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DESIGN AND IN-VITRO CHARACTERIZATION OF NICARDIPINE SUSTAINED RELEASE TABLETS

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ABSTRACT

The aim of the present study was to fabricate and evaluate sustained release tablets Nicardipine, using different natural polymers like Guar gum and Xanthum gum which is suitable for delivering the drug for sufficient long time and reduce frequency of dose. The Sustained released tablets containing Nicardipine SR tablets were successfully prepared by wet granulation method. The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. 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.The optimized formulation F7 which releases the Nicardipine in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours.

Keywords: Nicardipine, granulation method, average weight, average hardness, average thickness

1. INTRODUCTION

To the date, for every disease or disorder state of the patient, proper medication is of prime importance to maintain the patient in good health. To achieve this, the medicine or drug is administered conventionally by one or more of several well defined and popular routes of drug administration including oral, parenteral, rectal, alveolar, ocular, and topical. Traditionally patient only takes medication during the day time hours. Plasma levels can therefore fall to sub– therapeutic levels overnight. However, there are several major deficiencies of conventional dosage forms, few of which are listed here[1,2].
• Inconvenience and /or difficult use of drugs with very short duration of action or biological half-life. • Need for frequent dosing

2. LITERATURE REVIEW

LuanaPeriloli.,ValeriaAmbrogi etal.,[3] designed the sustained release mucoadhesive tablets of Flurbiprofen for the topical administration in the oral cavity. The first layer, responsible for the tablet retention on the mucosa, was prepared by compression of a cellulose derivative and polyacrylic derivative blend. The second layer, responsible for buccal drug delivery, was obtained by compression of a mixture of the same (first layer) mucoadhesive polymers and hydrotalcite containing flurbiprofen.
Juan Manuel Llabot., Ruben HilarioManzo etal.,[4] designed the mucoadhesiveBilayered of both immediate release and sustained release tablets of nystatin. The mucoadhesive tablet formulated in this work releases nystatin quickly from the lactose layer and then in a sustained way, during approximately 6 hours, from the polymeric layer. The mixture CB: HPMC 9:1 showed good in vitro mucoadhesion. A swelling-diffusion process modulates the release of nystatin from this layer. A non-Fickian (anomalous) kinetic was observed.

3. AIM AND OBJECTIVE

The aim of the present study was to fabricate and evaluatesustained release tablets Nicardipine, using different natural polymers like Guar gum and Xanthum gum which is suitable for delivering the drug for sufficient long time and reduce frequency of dose.

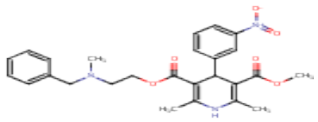
- To perform the drug – excipient compatibility studies as per ICH guidelines.
- To optimize the concentration of Polymer for sustained release tablets of Nicardipine.

- To evaluate the formulation parameters like weight variation, hardness, friability, assay.
- To evaluate the In-vitro studies for the sustained tablets.
- To conduct the accelerated stability studies for the prepared tablets as per ICH guidelines

4. DRUG PROFILE

Nicardipine

Structure:



Weight: 479.525
Chemical Formula: $C_{26}H_{29}N_3O_6$
IUPAC Name: 3-{2-[benzyl(methyl)amino]ethyl} 5-methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4- dihydropyridine-3,5-dicarboxylate

5. MATERIALS AND METHODS

List of materials used to carry out present research work

S.No	Materials	Source
1	Nicardipine (drug)	Provided by Chandra labs, Hyderabad.
2	Guar gum	S.D. Fine Chem. Ltd, Mumbai, India
3	Xanthine Gum	S.D. Fine Chem. Ltd, Mumbai, India
4	Polyvinylpyrrolidone	S.D. Fine Chem. Ltd, Mumbai, India
5	Iso propyl alcohol	S.D. Fine Chem. Ltd, Mumbai, India
6	Microcrystalline cellulose	S.D. Fine Chem. Ltd, Mumbai, India
7	Magnesium stearate	S.D. Fine Chem. Ltd, Mumbai, India
8	Talc	S.D. Fine Chem. Ltd, Mumbai, India

List of equipments used to carry out present research work

Sl.No	Equipments	Manufacturer
1	Electronic balance	Shimadzu AUX220, Japan.
2	pH meter	Survewell Instruments Pvt. Ltd., Bangalore
3	Sieves	United engineering Ltd
4	Tap density tester	Electrolab ETD-1020
5	Vernier Caliper	Mitutoyo
6	FTIR spectrophotometer	Shimadzu 8400S
7	UV-Visible Spectrophotometer	Shimadzu UV-1800, Japan
8	Tablet compression machine	Ridhdhi pharma machinery Ltd., India
9	Tablet hardness tester	Monsanto hardness tester
10	Friability test apparatus	Roche Friabilator(USP), Electrolab, India
11	Disintegration test apparatus	Disintegration test apparatus
12	Dissolution test apparatus	Electrolab, India

Composition Of Sustained Release Tablets

Table 1: Formulation table for sustained release tablets

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F9	F10	F11	F12	F13
Nicardipine	20	20	20	20	20	20	20	20	20	20	20	20	20
Ethyl cellulose	30	-	-	45	-	-	30	30		45	45		30
HPMC	-	30	-	-	45	-	30	-	30	45		45	30
Xanthum gum	-	-	30	-	-	45	-	30	30		45	45	30
MCC	190	150	110	70	190	150	110	70	70	40	40	40	40
PVP K-30	15	15	15	15	15	15	15	15	15	15	15	15	15
Magnesium stearate	9	2	2	2	2	2	2	2	2	2	2	2	2
Talc	9	8	8	8	8	8	8	8	8	8	8	8	8
Total weight	300	300	300	300	300	300	300	300	300	300	300	300	300

PVP- Polyvinyl pyrrolidone, IPA- Isopropyl alcohol. All the ingredients are in 'mg'

EVALUATION OF GRANULES

% Compressibility index & Hausner's ratio

Percentage Compressibility (or) Carr's index (%)

Based on the apparent bulk density and the tapped density, the percentage Compressibility of the bulk drug was determined by the following formula.

Carr's index (%) = [(Tapped Density-Bulk Density) / Tapped Density] X 100

Evaluation Of Tablets

The quantitative evaluation and assessment of a tablet's 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

In vitro Dissolution Studies

In vitro drug release studies were carried out using USP XXIV dissolution apparatus type II, with 900ml of dissolution medium maintained at 37±1°C for 12 hr, at 50 rpm, pH 6.8 phosphate buffer for 12hrs for sustained release tablets. 5ml of sample was withdrawn at predetermined time intervals replacing with an equal quantity of drug free dissolution fluid.

8. RESULTS AND DISCUSSION

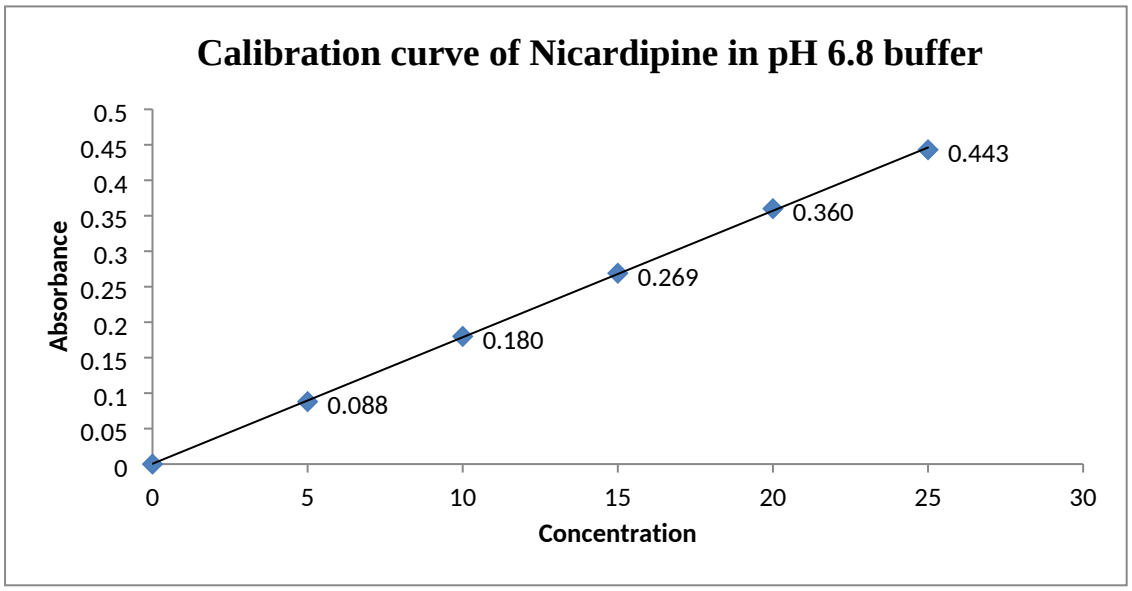


Fig 1: Calibration curve of Nicardipine in 6.8pH Phosphate buffer

Compatibility Studies

The spectrum obtained after the analysis is shown in Fig 1. The spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. All the characteristic peaks of Nicardipine mentioned in Table No: were also found in the spectrum formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and excipients.

Pre-Compression Parameters

Table 2: Pre compression parameters for SR tablets

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
F9	26.51±0.02	0.682±0.01	0.893±0.02	17.34±0.03	1.53±0.02	Excellent
F10	25.65±0.03	0.671±0.01	0.720±0.03	21.12±0.03	1.18±0.02	Excellent
F11	27.14±0.07	0.686±0.02	0.821±0.02	17.19±0.05	1.46±0.04	Excellent
F12	28.51±0.02	0.658±0.01	0.654±0.04	18.34±0.03	1.43±0.02	Excellent
F13	24.65±0.03	0.666±0.02	0.827±0.03	22.14±0.03	1.28±0.02	Excellent

From the above pre-compression parameters it was clear evidence that granules has excellent flow properties.

In-Vitro Drug Release Studies for SR tablets

Table 3: Cumulative percentage drug release from sustained release tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
1	12	11.5	10.2	7.5	11.3	12.5	9.3	9.5	7.5	11.3	12.5	9.3	9.5
2	20	16	13	12.3	15.2	20	15	13.9	12.3	15.2	20	15	13.9
3	34	28	27	25	36.4	35	34	33	25	36.4	35	34	33
4	45	37	35	34	45.2	46	42	45.8	34	45.2	46	42	45.8
5	61	55	52	42	42.4	59	57	60	42	42.4	59	57	60
6	70	71	67	53	50.2	68	70	74.5	53	50.2	68	70	74.5
8	82	80.5	74	65	65.3	77	79.6	79.3	65	65.3	77	79.6	79.3
10	--	--	80	78	83.2	90	83.4	80.8	78	83.2	90	83.4	80.8
12	--	--	--	84.7	--	--	94.7	89.7	79.8	80.4	86.3	80.9	78.4

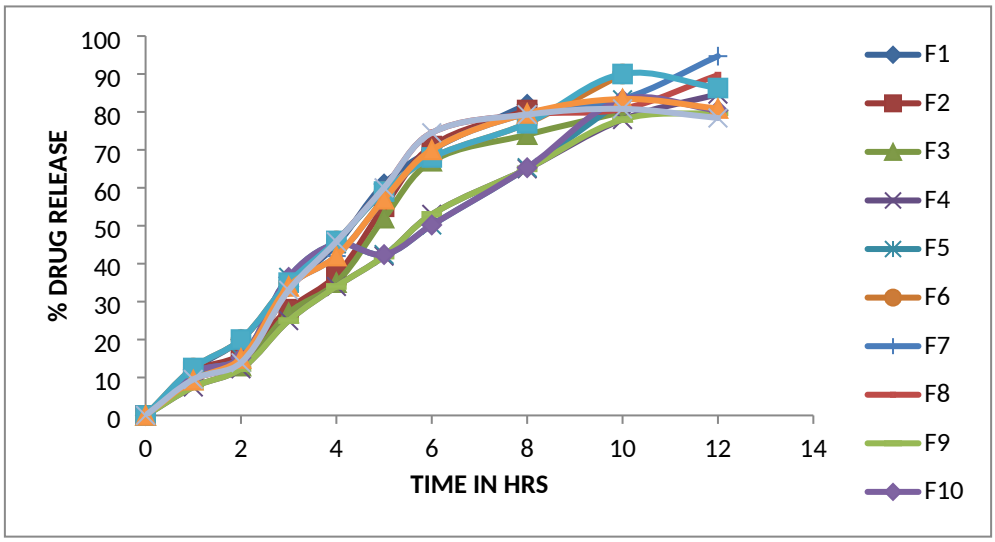


Fig 2: Dissolution graph for sustained release formulations

Table 4: Release kinetics for F7 formulation for sustained release 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

Discussion of dissolution test

The results of *in-vitro* drug release studies in 6.8 phosphate buffer (from 1 to 12 hours) are presented in Fig.. Initially our aim was to select optimum concentration of individual polymers of different concentration for SR tablets.

Hence the tablets containing, SR tablets of drug (Nicardipine) were prepared by altering the concentration of different natural polymers.

Discussion for in-vitro release of Nicardipine sustained release tablets

From the table, it was confirmed that the F7 formulation SR tablets fulfill the sustained release theory, In that the Guar gum was used separately in the formulations, but increasing the polymer concentration, it was clearly identified that the drug release was retarded. And also from the table, it was also confirmed that the formulation made with guar gum (F4 and F8) showed sustained drug release compared to the formulations made with xanthum gum (F1 to F4).

9. SUMMARY AND CONCLUSION

The Sustained released tablets containing Nicardipine 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 prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. 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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