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FORMULATION AND EVALUATION OF NIFEDIPINE SUSTAINED RELEASE TABLETS BY USING DIFFERENT POLYMERS

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ABSTRACT:
Oral drug delivery has been known for many years because the most generally utilized route of administration among all the routes that are explored for the general delivery of medication via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such quality could also be partly attributed to its simple administration moreover because the ancient belief that by oral administration the drug is well absorbed because the food stuffs that area unit eaten daily. In fact the event of a pharmaceutical product for oral delivery, no matter its physical kind involves variable extents of optimization of dose kind characteristics at intervals the inherent constraints of GI physiology. The rationale for development of a extended release formulation of a drug is to enhance its therapeutic benefits, minimizing its side effects while improving the management of the diseased condition. The aim of the present investigation is to formulate and evaluate matrix tablets of Nifedipine using a mixture of polymers in view to sustain the drug release, reduce frequency of administration and improved patient compliance. In this research paper all evaluation parameter and stability studies also well discussed in well manner.
Keyword Matrix Tablets, Coating, Novel Drug Delivery System, Sustained Release Tablets

INTRODUCTION:

Sustained- release dosage forms it is defined as "any drug or dosage form modification that prolongs the therapeutic activity of the drug". Sustained release formulations can offer many pharmacokinetic and Pharmacodynamic advantages over conventional dosage forms, including maintenance of constant therapeutic levels for a longer period of time and reduction of fluctuations in plasma drug concentrations. Sustained release formulations can reduce the risk of treatment failure due to inadequate dosing of antibiotics. Nifedipine has bioavailability of 45-56%, protein binding of 92-98% and its half-life is about 2 hours and it undergoes gastrointestinal and hepatic metabolism So, In the present study, aim is for preparation and evaluation of sustained release matrix tablets of Nifedipine, in order to overcome first-pass effect, dose related side effects, dosing frequency, problems in disease control and many other difficulties.

MATERIALS AND METHOD

Chemicals and Reagents

Nifedipine Hydrochloride was supplied by Glow Pharma Ltd, Vasai, Maharashtra and Hydroxypropylmethylcellulose K100M, Ethylcellulose, Polyvinyl pyrollidone K-30, Magnesium Stearate, Aerosil, Lactose, Talc was also supplied by Glow Pharma Ltd, Vasai, Maharashtra

Preformulation Studies

Preformulation testing is the first step in rational development of dosage forms of a drug Substance. Preformulation study is the process of optimizing the delivery of drug through Determination of physicochemical properties of the excipients that could affect drug performance and development of as efficacious, stable and safe dosage form. [1] It provides a framework for the drug combination with pharmaceutical excipients in the dosage form. Determination of λ max of Nifedipine was dissolved

in methanol further diluted with the same and scanned for Maximum absorbance in UV double beam spectrophotometer (Shimadzu 1800) in the range from190 to 380 nm.

Appearance:

Visual Examination- A small quantity of Nifedipine was taken in a butter paper and viewed in well illuminated Room.

Solubility

The solubility of Nifedipine is determined by acetone in chloroform, ethanol and water.

Table 1: Solubility Parameter [2]

Descriptive team	Parts of solvent required for 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 o 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10000
Practically insoluble or insoluble	Greater than or equal to 10,000.

Melting point

Melting point of the Nifedipine was determined by capillary method in triplicate.

Assay

Weigh 25 mg Nifedipine ,dissolve a mixture of 100ml of methanol and take blank 2 ml of 0.1M hydrochloric acid and sample equivalent to 25 mg Nifedipine ,dissolve a mixture of 100ml of methanol and take blank 2 ml of 0.1M hydrochloric acid and take U.V. spectroscopy λ max of Nifedipine observe at 340nm.

Compatibility studies

The proper design and formulation of a dosage from require consideration of the physical, chemical and biological characteristics of the ingredients used in fabricating the formulation i.e. drug and excipients in the formulations. The drug an excipients should be compatible with one another to produce stable efficacious, attractive an easy to administer and safe dosage form. If the excipients are new and not been used in the formulation containing the active substance, the compatibility are of paramount importance .hence FTIR spectra Active with Nifedipine is compared with different excipients.[3]

Spectroscopy

FT-IR spectroscopy was carried out to check the compatibility between drug and excipients.

Infrared spectroscopy was conducted using burker and the spectrum was Recorded in the region of 4000 to 400 cm-1. The samples (drug and drug-excipient mixture in 1:1 ratio. The interaction between drug-excipients was observed from IR-spectral studies by observing any shift in peaks of drug in the spectrum of physical mixture of drug excipients.[4, 23, and 24,25,26,27]

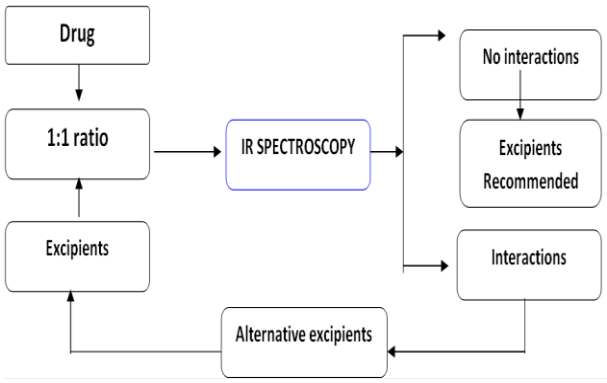


Fig 1 FT-IR spectroscopy[5]

Manufacturing Process of the Sustained Release Tablets of Nifedipine

In the present investigation sustained release tablets of Nifedipine tablets were prepared by using wet granulation technique.[6] Steps included in the manufacturing process are by sifting & dry mixing:

- The active material and excipeints were passed through 60# and 100 # sieve respectively
- And then mix the material in granulator close the lid and allow it to rotate for 5 mins.
- Total time required was 15 mins

Binder Preparation

- Mix the material in the vessel and pour the solvent continuously stir it using the ladle.
- Stir it constantly until the desired consistency is observed.
- Allow the paste to cool at room temperature.

- Total time required for preparation of binder was 30 mins using isopropyl alcohol lactose ad ethyl cellulose

Wet granulation

- Mix the binder solution with the powder mixture to form wet mass
- Wet granulation is used using the RMG.
- All the material were mixed at slow speed and fast speed .
- An stopped when the ampere reading reached at 25 am

Drying

- Drying is done using FBD.
- Load the material in the FBD and FBD bags are fitted. And the temperature is adjusted in the inlets and outlet by putting on the heater.
- Start the FBD 15 min and put off the heater and adjust the heater and stop after 15 min.
- Rake the material in bowl up and down with spatula for 3 min.
- Put the heater and adjust the temperature.
- Put off the heater And Stop the FBD and shake the FBD Bags.
- Total time required to complete drying is 45 min.

Sizing

- Check and ensure that all sieves are cleaned.
- Sift the material through 18 # sieve and dried material through vibratory sifter and collect.
- Mill the leftover through multimills.
- Granules should be cooled before lubrication.
- Screen size should be 1.5 mm.

Lubrication

- Collect the sifted material through 60#and 40 #.
- And magnesium stearate was passed through 100 # and it was added after sifting in a different container
- First take out the fines.
- Then mix the lubricants for Close the octagonal blender and Allow to rotate the blender.
- Stop octagonal blender.
- And collect the granules in the container.

Compression

- Set the rotary tablets compression machines & set the machine as per the physical parameter mentioned.
- Add granules in the hopper of the compression machine and check the flow of granules to feed frames
- All tablets were compressed on single punch i.e. 8.6 mm single punch as per company requirement with circular flat look with a breakline on one side

Coating

- Transfer the tablets uncoated tablets area to coating tablets.
- Fit spray gun and nozzle transfer the coating solution to the coatin solution.
- Start the pan to roll and start spaying the coating solution over the tablet bed after adjusting the parameter including.

1. Air pressure
2. Temperature of hot air blower
3. Bed temperature.
4. Exhaust

Coating conditions

Table 2: Coating Conditions [7]

Parameters	Conditions
Pan speed	8 to 10 rpm
Inlet air temperature	30 to 40 °C
Exhaust air temperature	30 to 35 °C
Bed temperature	30 to 35 °C
Atomizing air pressure	3 to 4 kg /cm^2
Spray gun nozzle diameter	1.0 mm
Spray rate	6.0 to 8.0 ml /min

Preparation of Coating Solutions [8]

- All the ingredients were weighed and dispensed.
- Color sunset yellow lake and Titanium Dioxide was added in IPA.
- PEG-600 , HPMC and purified talc were added in Methylene dichloride
- Both were mixed together and stirred together to get a homogenous mixture
- The prepared suspension is strained through 100 #sieve.

The initial check on the tablet were carried out after film coating, appearance, average weight, Thickness of tablet ,Disintegration time and drug release were also checked .

Blister Packing of Tablets [9]

White colored PVC-PVDC base foil and Aluminium lidding foil are loaded in the machine .The tablets were loaded in the hopper. The base foil passes through the forming units with Teflon heads and cavities are formed. Tablets in the hopper coming down through inclined feeding channel and singling

unit and are introduced into the cavities formed. The heat sealable Aluminium lidding foil is introduced and the sealing of the foils was done in the sealing station. The non-filled cavities are detected using non fill detecting system and are rejected. The cutting assembly and the trimming station cuts the blister into appropriate size and shape. Here the thickness of PVC/ PVDC layer is 0.850mm while thickness of Aluminium foil is 0.400mm.

Evaluation of Preformulation Parameters:

Angle of Repose [10]

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using equation. $\theta = \tan^{-1}(h/r)$

Where, θ = the angle of repose

h = height of the heap of the powder

r = radius of the heap of the powder

Table 3: Angle of Repose [11]

Sr. No	Angle of Repsoe(θ)	Type of flow
1	< 25	Excellent
2	25-30	Good
3	30-40	Passable
4	> 40	Very poor

Determination of bulk density and tapped density [12, 13]

A quantity of 2 g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using following formulas.

Db = Mass of powder
Bulk volume of the powder

Dt = Mass of powder
Tapped volume of the powder

Carr's index [14]

It helps in measuring the force required to break the friction between the particles and the hopper. It is expressed in % and given by

Carr's index % = Tapped Density – Bulk Density X100/Tapped Density

Table 4: % Compressibility Index

Sr. No	% Compressibility	Index Property
1	5-12	Free flowing
2	12-16	Good
3	18-21	Fair
4	23-35	Poor
5	33-38	Very poor
6	6 > 40	Extremely poor

Hausner's ratio [15]

Hausner's ratio is a indirect index of ease of powder flow. Hausner's ratio was measured by the ratio of tapped density to bulk density.

Hausner's ratio = Tapped Density/Bulk density

Table 5: Hausner's ratio

Sr no.	Hausner's ratio Property	Property
1	0-1.2	Free flowing
2	1.2-1.6	Cohesive flowing

EVALUTION OF COMPRESSED TABLETS[16]

Evaluation of Nifedipine sustained release Tablet

The tablets prepared were evaluated for the following parameters like weight variation, hardness, friability, drug content, *in-vitro* dissolution studies and, stability studies.

Weight Variation Test [17, 18]

To study weight variation, 20 tablets of each formulation were weighted using electronic balance and the test was performed according to the official method.

Table 6: IP standards of Uniformity of weight

Sr no.	Avg. Wt of Tablet (mg)	% Deviation
1	> 80 mg	10%
2	80 mg – 250 mg	7.5%
3	≥250 mg	5%

Hardness [19]

Hardness of tablets was tested using the Monsanto hardness tester .the tester consist of barrel containing a compressible spring held between two plunger .the lower plunger is placed in contact with tablet with a zero reading taken. The upper plunger is than forced against a spring by turning a threaded bolt until the tablet fractures and then the force of fracture was recorded .in all the average of six tablets were used for determination .

Friability [19]

Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients.10 gm were weighed and the initial weight of these tablets was recorded and placed in Roche friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator dusted off the fines and again weighed and the weight was recorded. Percentage friability was calculated by using the formula.

% Friability = Weight of initial tablets- Weight of final tablets X 100/ Weight of initial tablets

Tablet Thickness

Thickness of the tablet is important for uniformity of tablet size. Thickness was measured using Vernier Calipers. It was determined by checking the thickness of ten tablets of each formulation. Vernier caliper consists of metric and imperial scales. The main matric scale is read first then read “hundredths of mm” of imperial scale (count the number of division until the lines concedes with the main metric scale. The imperial scale number is multiply with 0.02. Then that number obtained from imperial scale added with main metric scale to get final measurement.

Disintegration time [5, 19]

The disintergration time was determined using disintegration test apparatus at 37°C ± 2°C. A tablet was placed in each of the six tubes of the apparatus a one disc is added to each tube .then time taken for the complete disintegration of the tablets with no palpable mass in the apparatus was noted.

***In vitro* dissolution studies of sustained release layer** [20, 21]

The in vitro release of sustained release layer was carried out for hours using USP type-II apparatus (DT-1200) at 150 rpm for the first 120mins in 900 ml 0.1N HCL at 340 nm maintaining at 37 ±0.50C and then at phosphate buffer pH 6.8 in 900ml for another 6 hour. A 5 ml was withdrawn at different time intervals and replaced with an equal volume of fresh medium. The samples were suitably diluted with blank dissolution medium, filtered and analyzed on UV spectrophotometer at 340 nm.

Drug Content for Sustained Release layer

Ten tablets were weight and average weight is calculated. All tablets were crushed and powder equivalent to 100 mg drug was dissolved in pH 6.8 phosphate buffer and the volume was made up to 100 ml with pH 6.8 phosphate buffer. The solution was kept in solicitor for 1 hr. From the stock solution, 1ml solution was taken in 10 ml volumetric flask and the volume was made with pH6.8 phosphate buffer. Solution was filtered and absorbance was measured spectrophotometrically at 350 nm against pH6.8 phosphate buffer as a blank. Amount of drug present in one tablet was calculated.

Mathematical Modeling of drug Release Profile [23, 24,25,26,27]

The cumulative amount of release from the formulated tablets at Different time intervals were fitted to Zero order kinetics, first order kinetics, Higuchi model and korsmeyer-peppas model to characterize mechanism of drug release.

1. Zero-order Kinetic model – Cumulative %drug release versus Time.
2. first-order Kinetic model – Log cumulative % drug remaining versus Time.
3. Higuchi’s model – cumulative percent drug released versus square root of time.
4. Korsmeyer equation / peppa’s model- Log cumulative percent drug released versus log time.

Zero order kinetic

It describes the system in which the release rate is independent of its concentration.

$Qt=Q_0 + K_0t$

Where, Qt = amount of drug dissolved in time t

Q_0 = initial amount of drug in the solution

K_0 = zero order release constant

If the zero order drug release kinetic is obeyed, a plot of Qt versus t will give straight line with a slope of K_0 and an intercept at Q_0.

First order kinetics

The application of this model to drug dissolution studies was first proposed byGibaldi and Feldman

(1967) and later by Wagner. The dissolution phenomena impliesa surface action, as can be seen by Noyes–Whitney equation,

$\frac{dc}{dt} = K(Cs - C)$

Where, C = Concentration of solute in time t, CS = solubility in equilibrium at experience temperature, k =First order proportionality constant

Hixson and Crowell adapted the above equation as

$\frac{dw}{dt} = K(Cs - C)$

Where, w = amount of solute in solution at time t, S = Solid area accessible to dissolution.

$\log Q_t = \log Q_0 + K1.t / 2.303$

Where, Q_t = amount of drug release in time t, Q_0 = initial amount of drug in solution,

K_1 = First order release constant.

Above equation also represents this model.

The pharmaceutical dosage form following this dissolution profile, such asthose containing water soluble drugs in porous matrices release drug in a way that is proportional to amount of drug remaining in its interior in such a way that amount of drug released by unit of time diminish.

Higuchi Model

Higuchi developed mathematical expressions for drugs particles dispersed in a uniform matrix behaving as diffusion media. To study the dissolution form a planar system having a homogeneous matrix, the relation obtained was

$Ft = Q = \sqrt{(2C - Cs)Cst}$

Where, Q = Amount of drug released in time t per unit area, C = Drug initial concentration

CS = drug solubility in matrix media, D = Diffusivity of drug molecules in matrix substance.

The solid line represents the variation of drug concentration in the pharmaceutical system after time t. To distance h, the concentration gradient will be constant, provided $C >> C_s$. The linearity order follows the Fick's law.

$Q = \sqrt{tDCs(2C - Cs}$

Relation is valid during all time except when the total depletion of drug in therapeutic system is achieved .Higuchi developed other models for release from heterogeneous matrix, when the drug concentration in matrix is lower than its solubility and the release occurs through pores in matrix, the obtained relation is:

$Ft = Q = \sqrt{DE/T(2C - \mathcal{E}Cs}\,)Cst$

Korsmeyer and Peppas model

This equation is useful to study the diffusion / relaxation release of dosage form as well zero order release kinetics. The equation can be described as

$\frac{Mt}{M\infty} = Kt^n$

$\frac{Mt}{M\infty}$= fraction of drug release in time t,

K = constant incorporating structural and geometric characteristics of controlled release device.

n = diffusion release exponent indicative of release Mechanism. For release from swellable cylinders Ritger and Peppas have indicated,

n = 0.45 for Fickian diffusion,

n > 0 .45 and < 0.89 for anomalous diffusion or non Fickian diffusion (0.5 < n < 1)

n = 0.89 for zero order release

n = 1 or > 1 for super case

STABILITY STUDIES [23, 24,25,26,27]

Stability Testing of the Optimized Formulation

Stability studies of the drug has been defined as the ability of a particular formulation in \a specific container to remain within its physical ,chemical, therapeutic and toxicological specifications. The purpose of stability study is to provide evidence on the quality of a drug substance or drug product which Varies with time under the influence of variety of environmental factors such as temperature ,humidity and light .recommended storage conditions ,re-test period and shelf lies are to be established. The international conference of harmonization (ICH) Guidelines titled, "stability testing of a new drug Substances and products" describes the stability test requirement for drug registration application of European Union, Japan and USA.

Long term stability

(I) 30 + 2 ^{o} C and RH 65 % + 5%

Accelerated studies

(II) 40 + 2 ^{o} C and RH 75 % + 5%

Tablets were withdrawn after a period of 1, 2, 3 months and analyzed for physical characterization (appearance, moisture content), study and percentage assay.

Table 7: Formulation of Nifedipine

Ingredients	NF_1	NF_2	NF_3	NF_4	NF_5
Drug	20 mg	20 mg	20mg	20 mg	20 mg
MCCP	95 mg	85 mg	78 mg	65 mg	70 mg
Starch	30 mg	34 mg	38 mg m	36 mg	40 mg
P.V.P.K -30	10 mg	12 mg	14 mg	15 mg	9 mg
Lactose	30 mg	34 mg	36 mg	32 mg	40 mg
Ethyl cellulose	7.5 mg	9.5 mg	8.4 mg	11 mg	11.5 mg
Talc	4 mg	5 mg	6 mg	5 mg	5.5 mg
Aerosil	1 mg	1.2 mg	1.4 mg	1.2 mg	1.6 mg
Magnesium stearate	0.3 mg	0.5 mg	0.6 mg	0.5 mg	0.6 mg
HPMC K-100	15 mg	21 mg	23.2 mg	38 mg	32 mg m
Ethyl cellulose	9 mg	9.5 mg	8.5 mg	--	---
Total weight	231.9 mg	233.7 mg	235 mg	223.7 mg	230.2 mg

Table 8: Formulation of Nifedipine Coating Solution

Ingredients	Quantity
HPMC	6.06 mg
Purified talc	7.580 mg
Titanium dioxide	0.400 mg
PEG 6000	1.010 mg
Col Sunset Yellow	0.303 mg
Isopropyl Alcohol	60 ml
Methylene dichloride	101 ml

RESULT

Table 9:

Test	Specification	Observation
Color	Yellow to light yellow	Yellow to light yellow
Odour	Odorless	Odorless
Appearance	Yellow crystalline powder	Yellow crystalline powder
Loss on drying	NMT than 0.5%	0.33%
Melting point	173-175°C	173 °C

Table 10: Solubility of Nifedipine in different solvents

Sr No.	Solvent	Inference
1	Water	Insoluble
2	Chloroform	Freely soluble
3	Ethanol	Sparingly soluble
4	Acetone	Freely soluble

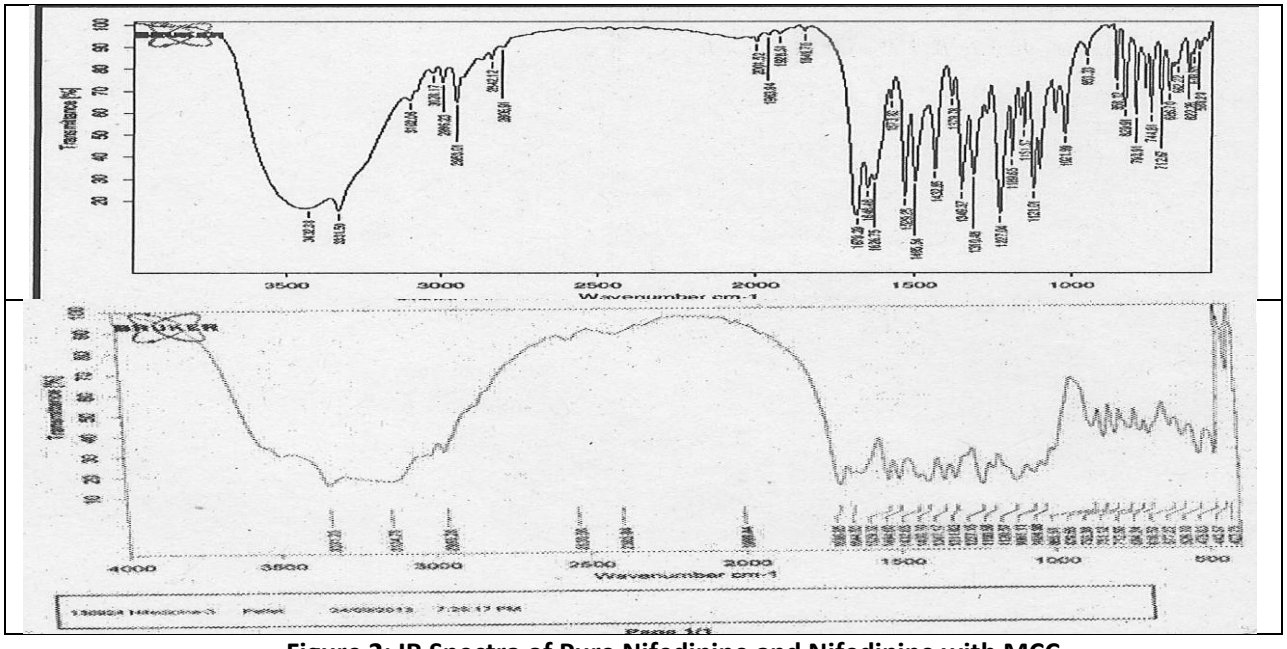


Figure 2: IR Spectra of Pure Nifedipine and Nifedipine with MCC

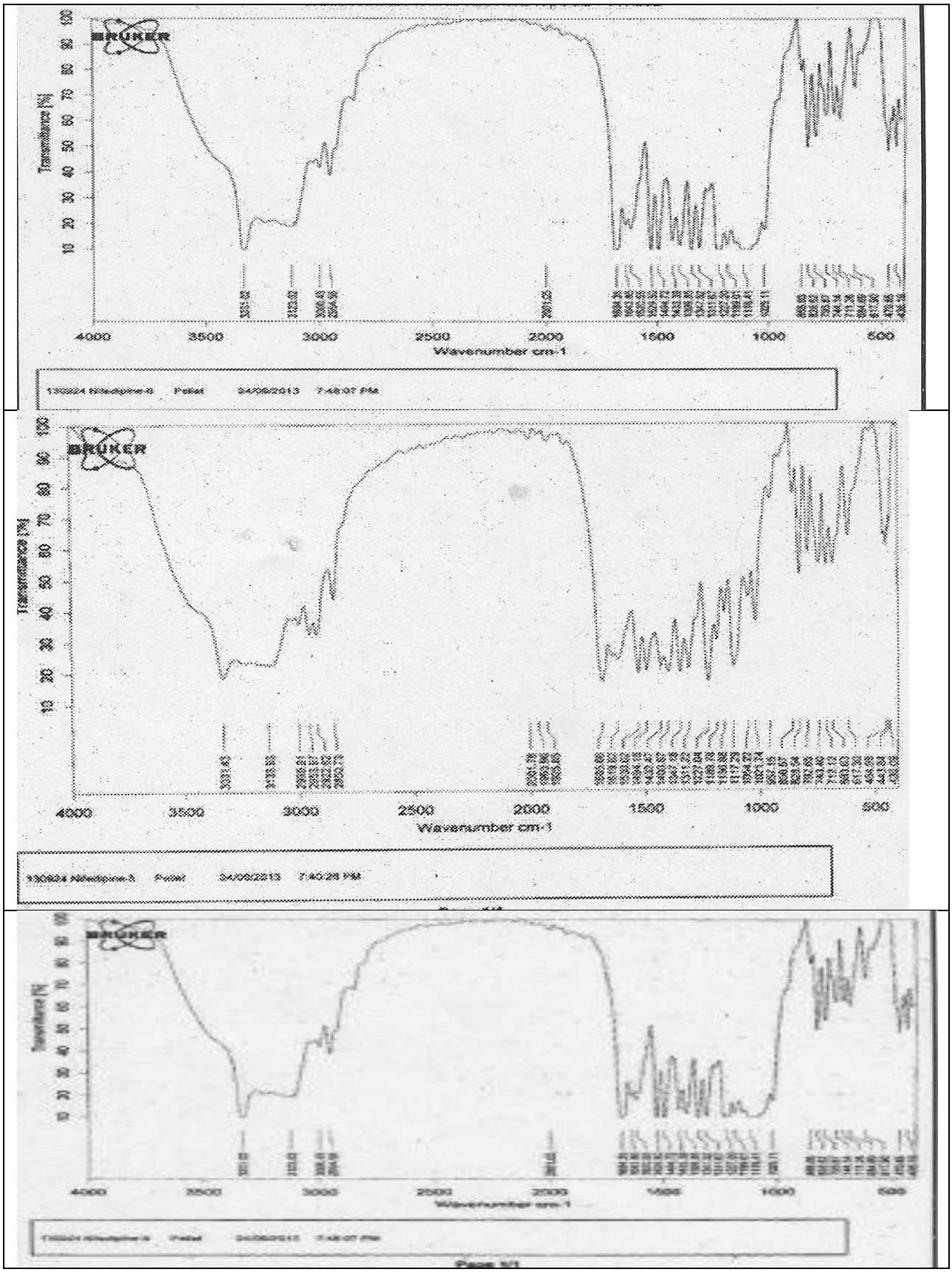


Figure 3: Nifedipine with PVPK-30 and Magnesium Sterate

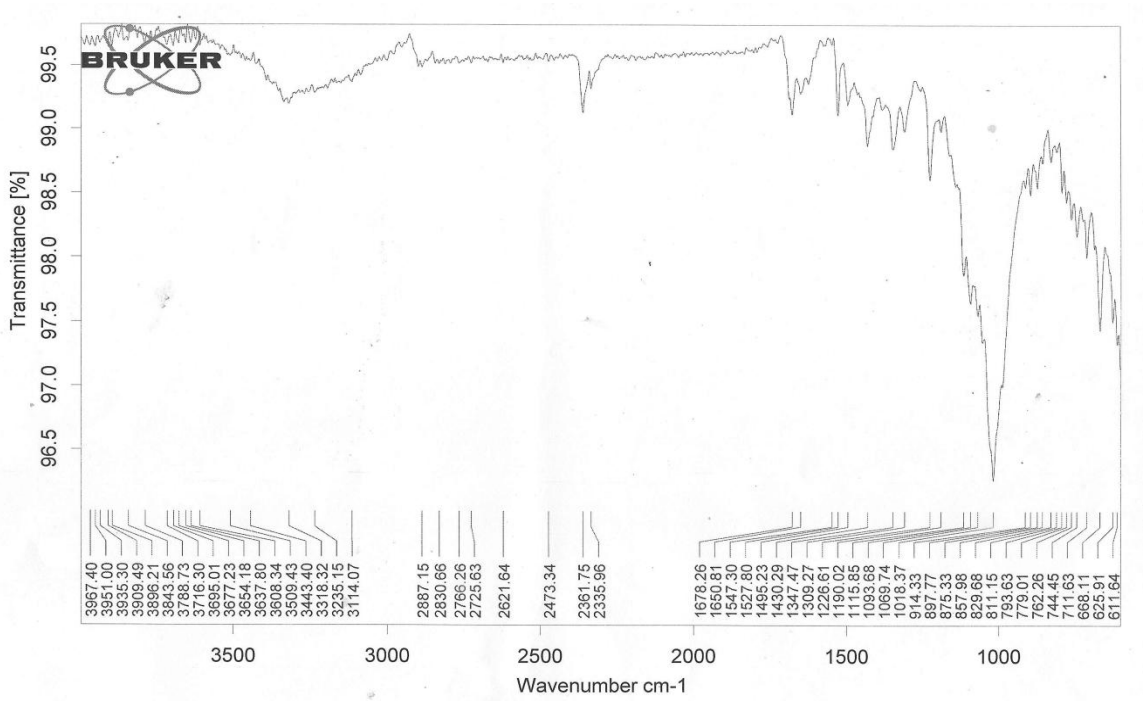


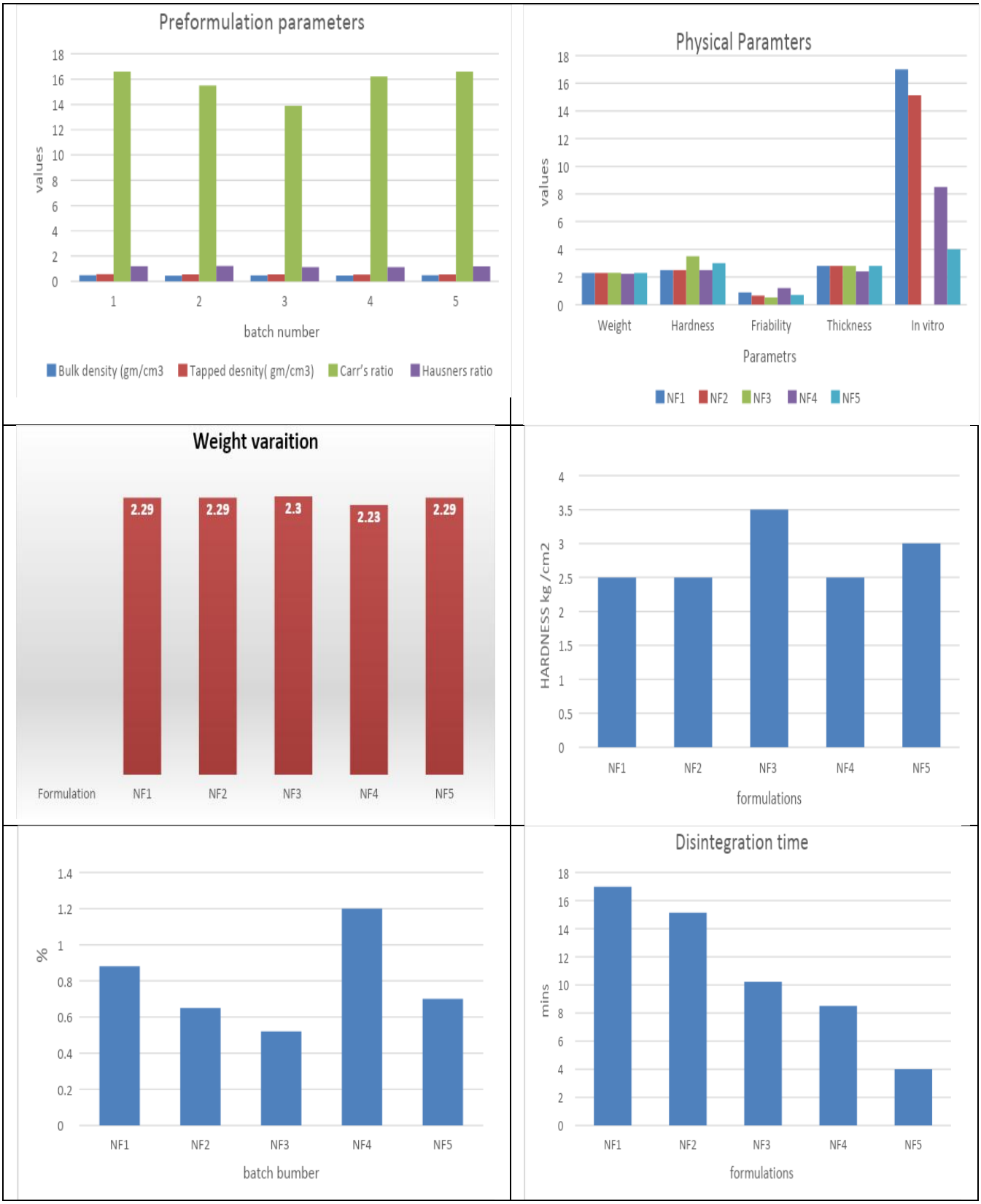
Figure 4: NIFEDIPINE WITH ALL EXCIPIENTS

Table 11: Evaluations of Pre-Compression Parameters

Property	NF1	NF2	NF3	NF4	NF5
Angle of repose (°)	33°59	33°05	34°02	33°31	33°14
Bulk density (gm/cm^3	0.488	0.455	0.476	0.466	0.488
Tapped destiny(gm/cm$^{3)}$	0.572	0.556	0.556	0.541	0.550
Carr's ratio	16.6	15.5	13.9	16.20	16.6
Hausners ratio	1.20	1.22	1.13	1.13	1.19
Flow property	Good	Good	Good	Good	Good

Table 11: POST-COMPRESSION EVALUATION PARAMETERS

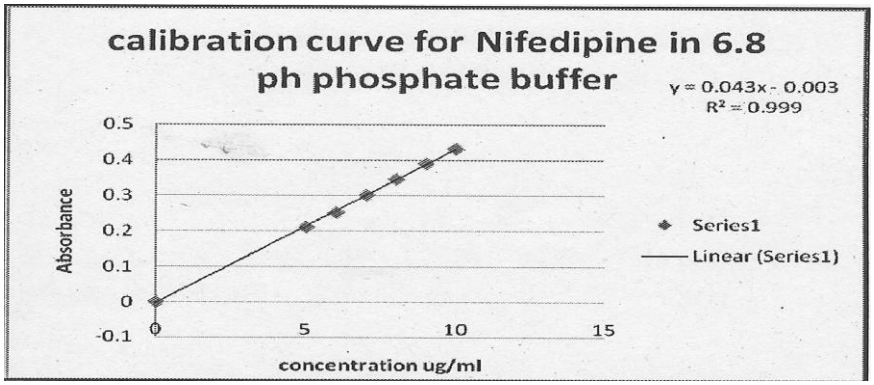
Formulation	Weight variation Mean	Hardness (kg/cm2) Mean	Friability (%) Mean	Thickness Mean	*In vitro* disintegration time (sec) Mean
NF1	2.29	2.5	0.88	2.80	17 Mins
NF2	2.29	2.5	0.65	2.80	15 min &14 sec
NF3	2.30	3.5	0.52	2.80	10 min & 22 secs
NF4	2.23	2.5	1.2	2.40	8 min 5 Sec
NF5	2.29	3	0.7	2.80	4 mins



Graph 1: Preformulation Parameter, Weight variation, hardness, disintegration time

Table 12: Absorbance of Nifedipine

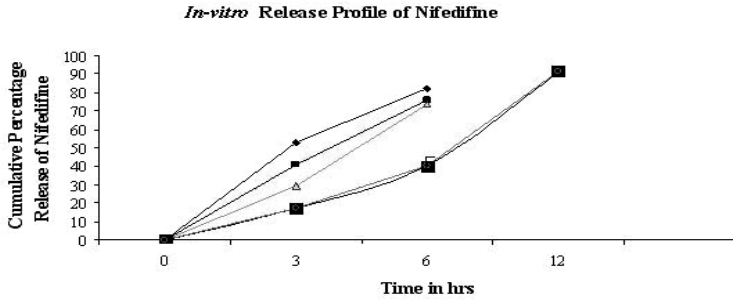
Sr no	Concentration (mcg/ml)	Absorbance 237 nm
1	0	0
2	5	0.211
3	6	0.252
4	7	0.301
5	8	0.346
6	*9*	*0.390*
7	*10*	*0.432*



Graph 2: Calibration curve for Nifedipine in 6.8 pH in phosphate buffer

Table 13: In-vitro dissolution study

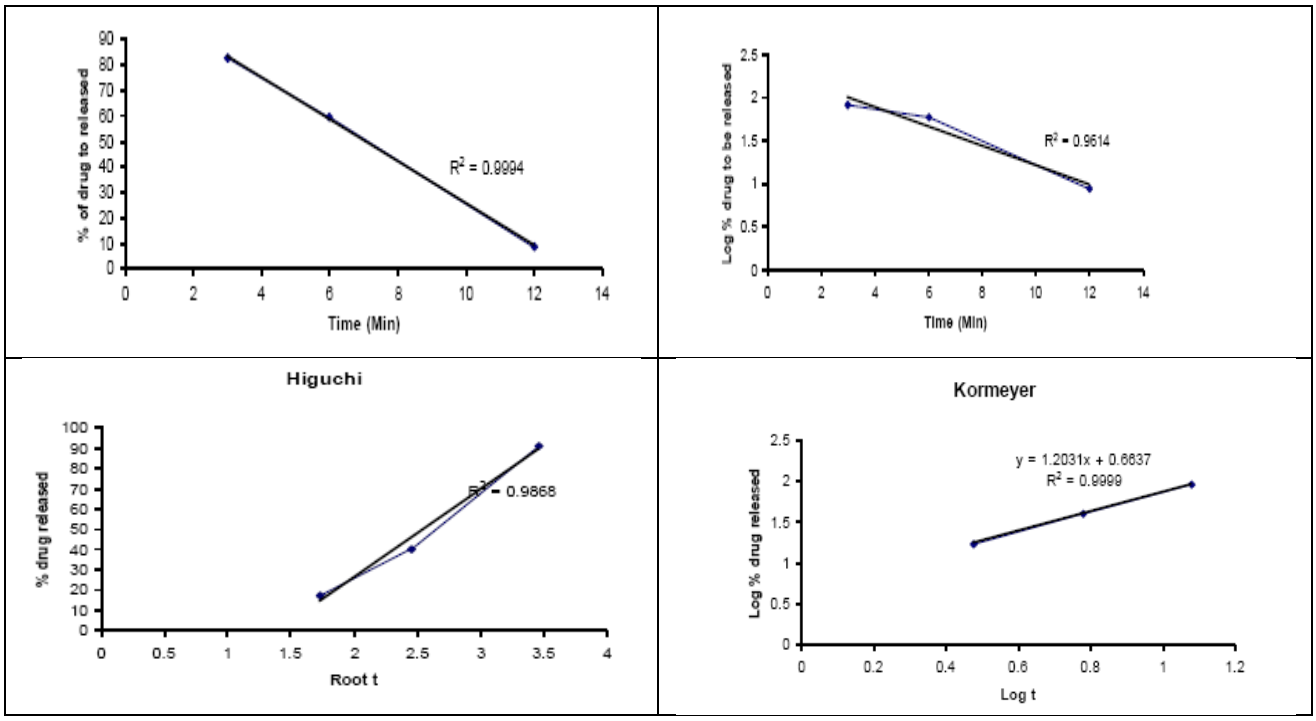
Drug release test at hrs	Specification	Batch I NF1	Batch II NF2	Batch III NF3	Batch IV NF4	Batch V NF5
At 0 hrs	Between 00% and 00%	00	00	00	00	00
At 3 hrs	Between 10% and 30%	15.16	17.22	17.19	53	41
At 6 hrs	Between 40% and 65%	38.23	40.19	40.24	82	76
At 12 hrs	Not less than 80%	91.10	91.08	91.12	00	00



Graph 3: Release profile

Table 14: In-vitro Release of drug of NF3

Time (h)	√t	Log t	Amount released (mg)	% drug released	% drug to be released	Log % drug released	Log % drug to be released
3	1.732	0.4471	3.12	17.19	82.81	1.23527	1.91808
6	2.449	0.7781	8.05	40.24	59.76	1.60465	1.77641
12	3.464	1.0791	18.32	91.12	8.8	1.95961	0.94841



Graph 4: Kinetic release of Nifedipine of Zero Order Reaction, Nifedipine of First Order Reaction , Kinetic release of Nifedipine Higuchi Kinetic release of Nifedipine Kormeyer

STABILTY DATA

Table 15: REAL TIME STABILITY REPORT

Product: Nifedipine Sustained Release Tablets 20 mg
Storage Conditions: Temperature 30°C + 2°C and RH 65 % + 5 %.

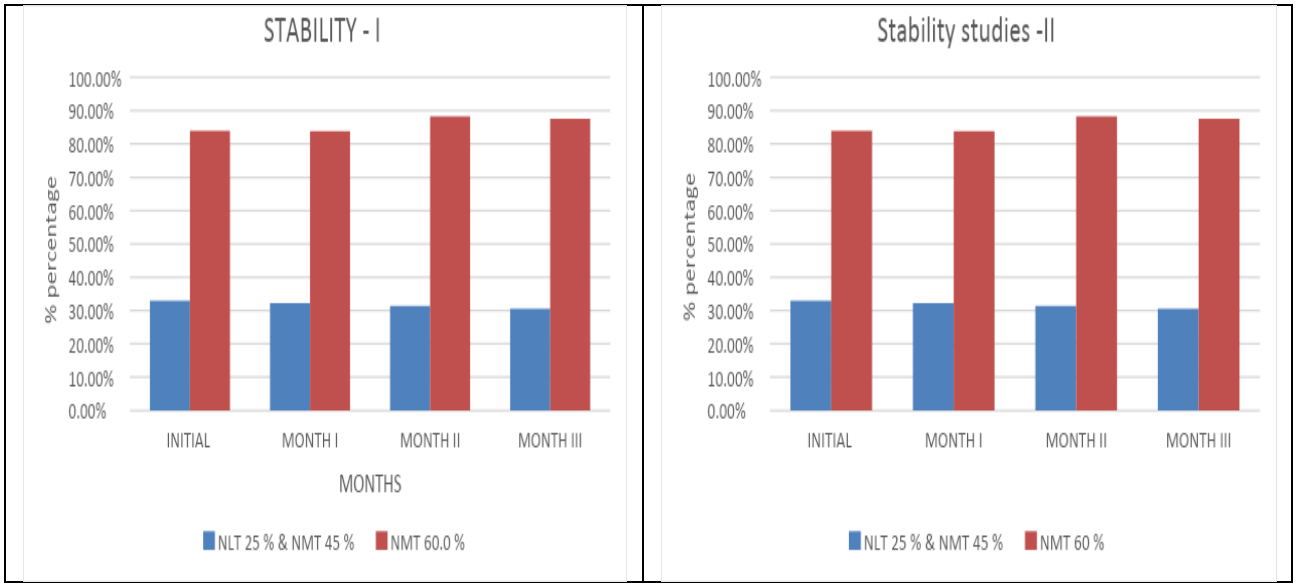
Sr. No	Tests	FREQUENCY OF TESTING			
		Initial	1 months	2 months	3 months
1	Description: Light orange Coloured, circular, biconvex, sustained released film coated tablet.	Complies	Complies	Complies	Complies
2	Identification: Must comply as per standard	Complies	Complies	Complies	Complies
3	Weight of 20 Tablets: 4.6000 gm	4.6082 gm	4.5996 gm	4.5877 gm	4.5739 gm
4	Average Weight of a Tablet: 0.2300 gm	0.2304 gm	0.2298 gm	0.2294 gm	0.2287 gm
5	Uniformity of Weight: ± 7.5 % Avg. Weight	Complies	Complies	Complies	Complies
6	Disintegration Time: NMT 30 minutes	10 min. & 22 sec.	11 min. & 00 sec.	11 min. & 13 sec.	11 min. & 37 sec.
7	Dissolution Test:				
	A) NLT 25.0 %&NMT 45.0 %	33.00 %	32.27 %	31.41 %	30.58 %
	B) NLT 60.0 %	84.00 %	83.86 %	88.25 %	87.58 %
8	Assay: Limit: 90.0 % to 110.0 %				
	Each sustained release film coated tablet contains:				
	Nifedipine	101.60 %	101.12 %	100.64 %	99.91 %

Table 16: ACCELERATED TIME STABILITY REPORT

Product: Nifedipine Sustained Release Tablets 20 mg

Storage Conditions: Temperature 40°C + 2°C and RH 75 % + 5 %.

Sr. No	Tests	FREQUENCY OF TESTING			
		Initial	1 months	2 Months	3 months
1	Description: Light orange coloured, circular, biconvex, sustained released film coated tablet.	Complies	Complies	Complies	Complies
2	Identification: Must comply as per IP	Complies	Complies	Complies	Complies
3	Weight of 20 Tablets: 4.6000 gm	4.6082 gm	4.5961 gm	4.5877 gm	4.5739 gm
4	Average Weight of a Tablet: 0.2300 gm	0.2304 gm	0.2298 gm	0.2294 gm	0.2287 gm
5	Uniformity of Weight: ± 7.5 % Avg. Weight	Complies	Complies	Complies	Complies
6	Disintegration Time: NMT 30 minutes	10 min. & 22 sec.	11 min. & 00 sec.	11 min. & 13 sec.	11 min. & 37 sec.
7	Dissolution Test:				
	A)NLT 25.0 %&NMT 45.0 %	33.00 %	32.27 %	31.41 %	30.58 %
	B) NLT 60.0 %	84.00 %	83.86 %	88.25 %	87.58 %
8	Assay: Limit: 90.0 % to 110.0 %				
	Each sustained release film coated tablet contains:				
	Nifedipine	101.60 %	101.12 %	100.64 %	99.91 %



Graph 5: stability Graph

DISCUSSION

The Drug selected for Research Work is Nifdipine Anti-Angina & Antihypertensive drug .the Drug Sample was firstly identified for various Pharmacopoeial test as well as analyzed by spectrometrically and By FTIR and the results showed Authencity and purity of drug sampl. The melting Point of the drug with Appearance Solubility, Odour and loss on drying were determined which is matched the standard. The Melting Point was Found 173-175°C which matched the standard. Solubility of drug was freely soluble I chloroform and acetone and completely insoluble in water. LOD was found to be 0.33% which was in the standard limit.Standard curve of Nifedipine was prepared by Shimadzu UV

Spectrophotometer . at 237 nm .The results showed that it follows the concentration range and follows Beer Lambert law. Drug Excipients interaction was determined by infrared Spectroscopy. The IR Mixture of the drug sample and excipients was found to be within the specified range .Hence there is no interaction between sample and excipients .and excipients likely to be used in the formulation n hence can be used in the formulations. The flow properties of the samples were found optimum and in standard Limit, The Sample NF3 was found optimal in the Parameters and was subjected to further studies in Assay and Stability Studies. The Dissolution Profile also concluded that NF3 release the drug as per the specifiecations. Dissolution of NF1 & NF2 were also in the standard range As comapared to that Of NF4 & NF5 Release of NF3 was better after 3, 6& 12 hrs . The drug release after 12 hrs was 91.12 %. From these graphs the kinetic values were calculated by linear regression (r2) analysis and least square techniques. The data was plotted as % drug released (Vs) time has indicated that the release rate is almost linear. The linear regression value was found to be 0.9994, which indicates that the release rate is satisfying the zero order kinetics. The graph is shown in above figure The data was also drawn according to first order rate kinetics and the plot is shown in above figure The linear regression value was found to be 0.9614. The data has satisfied zero order release of the drug than first order rate of release. Higuchi's square root dependent diffusion equation in which the % drug release was plotted against time and plot is shown in figure 21 . The plot is linear. This indicates that the diffusion mechanism is operative. The linear regression value 0.9868. So the drug release obeys diffusion mechanism, with zero order rates. Peppas exponential equation in which the log % drugs release was plotted against log time. The plot was found to be the linear regression value was 0.999. This indicates that there is significant swelling in the matrix during dissolution time and the mechanism of drug release is anomalous diffusion. The stability Studies of NF3 also found satisfied. Which indicated that drug was stable for 3 months .Which was done as Per the ICH guidelines on real time and accelerated. Accelerated Temperature 40°C + 2°C and RH 75 % + 5 %, real time Temperature 30°C + 2°C and RH 65 % + 5 %. The sample complies with all the parameters included.

CONCLUSION

NIifedipine is very efficient for anti-anginal and hypertension. In present Study sustained Release nifedipine tablets were prepared and evaluated .work has shown that Sustained Release may be an interesting choice for hypertension. It Provide a sustained release over the period of 12 hrs. Nifedipine was prepared with HPMC & ethyl cellulose and were sustained Release, efficiency, Drug release, Stability and assay with all physical parameter.

- Preformulation studies were carried on various Parameter were Performed Like – Physiochemical Properties, Solubility ,pH and Identification of drug .
- Suitable method based on UV Visible Spectrophotometer was developed at 237 nm and interference was verified and found that Nifedipine did not interfere with the polymer and excipients used.
- Matrix formation was used to prepare the tablets.
- Evaluation Was within Permissible limit of formulation.
- In-vitro drug Release Study of all the formulation was carried out and based on the result NF3 batch of sustained Release tablet was identified as the best Formulation among all the formulations

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