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Research

Formulation development and characterization of Sustained release tablets of nicardipine

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Abstract

The aim of this study was to develop and characterize sustained-release tablets of nicardipine hydrochloride, a calcium channel blocker used to treat hypertension and angina. Sustained-release formulations improve patient compliance by reducing dosing frequency and maintaining stable plasma drug concentrations. Nicardipine short half-life and high first-pass metabolism make it an ideal candidate for sustained-release delivery systems. The tablets were prepared using the wet granulation technique, employing various hydrophilic and hydrophobic polymers such as Xanthum gum, Guar gum as release-controlling agents. Formulations were optimized by evaluating pre-compression parameters like bulk density, tapped density, compressibility, and angle of repose, as well as post-compression characteristics such as hardness, friability, drug content, weight variation, and in vitro dissolution profiles. In vitro drug release studies were conducted in simulated gastric fluid (pH 1.2) for the initial 2 hours, followed by simulated intestinal fluid (pH 6.8) for 10 hours, using USP Type II dissolution apparatus. The release data were analyzed using kinetic models such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas to determine the release mechanism. The optimized formulation demonstrated sustained drug release for up to 12 hours, following a non-Fickian diffusion mechanism. The results suggest that the combination of Xanthum gum, Guar gum provides effective control over drug release, ensuring prolonged therapeutic effects. Stability studies conducted as per ICH guidelines confirmed the robustness of the formulation. This study highlights the potential of sustained-release nicardipine tablets in improving treatment outcomes and patient adherence.

Keywords: Nicardipine, sustained-release tablets, Xanthum gum, Guar gum.

INTRODUCTION

Hypertension is a major, worldwide health problem owing to its high prevalence and association with increased morbidity and mortality[1]. Hypertension is a key risk factor for cardiovascular morbidity and mortality and

approximately 7.1 million deaths per year can be directly attributed to poor control of blood pressure[2]. Hypertension is also a major risk factor for stroke (Ischaemic and Haemorrhagic), myocardial infarction, heart failure, chronic kidney disease, peripheral vascular disease, cognitive decline and premature death [3]. Hypertension is classified as either primary (essential) hypertension or secondary hypertension; about 90-95% of cases are categorized as "primary hypertension" which means high blood pressure with no obvious underlying medical cause [4]. The remaining 5-10% of cases (secondary hypertension) caused by other conditions that affect the kidneys, arteries, heart or endocrine system [5].

A sustained release formulation that is retained in the stomach and releases the active ingredient over an extended period of time in the gastric fluids is quite suitable for drugs such as nicardipine hydrochloride. This is due to the fact that the drug is readily soluble in gastric juice and slightly soluble in intestinal fluid [6] being a weakly basic drug of pKa 7.2[7]. In this way, the drug reaches the jejunum and ilieum, its optimum absorption sites [8], over a sustained period of time and in a soluble form ready for absorption. The controlled release properties of such a formulation can maximize the blood level profile and consequently the pharmacological response in a unique fashion that is not possible by conventional controlled release technology.

Methodology

Identification

IR Spectroscopy

The FT-IR spectrum of the obtained drug sample was compared with the standard FT-IR spectra of the pure drug.

Compatibility Studies of Drug & Polymers

Preparation of the standard calibration curves of ncdpn

Standard calibration linearity curve of NCDPN in pH 6.8 Phosphate buffer

NCDPN(100mg) was dissolved in 10ml of methanol and volume was made up to 100 ml in volumetric flask using Phosphate buffer pH 6.8. From this stock solution 10 ml was withdrawn and is diluted to 100ml in volumetric flask which gives the concentration of 100 µg/ml. From this stock solution aliquots were withdrawn in volumetric flask to give concentrations 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml. Absorbance of each solution was measured at 355 nm using Shimadzu UV- 1700 UV-Vis double beam spectrophotometer with Phosphate buffer pH 6.8 as a reference standard.

Formulation of SR tablets

This SR tablets was prepared by wet granulation method

Sieving

Dry mixing

Preparation of binder solution

PVP-K30

IPA

Weigh PVP K-30 accurately and it is mixed with IPA to form a solution is used as binder solution and kept separately. Then the granulation, drying and sieving were followed by lubrication for final compression. Magnesium stearate and talc were weighed and they were passed through sieve#20.Then mixed with dried granules of NCDPN in a polybag for 5minutes to get a uniform blend. Then the lubricated granules of NCDPN were weighed accurately and fed into the die of single punch machinery and compressed. For this 9mm round punch was used for compression.

Formulation of SR tablets

Table.1 Formulation table for sustained release tablets

Formulation	F1	F2	F3	F4	F5	F6	F7	F8
NCDPN	40	40	40	40	40	40	40	40
Xanthum gum	40	80	120	160				
Guar gum					40	80	120	160
MCC	190	150	110	70	190	150	110	70
PVP K-30	20	20	20	20	20	20	20	20
IPA	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Magnesium stearate	2	2	2	2	2	2	2	2
Talc	8	8	8	8	8	8	8	8
Total weight	300	300	300	300	300	300	300	300

Evaluation of granules

1) Apparent Bulk Density
2) Tapped Density
3) Percentage Compressibility (or) Carr's index (%)
4) Hausner's Ratio
5) Angle of Repose

Evaluation of tablets

The quantitative evaluation and assessment of a tablets chemical, physical and bioavailability properties are important in the design of tablets and to monitor product quality.

There are various standards that have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets.

These include the diameter, size, shape, thickness, weight, hardness, Friability and In vitro-dissolution characters.

Physical Appearance

The general appearance of a tablet, its identity the uniformity of the tablet. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

RESULTS AND DISCUSSION

Concentration and absorbance's of NCDPN in 6.8 pH Phosphate buffer

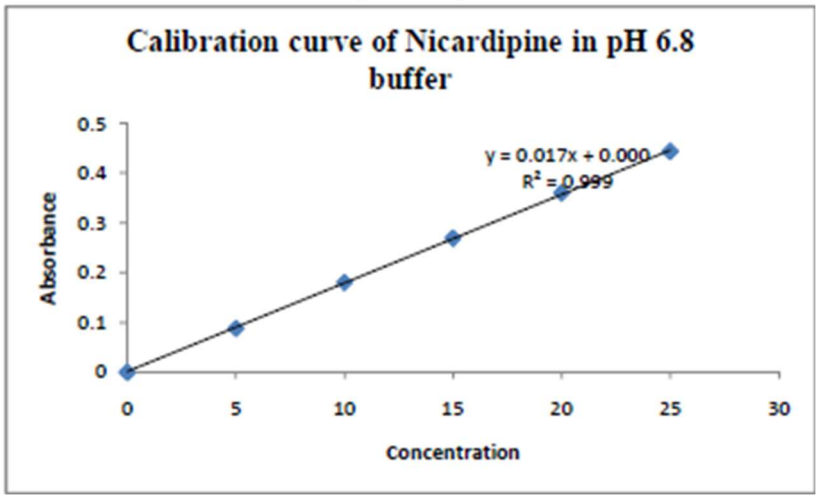

Fig 1: Calibration cure of nicardipine in 6.8pH buffer

Pre compression parameters

Table 2: Pre compression parameters

Formulations	Angle of Repose (θ)	Loose Bulk Density (g/ml)	Tapped Bulk Density(g/ml)	%Compressibility	Hausner's ratio	RESULT
F1	28.38±0.06	0.614±0.01	0.754±0.04	18.56±0.05	1.22±0.03	Excellent
F2	27.36±0.04	0.661±0.01	0.812±0.03	18.59±0.06	1.22±0.02	Excellent
F3	25.55±0.03	0.648±0.02	0.793±0.02	18.27±0.03	1.23±0.03	Excellent
F4	29.11±0.06	0.612±0.01	0.766±0.03	20.12±0.03	1.25±0.02	Excellent
F5	27.72±0.07	0.668±0.01	0.828±0.02	19.34±0.03	1.23±0.02	Excellent

F6	28.14±0.07	0.663±0.03	0.820±0.03	19.19±0.05	1.23±0.02	Excellent
F7	28.39±0.06	0.676±0.02	0.847±0.03	20.19±0.02	1.25±0.04	Excellent
F8	26.31±0.02	0.659±0.02	0.831±0.02	20.67±0.01	1.26±0.04	Excellent

Post compression parameters

Table 3: Post compression parameters

F.Code	Hardness (kg/cm^2) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)
F1	7.25±0.02	3.40±0.03	300±0.01	0.58±0.05
F2	7.53±0.02	3.32±0.03	300±0.03	0.50±0.05
F3	7.46±0.01	3.40±002	300±0.03	0.52±0.05
F4	7.31±0.03	3.40±0.01	300±0.02	0.33±0.05
F5	7.59±0.03	3.41±0.01	300±0.03	0.31±0.03
F6	7.87±0.02	3.41±0.01	300±0.03	0.32±0.05
F7	7.94±0.05	3.11±0.02	300±0.05	0.45±0.04
F8	7.81±0.06	3.11±0.03	300±0.04	0.49±0.01

In-Vitro Drug Release Studies for SR tablets
Cumulative percentage drug release from SR tablets

Table 4: cumulative percentage drug release from sustained release tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8
1	12	11.5	10.2	7.5	11.3	12.5	9.3	9.5
2	20	16	13	12.3	15.2	20	15	13.9
3	34	28	27	25	36.4	35	34	33
4	45	37	35	34	45.2	46	42	45.8
5	61	55	52	42	42.4	59	57	60
6	70	71	67	53	50.2	68	70	74.5
8	82	80.5	74	65	65.3	77	79.6	79.3
10	--	--	80	78	83.2	90	83.4	80.8
12	--	--	--	84.7	--	--	94.7	89.7

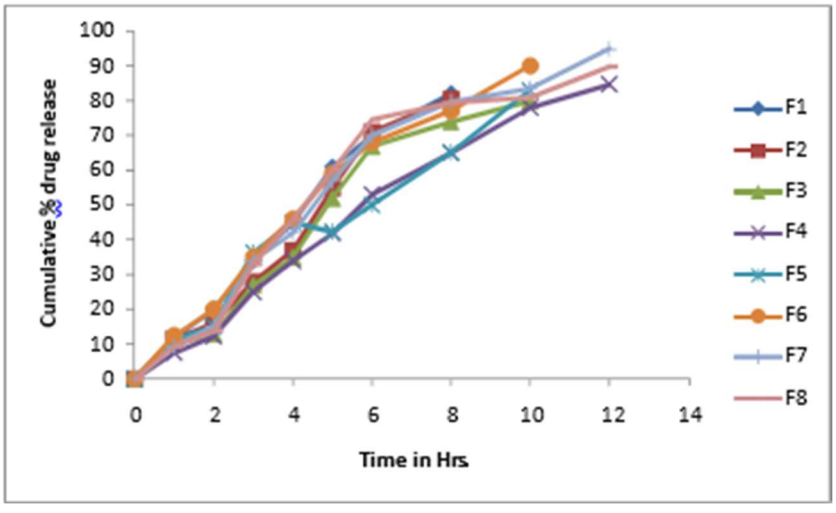

Fig 2 %Drug release

Kinetic release models

Zero Order

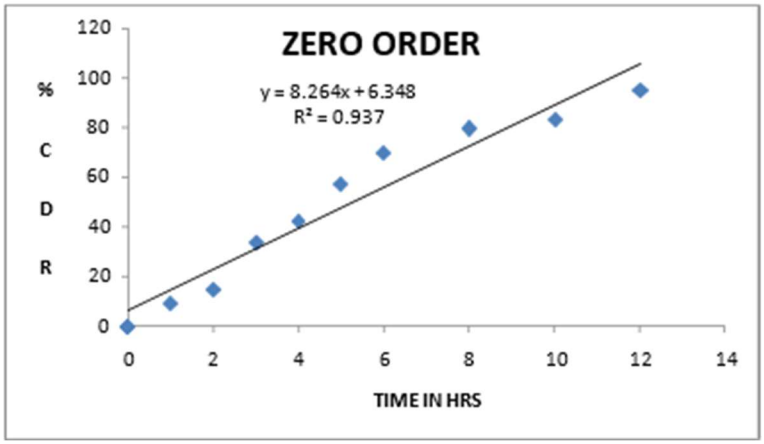

Fig 3: zero order release graph for F7 SR formulation

First Order

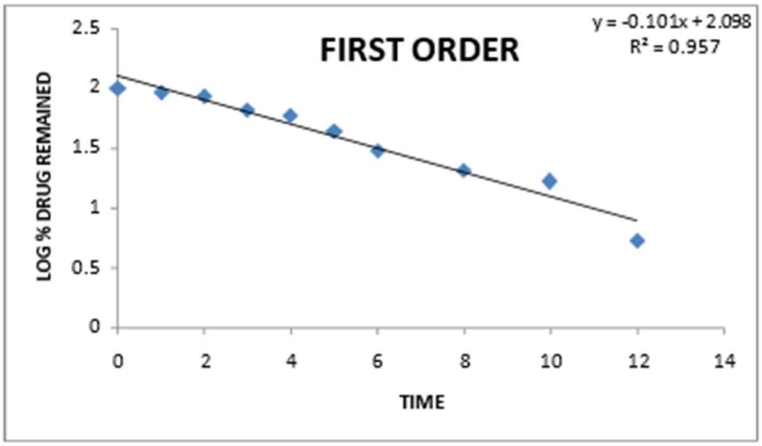

Fig 4 : First order release graph for F7 SR formulation

Higuchi Plot

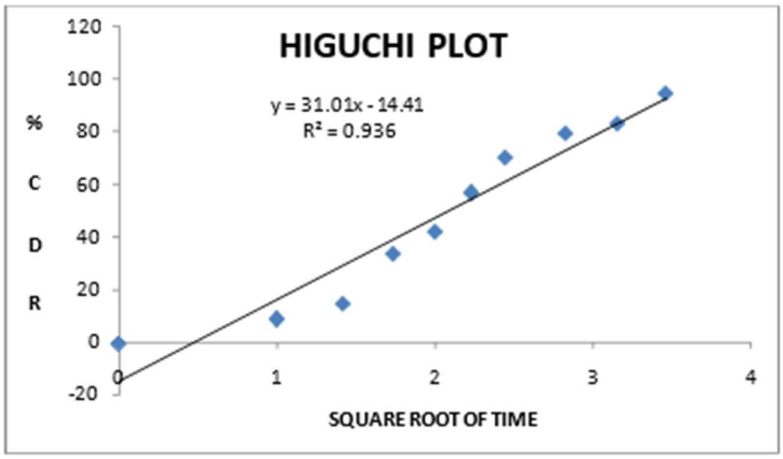

Fig 5: Higuchi model graph for F7 SR formulation

Peppas Plot

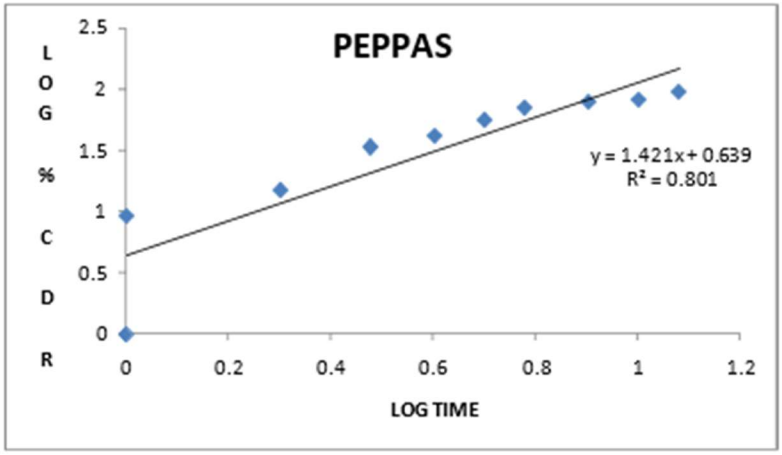

Fig 6: peppas model for F7 SR formulation

Table 5: Release kinetics for F7 formulation for SR tablets

	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	8.264938805	0.100994807	31.0147686	1.421895774
Intercept	6.348812095	2.098533714	14.41850882	0.639539655
Correlation	0.968384256	0.978301696	0.967474051	0.895062581
R 2	0.937768067	0.957074209	0.936006039	0.801137024

SUMMARY& CONCLUSION

The SR tablets containing NCDPN SR tablets were successfully prepared by wet granulation method. The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index. The optimized formulation F7 which releases the NCDPN in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours. The SR tablets containing NCDPN SR tablets were successfully prepared by wet granulation method. "The optimized formulation contains the average thickness of" 3.11±0.02, "average hardness" of 7.94±0.05, "average weight of" 300±0.05, "friability of" 0.45.

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