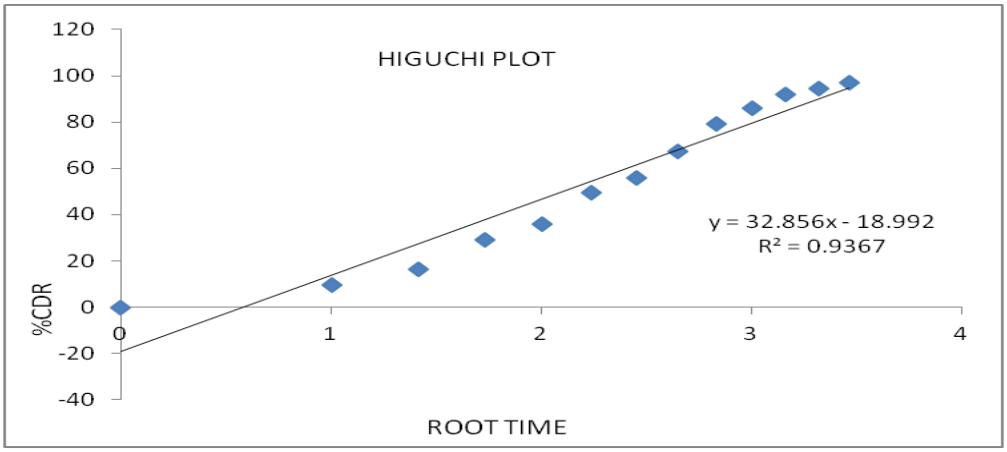
Zero Order



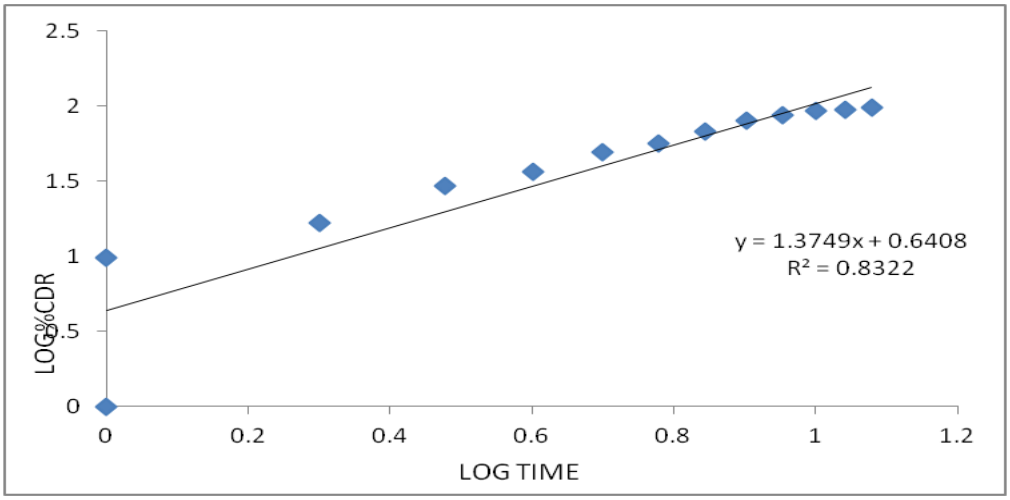
First order



Higuchi plot



PEPPAS PLOT



Release kinetics of Nimodipine hydrogel beads

The invitro dissolution data for best formulation F3 were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer - peppas equation. Optimized formulation F3 shows R^2 value 0.982. As its value nearer to the '1' it is conformed as it follows the zero order release. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot.

The 'n' value is 1.379 for the optimised formulation(F3) i.e., n value was >0.89 this indicates Super case II transport.

CONCLUSION

- Preformulation studies like melting point, solubility and UV analysis complied with standards. The FTIR Spectra revealed that, there was no interaction between Nimodipine and polymers. Surface smoothness of the Nimodipine beads was confirmed by SEM. As the ratio of polymer was increased, the mean particle size of Nimodipine floating beads was decreased. Nimodipine floating beads with normal frequency distribution were obtained. Entrapment efficiency increased with increase in the polymer concentration. From the results it can be inferred that there was a proper distribution of Nimodipine in the beads and the deviation was within the acceptable limits. The study also indicated that the amount of drug release decreases with an increase in the polymer concentration. The *in vitro* performance of Nimodipine Hydrogel beads showed prolonged and controlled release of drug.

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