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Formulation of Time Dependent Controlled Release Tablet of Nimodipine and its Evaluation using Linear Regression analysis

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ABSTRACT

The objective of the present study is to identify a release profile and propose of mechanism of dissolution of a Controlled release tablet of Nimodipine. 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. Direct compression method was used to prepare the tablets using different polymers include HPMC K4M and HPMC K15M. Formulations were prepared by varying the amount of polymers. Nimodipine is one such anti- hypertensive drug, where these problems are incurred. The objective of the proposed work was to design and develop Controlled release tablets of the given drug and to ensure time-dependent, controlled release formulation with optimizing the process variables. The prepared tablets were evaluated for both precompression and postcompression parameters. The compatability of drug with polymers is identified by FTIR studies. The results obtained showed that the drug is compatible with all the polymers used.

Key words: *Nimodipine, HPMC K4M and HPMC K15M, Carbopol, Direct compression method.*

INTRODUCTION

Over the past 30 years, as the expense and complications involved in marketing new entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery of, greater attention has been focused on development of controlled release drug delivery systems. It is generally been recognized that for most disease states, a substantial number therapeutically effective compounds already exists. The effectiveness of these drugs, however, is often limited by side effects or the necessity to administer the compound in a clinical setting. The goal in designing a controlled delivery system is to reduce the frequency of dosing or to increase the effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery [1, 2].

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such immediate-release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects [3]. However, after absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached, another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is a typically seen using immediate-release dosage form [4, 5].

The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized".

Nimodipine is a 1,4 dihydropyridine calcium channel blocker. It acts primarily on vascular smooth muscle cells bystabilizing voltage-gated l- type calcium channels in their inactive conformation. By inhibiting the influx of calcium in smooth musclecells, nimodipine prevents calcium-dependent smooth muscle contraction and subsequent vasoconstriction. Following are the pharmacokinetic parameters of conventional parameters and need for controlled release. The usual goal of an oral controlled - release dosage form is to maintain therapeutic blood levels, over an extended period of time several works has been done on Nimodipine to improve its bioavailability since it has high first pass metabolism.

A drug must be absorbed and enter the circulation at approximately the same rate at which it is eliminated. The elimination rate is quantitatively described by the half - life (t 1/2). Each drug has its own characteristic elimination rate, which is the sum of all elimination process, including metabolism, urinary excretion, and all other processes that permanently remove drug from the bloodstream. Thus this dosage form improves the bioavailability as well as improves patient compliance.

MATERIALS AND METHOD

Materials:

Nimotidine was obtained as a gift sample from Biocon India Ltd Bangalore, India. All other chemicals were standard grade obtained from SD Fine chemicals.

Methodology:

Preformulation studies: [8, 9]

Before formulation of drug substances into a dosage form, it is essential that drug and polymer should be chemically and physically characterized. Preformulation studies give the information need to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excipients in the fabrication of a dosage form.

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Calibration curves of Nimotidine in different media:

Principle: The calibration curve is based on the spectrophotometry. The maximum absorption of Nimotidine was observed at 238nm. It obeyed Beer's law in the concentration range of 1 -10 µg/ml.

a) Determination of absorption maxima:

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl and pH 6.8 Phosphate buffer UV spectrums was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

b) Preparation calibration curve:

100mg of Nimodipine pure drug was dissolved in 100ml of Methanol (stock solution) 10ml of above solution was taken and make up with100ml by using 0.1 N HCl (100µg/ml).From this 10ml was taken and make up with 100 ml of 0.1 N HCl (10µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 5,10,15,20,25,30,35 and 40µg/ml of Nimodipine per ml of solution. The absorbance of the above dilutions was measured at 238 nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

Drug – Excipient compatibility studies:

Fourier Transform Infrared (FTIR) spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

Formulation:

A. Preparation of Repaglinide tablets:

Direct compression method: Different tablets formulations were prepared by direct compression technique. All powders were passed through 60 mesh. Required quantities of drug and polymers were mixed thoroughly Magnesium stearate was added as lubricant. Talc was used as glidant. Micro crystalline cellulose was used as diluent. Finally the powder mix was subjected to compression after mixing uniformly in a polybag. Prior to compression, the blends were evaluated for several tests.

Table No. 1: Composition of Formulations of Nimotidine

Formulation	Drug	Carbopol	HPMC K4m	HPMC K15m	Sodium CMC	Mg Stearate	AEROSIL
F_1	40 mg	150 mg	-------	-------	-------	5 mg	5 mg
F_2	40 mg	75 mg	75 mg	-------	-------	5 mg	5 mg
F_3	40 mg	50 mg	100 mg	-------	-------	5 mg	5 mg
F_4	40 mg	100 mg	50 mg	-------	-------	5 mg	5 mg
F_5	40 mg	75 mg	-------	75 mg	-------	5 mg	5 mg
F_6	40 mg	50 mg	-------	100 mg	-------	5 mg	5 mg
F_7	40 mg	100 mg	-------	50 mg	-------	5 mg	5 mg
F_8	40 mg	-------	150 mg	-------	-------	5 mg	5 mg
F_9	40 mg	-------	-------	150 mg	-------	5 mg	5 mg
F_{10}	40 mg	-------	-------	75 mg	75 mg	5 mg	5 mg
F_{11}	40 mg	-------	-------	50 mg	100 mg	5 mg	5 mg
F_{12}	40 mg	-------	-------	100 mg	50 mg	5 mg	5 mg

Post Compression Parameters:

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table No. 2: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [(W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:

Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Meloxicam 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* drug release studies:**

Dissolution parameters:

Apparatus	-- USP-II, Paddle Method
Dissolution Medium	-- 0.1 N HCl , p H 6.8 Phophate buffer
RPM	-- 50
Sampling intervals (hrs)	-- 0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature	-- 37°c ± 0.5°c

Procedure:

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 2 hours and then the medium 0.1 N HCl was removed and pH 6.8 phosphate buffer was added process was continued from upto 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 238 nm using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics: To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$Log (100-F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\, t1/2$$

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t/ M_\infty = K t^n$$

Where, M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Q_t)^{1/3} = 100^{1/3} – K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

RESULTS & DISCUSSION

Pre-Formulation studies:

The present study was aimed to developing Sustained release tablets of Nimodipine using various polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Analytical Method:

Graphs of Nimodipine was taken in Simulated Gastric fluid (pH 1.2) and in p H 6.8 phosphate buffer at 238 nm and 234 nm respectively.

Table No. 3: Observations for graph of Nimodipine in 0.1N HCl (238nm)

Conc [µg/l]	Abs
5	0.112
10	0.230
15	0.336
20	0.410
25	0.567
30	0.645

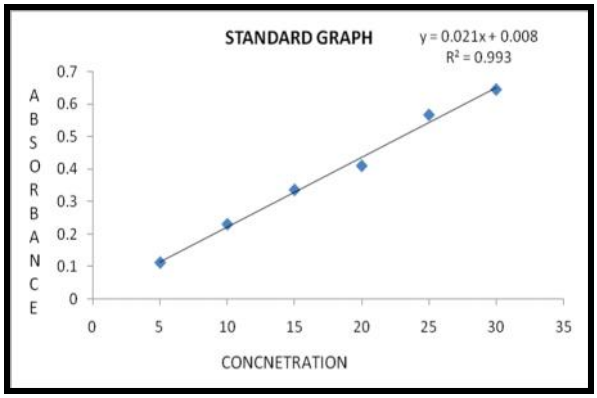

Fig. 1: Standard graph of Nimodipine in 0.1N HCl

Table No. 4: Observations for graph of Nimodipine in p H 6.8 phosphate buffer (234nm)

Conc [µg/l]	Abs
5	0.123
10	0.210
15	0.320
20	0.411
25	0.501

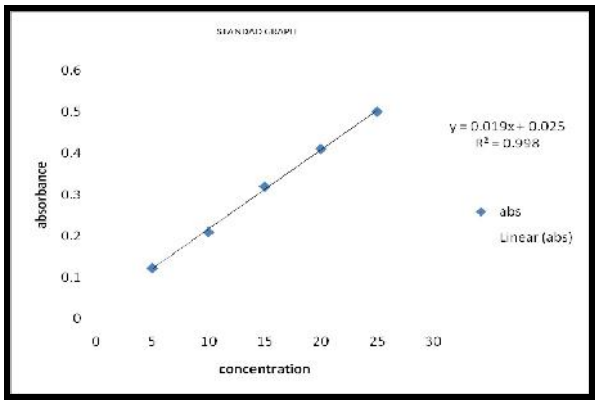

Fig. 2: Standard graph of Nimodipine pH 6.8 phosphate buffer (234nm)

Drug – Excipient compatability studies:
Fourier Transform-Infrared Spectroscopy:

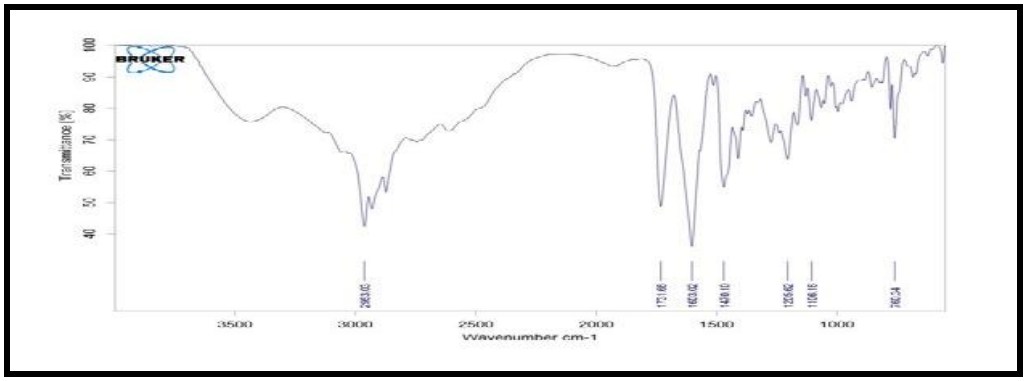

Fig. 3: FT-TR Spectrum of Nimodipine pure drug

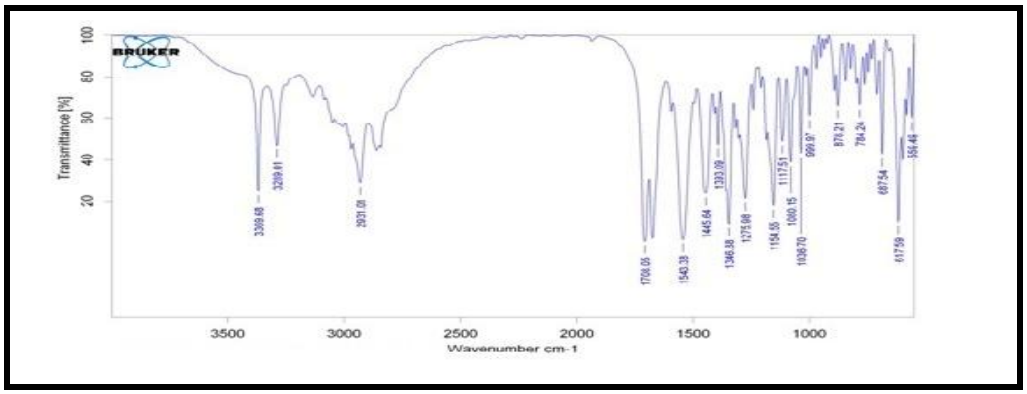

Fig. 4: FT-IR Spectrum of Drug+Carbopol

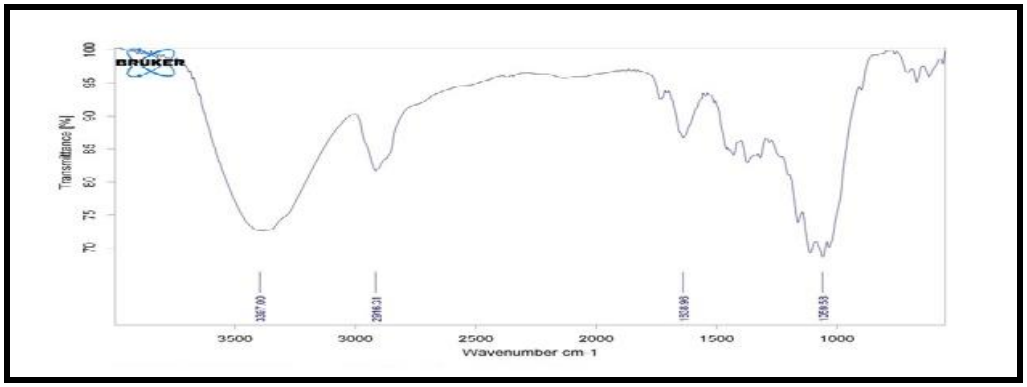

Fig. 5: FT-IR Spectrum of Drug+HPMC K4M

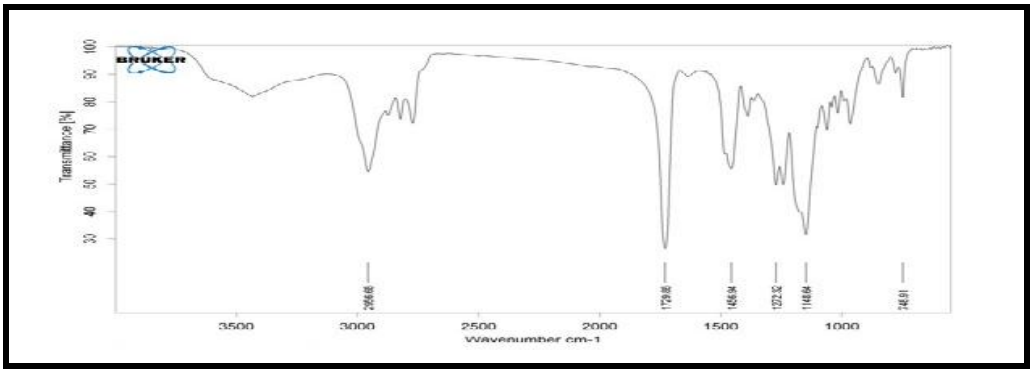

Fig. 6: FT-IR Spectrum of Drug+HPMC K 15 M

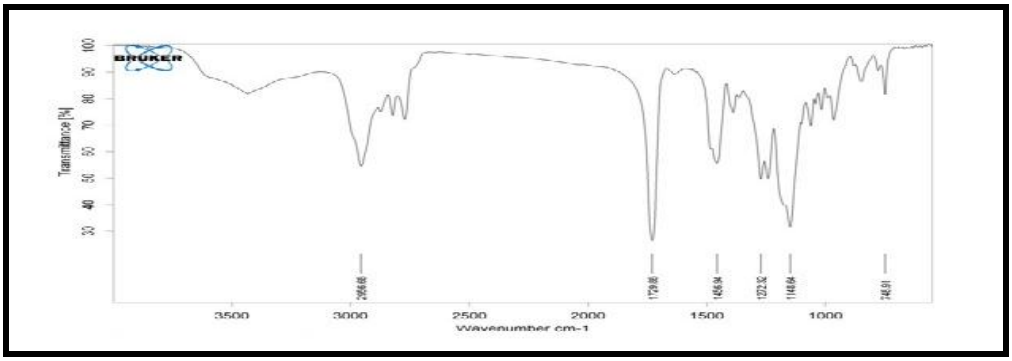

Fig. 7: FT-IR Spectrum of Drug+Sodium CMC

Pre-Formulation parameters of powder blend:

Table No. 5: Pre-Formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Hausner's Ratio
F1	28.9±0.91	0.45±0.01	0.67±0.01	1.5
F2	27.7±1.20	0.35±0.02	0.53±0.04	0.9
F3	29.3±0.72	0.47±0.04	0.75±0.02	1.18
F4	26.6±0.42	0.38±0.02	0.65±0.02	1.2
F5	25.5±1.21	0.43±0.03	0.59±0.03	0.8
F6	29.8±0.75	0.42±0.03	0.64±0.02	0.99
F7	30.2±0.69	0.38±0.02	0.59±0.01	0.7
F8	26.6±0.96	0.41±0.05	0.63±0.04	1.15
F9	29.5±1.34	0.39±0.01	0.71±0.05	0.92
F10	27.7±1.20	0.35±0.02	0.53±0.04	0.9
F11	29.3±0.72	0.47±0.04	0.75±0.02	1.18
F12	26.6±0.42	0.38±0.02	0.65±0.02	1.2

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 0.35±0.07 to 0.47±0.06 (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 0.53 to 0.75 showing the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Quality Control 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 compression coated tablet.

Table No. 6: Invitro quality control parameters for tablets

Formulation code	Weight variation (mg)	Hardness (kg/cm²)	Friability (%)	Thickness (mm)	Content uniformity (%)
F1	300±0.05	3.2±0.32	0.54±0.12	3.56±0.12	99.9±0.04
F2	299±0.01	3±0.41	0.55±0.09	3.59±0.09	101±0.11
F3	299±0.03	3.1±0.47	0.61±0.13	3.68±0.21	99.9±0.05
F4	301±0.04	2.9±0.29	0.57±0.20	3.67±0.23	99±0.07
F5	299±0.02	3±0.18	0.71±0.03	3.58±0.04	99.8±0.13
F6	299±0.42	2.9±0.07	0.59±0.09	3.71±0.06	101±0.09
F7	300±0.72	3±0.11	0.54±0.02	3.83±0.12	100±0.01
F8	299±0.91	3±0.23	0.63±0.07	3.62±0.03	101.3±003
F9	300±0.05	3±0.27	0.79±0.11	3.89±0.06	100±0.12
F10	299±0.03	3.1±0.47	0.61±0.13	3.68±0.21	99.9±0.05
F11	301±0.04	2.9±0.29	0.57±0.20	3.67±0.23	99±0.07
F12	299±0.02	3±0.18	0.71±0.03	3.58±0.04	99.8±0.13

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

***In-Vitro* Drug Release Studies**

Table No. 7: Dissolution Data of Nimodipine Tablets (F1, F2, F3 ,F4 formulations)

TIME (Hrs)	F1	F2	F3	F4
0.5	18.29±0.46	5.23±0.34	4.29±0.52	6.46±0.74
1	32.48±0.78	9.23±0.68	11.19±0.47	20.67±0.68
2	56.87±1.24	24.75±0.47	21.79±0.64	37.46±0.48
3	71.09±1.22	38.96±0.84	26.48±0.74	48.76±0.64
4	82.86±1.09	44.76±0.48	28.67±0.53	59.49±0.84
5	94.86±0.75	58.23±0.57	38.63±1.06	68.62±0.98
6	97.32±.68	68.18±0.38	52.16±1.04	83.16±0.78

7	98.82±.54	79.65±0.47	64.37±1.12	87.49±0.81
8	99.94±0.74	88.79±0.24	80.42±0.98	97.23±0.34
9	----------	92.38±0.68	82.67±0.84	99.59±0.54
10	----------	94.49±0.74	85.46±0.67	----------
11	----------	96.16±0.84	86.79±1.03	----------
12	----------	97.79±0.48	88.97±0.68	----------

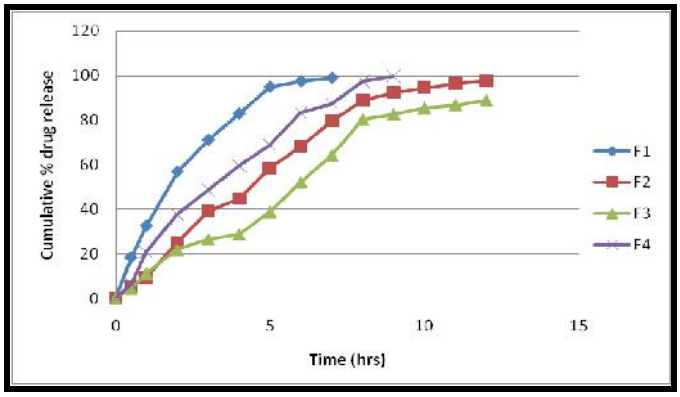

Fig. 8: Dissolution profile of Nimodipine (F1, F2, F3, F4 formulations)

Table No. 8: Dissolution Data of Nimodipine Tablets (F5, F6, F7 ,F8 formulations)

TIME (Hrs)	F5	F6	F7	F8
0.5	5.23±0.47	6.23±0.68	7.23±0.43	3.98±0.34
1	16.76±0.68	17.49±0.75	21.76±0.78	8.23±0.74
2	24.43±0.74	36.38±0.43	38.46±1.06	10.75±0.34
3	38.96±0.98	42.76±0.34	41.03±1.08	16.42±0.76
4	51.29±1.02	58.96±0.28	53.49±0.98	21.31±0.84
5	58.46±0.84	64.76±0.98	57.84±0.84	31.47±0.98
6	63.86±0.98	69.23±0.84	61.98±0.68	41.75±0.91
7	69.16±0.48	71.46±0.67	70.72±0.73	52.46±0.1.02
8	74.69±0.68	73.34±0.68	78.67±0.43	58.69±0.77
9	75.46±0.84	74.31±0.84	83.38±0.57	64.46±0.67
10	82.46±0.76	76.69±0.76	85.64±0.48	63.78±0.58
11	84.76±0.84	78.46±0.48	88.46±0.74	65.82±0.84
12	86.16±0.67	80.23±0.78	91.23±0.66	68.49±0.67

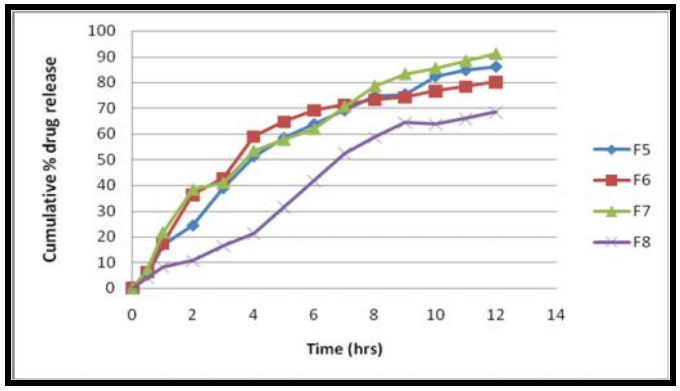

Fig. 9: Dissolution profile of Nimodipine (F5, F6, F7 ,F8 formulations)

Table No. 9: Dissolution Data of Nimodipine Tablets (F9, F10, F11,F12 formulations)

TIME (Hrs)	F9	F10	F11	F12
0.5	4.32±0.54	14.39±1.02	13.14±1.04	9.54±1.24
1	6.72±0.84	23.88±0.94	17.82±0.35	9.57±0.84
2	14.16±0.71	49.32±1.32	18.9±0.48	22.68±0.72
3	18.46±0.67	53.92±0.84	31.13±0.78	26.1±0.98
4	28.56±0.87	63.07±0.67	60.84±1.01	28.09±1.04
5	37.44±0.67	71.77±1.24	75.6±1.28	55.8±1.32
6	45.12±0.78	77.85±0.98	92.7±0.68	69.3±0.37
7	59.4±0.49	83.76±1.09	93.18±1.38	76.5±0.67
8	60±0.97	86.34±0.98	94.08±0.84	83.1±0.84
9	61.2±0.54	93.6±1.24	94.59±1.24	83.6±0.47

10	62.25±0.78	93.67±1.42	95±0.84	84.6±1.24
11	64.08±0.38	95.86±0.67	95.67±0.69	85.09±0.86
12	65.86±0.49	97.7±0.82	96.24±0.84	85.79±0.78

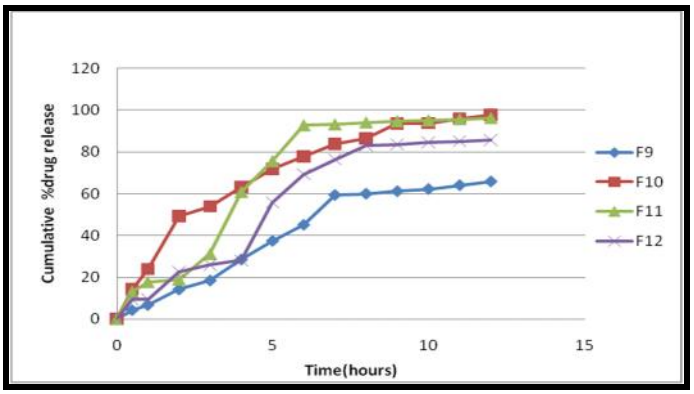

Fig. 10: Dissolution profile of Nimodipine (F9, F10, F11, F12 formulations)

In vitro drug release studies revealed that the release of Nimodipine from different formulations varies with characteristics and composition of matrix forming polymers as shown in Figure 5 to 7. The release rate of Nimodipine decreased with increasing concentration of HPMC K4M and HPMC K15 M in F3 and F5 to F6 and F8 to F9, respectively. These findings are in compliance with the ability of HPMC to form complex matrix network which leads to delay in release of drug from the device. Carbopol is more hydrophilic than HPMC; it can swell rapidly, therefore decrease of Carbopol content delays the drug release in F3 and F5 to F6. Drug release rate was increased with increasing amount of hydrophilic polymer. The maximum cumulative percent release of Nimodipine from formulation F1 could be attributed due to ionization of Carbopol at pH environment of the dissolution medium. Ionization of Carbopol leads to the development of negative charges along the backbone of the polymer. Repulsion of like charges uncoils the polymer into an extended structure. The counter ion diffusion inside the gel creates an additional osmotic pressure difference across the gel leading to the high water uptake. This water uptake leads to the considerable swelling of the polymer. The continued swelling of polymer matrix causes the drug to diffuse out from the formulation at a faster rate. Formulations F10, F11 showed relatively high rate of release of Nimodipine which is due to rapid swelling and erosion of NaCMC.

Table NO. 10: Coefficient Correlation (R) values from *Invitro* Dissolution rate test of Nimodipine Tablets

Formulation Code	Zero Order	First Order	Higuchi's	Peppas's
F1	0.9037	0.9704	0.9809	0.9769
F2	0.9541	0.9581	0.9679	0.9885
F3	0.9888	0.9751	0.9695	0.9882
F4	0.9689	0.8169	0.9834	0.9913
F5	0.9277	0.99555	0.9797	0.9568
F6	0.8330	0.9388	0.9512	0.9160
F7	0.9308	0.9886	0.9876	0.9459
F8	0.9642	0.9778	0.9394	0.9701
F9	0.9397	0.9544	0.9497	0.9812
F10	0.8756	0.9806	0.9801	0.9637
F11	0.8475	0.9212	0.9067	0.9123
F12	0.9141	0.9443	0.9191	0.9416

Various dissolution parameters computed for all the controlled release tablets. To examine further the release mechanism of Nimodipine from tablets, the results were analyzed according to the equation, $Mt/M\infty = Kt^n$ proposed by Peppa's and Korsemeyer40. The obtained values of release rate exponent (n), lie between 0.5901 and 0.8257 in all formulations for the release of Nimodipine. In general, the released pattern found to be non-Fickian tending to approach first order.

Several kinetic models describing drug release from immediate and modified released dosage forms. The model that best fits the release data was evaluated by correlation coefficient (r). The correlation coefficient (r) value was used as criteria to choose the best model to describe the drug release from the controlled release tablets. The 'r' values obtained for fitting the drug release data to first order, indicating that the drug release mechanism follows first order kinetics. From higuchi's equation, the high values of correlation coefficient 'r' indicating that the drug release mechanism from these tablets was diffusion controlled. The values of 'n' in Peppas model indicated the drug release follows non-Fickian diffusion.

From the above results it is concluded that the drug release from the formulated controlled release tablets of Nimodipine followed first order kinetics and was diffusion controlled.

DSC Studies:

Differential scanning colorimetry studies were carried out to determine the compatibility between drug and excipients in optimized formulation. From the studies it was evident that there were no prominent change in the melting point of pure drug alone and its melting point when it was combined with other excipients in optimized formulation.

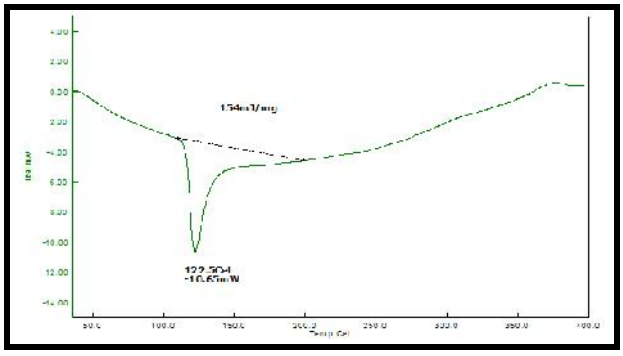

Fig. 12: Pure Nimodipine DSC

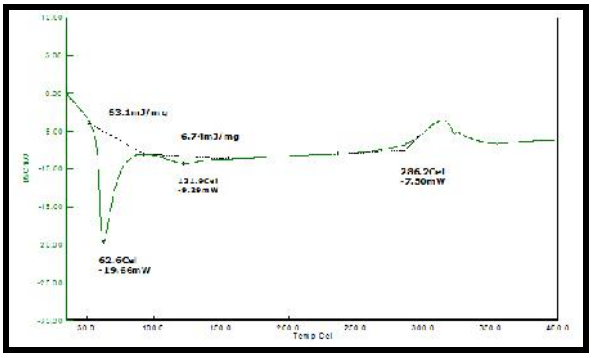

Fig. 12: optimized formulation of Nimodipine DSC

CONCLUSION

The aim of the present study was to develop an controlled release formulation of Nimotidine to maintain constant therapeutic levels of the drug for over 12 hrs. Various grades of HPMC were employed as polymers. Nimotidine dose was fixed as 40 mg. Total weight of the tablet was considered as 200 mg. Polymers were used in the concentration of 75 and 150mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F2) showed better and desired drug release pattern i.e.,97.79 % in 12 hours. It followed zero order release kinetics mechanism.

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