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Formulation and evaluation of fast dissolving tablet of nicardipine hydrochloride by using solid dispersion technique

Smita Aher, Ravindranath Saudagar and Mayuri Shinde

Abstract
The aim research was to prepare fast dissolving tablets of antihypertensive drug Nicardipine Hydrochloride. The solubility of poorly water soluble drug was enhanced by preparing solid dispersion of the drug with β Cyclodextrin in various ratios. The optimized solid dispersion were further kneaded with suitable proportions of superdisintegrant like crosspovidone and ingredients like microcrystalline cellulose, Talc, lactose, sodium saccharine, Magnesium stearate. Fast dissolving tablets of Nicardipine Hydrochloride was prepared by Direct Compression method. The pre-compressive parameters for blend and post-compressive parameters for the prepared tablets were evaluated. FTIR study showed no evidence of drug excipient interaction. DSC and XRD parameters performed on Drug and Solid Dispersion. The optimized formulation was found to be F8 Batch. It was Concluded that fast dissolving tablets of Nicardipine Hydrochloride can be prepared by solid dispersions of drug with β Cyclodextrin and with superdisintegrant provide better dissolution rate within in shorter period of time. Hence effective hypertensive treatment anywhere and anytime particularly for geriatric, pediatric, mentally ill, bedridden and patients who do not have easy access to water.

Keywords: Fast dissolving tablet, nicardipine hydrochloride, solid dispersion technique

1. Introduction
Tablets are the most widely used dosage forms because of the conveniences in terms of self-administration, compactness, stability, and ease in manufacturing. However, geriatric, bedridden and pediatric patients felt difficulty in swallowing conventional tablets. To overcome this drawback, innovative drug delivery systems known as fast dissolving tablets have developed. A tablet which can rapidly disintegrate or dissolved in saliva is an attractive and patient-oriented pharmaceutical preparation. The concept of rapid disintegrating drug delivery system emerged from the desire to provide patients with conventional mean of taking their medication. Difficulty in swallowing (Dysphagia) is a common problem especially in elderly and pediatrics, because of the physiological changes associated with these groups of patients [1]. Other categories that experience problems using conventional oral dosage forms includes the nauseated, mentally ill, and non cooperative patients, those with motion sickness, sudden episodes of allergic or asthma attack where an ultra-rapid onset of action is required [2]. The tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a greater deal of attention**.** The potential advantages such tablets include, administration without water, anywhere, anytime lead to their suitability to geriatric, pediatric, mentally ill, the bedridden and patients who do not have easy access to water. The benefit of such formulations includes patient compliance, rapid onset of action and increased extent of bioavailability. Before preparing fast dissolving tablets an effort to increase dissolution of drug is often needed. Methods available to improve dissolution include salt formation, micronization and addition of solvent or surface active agents. Solid dispersion is one of such methods and it involves a dispersion of one or more active ingredients in an inner carrier or matrix in solid state prepared by melting, dissolution in solvent or melting-solvent method etc. Solid dispersion technology has been successfully been used for improving the solubility of the poorly soluble drugs and hence bioavailability of such drugs [3].
The solubility of Nicardipine Hydrochloride can be successfully enhanced by preparing Solid dispersion of the drug with β Cyclodextrin with ratios 1:1, 1:2, 1:3, 1:4, 1:5 through Kneading Method. Crosspovidone is used as Superdisintegrant and other ingredients like microcrystalline cellulose, Talc, lactose, sodium saccharine, Magnesium stearate.

Nicardipine Hydrochloride is dihydropyridine calcium channel blocker is used alone or with an angiotensin-converting enzyme inhibitor to treat hypertension, chronic stable angina pectoris and prinzmetal's variant angina. Nicardipine is similar to other peripheral vasodilators. Nicardipine inhibits the influx of extra cellular calcium across the myocardial and vascular smooth muscle cell membranes possible by deforming the channel, inhibiting ion-control gating mechanisms and interfering with the release of calcium from the sacroplasmic reticulum [4, 5, 6].

2. Materials and Methods

2.1. Materials

Nicardipine Hydrochloride was obtained as a gift sample from Wockhardt Pharmaceutical Ltd, Aurangabad, Microcrystalline Cellulose, Sodium Saccharine, Magnesium Stearate, Talc, Lactose, β Cyclodextrin was obtained from Research lab, Mumbai.

2.2 Methods

2.2.1 Formulation of Tablets

Required quantity of Optimized solid dispersion (drug: polymer, 1:1 ratio) was triturated with different proportions of superdisintegrant Crosspovidone Mixed with other ingredients such as a Microcrystalline Cellulose, Sodium Saccharine, Talc, Lactose, Magnesium Stearate in geometric ratio of their weight and powdered in a mortar. The blend was directly compressed to obtained flat rounded tablets weighing 200 mg.

Table 1: Formulations of Nicardipine Hydrochloride fast dissolving Tablets.

Ingredients	Formulations(mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
SD equivalent to 10 mg of Drug	18.89	18.89	18.89	18.89	18.89	18.89	18.89	18.89	18.89
Microcrystalline Cellulose	40	80	120	40	80	120	40	80	120
Crosspovidone	2	2	2	3.5	3.5	3.5	5	5	5
Sodium Saccharine	1	1	1	1	1	1	1	1	1
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Lactose	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total	200	200	200	200	200	200	200	200	200

3. Characterization of Developed Formulation

3.1 Preformulation Study of Drug

Preformulation study is the first step in the rational development of dosage forms of a drug. It can be defined as an investigation of physical and chemical properties of drug substance, alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms, which can be mass-produced.

a) Organoleptic Properties

The sample of Nicardipine Hydrochloride was studied for organoleptic characteristics such as colour, odour and appearance [8].

b) Melting Point

Melting point of Nicardipine Hydrochloride was determined by taking a small amount of sample in a capillary tube closed at one end and placed in melting point apparatus. The melting point was noted in triplicate and average value was noted.

c) IR Spectroscopy

The FT-IR spectrum of the obtained sample of drug was compared with the standard FT-IR spectra of the pure drug [7, 10].

d) Solubility

The solubility of Nicardipine Hydrochloride was checked in different solvents: water, methanol, and phosphate buffer pH 6.8 of was added to 10 mg of Nicardipine Hydrochloride separately and shaken vigorously for 5 minute and placed in a constant temperature bath for 15minutes.

e) Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) was performed using differential scanning calorimeter (SW9.2, Mettler Star) equipped with a computerized data station on pure drug Nicardipine Hydrochloride to determine the melting point and exothermic and endothermic peaks. An empty standard aluminium pan was used as reference. DSC scans were recorded at heating rate of 10 °C/min in the temperature range 30°-300 °C and 40 ml/min of nitrogen flow.

f) Ultraviolet-Visible Spectroscopy

The UV spectrum of Nicardipine Hydrochloride was obtained using UV Visible Double Beam Spectrophotometer (UV 1800 Shimadzu). Accurately weighed 10 mg of the drug was dissolved separately in solvent (methanol) volume was made up to 100mL by the respective solvent to obtain a stock solution of final concentration 100 µg/mL. Aliquot (1mL) of stock solution of Nicardipine Hydrochloride was transferred into a series 10mL volumetric flask and volume was made up to the mark with the respective solvent to produce the concentration range 10 µg/mL. The resultant solution was scanned from 200 to 400 nm and the spectrum was recorded to obtain the value of maximum wavelength. The stock solution of 100µg/mL was used to prepare different dilutions in the range of 5-25 µg/mL. The absorbance values for resulting solutions were measured at λ max using respective solvent as blank by UV-visible spectrophotometer.

3.2 Compatibility Study

3.2.1 Physicochemical compatibility study

FTIR studies of Nicardipine Hydrochloride, Nicardipine Hydrochloride +Physical Mixture and Solid dispersion was carried out and shows no interaction between the drug and polymer. FTIR studies of Nicardipine Hydrochloride, Nicardipine Hydrochloride +Physical Mixture and Solid dispersion are shown in Fig 2, 3 and 6 resepectively [7].

3.3 Preparation of Solid dispersion

Drug and Polymer (β-CD) mixtures were dissolved in was weighed in different ratio 1:1,1:2,1:3,1:4 and 1:5 and transferred to mortar and kneaded for 45 min. using alcohol-

water mixture in ratio 1:1, sufficient solvent was added to maintained paste like consistency. The resulting paste was then dried in oven at 50°C for 24 hours. The dried dispersions were grounded in mortar for 2 min and passed through sieve no. 80. The prepared dispersions were stored in glass vials and used for further studies.

Table 2: Composition of Various Solid Dispersions by Kneading Method.

Sr. No	Drug	Polymer	Ratio	Method of Preparation
1	Nicardipine Hydrochloride	β-CD	1:1	Kneading Method
2	Nicardipine Hydrochloride	β-CD	1:2	Kneading Method
3	Nicardipine Hydrochloride	β-CD	1:3	Kneading Method
4	Nicardipine Hydrochloride	β-CD	1:4	Kneading Method
5	Nicardipine Hydrochloride	β-CD	1:5	Kneading Method

3.4 Evaluation of prepared Solid Dispersions

a) Production yield

The production yield formulation was calculated using the weight of final product after drying with respect to the initial total weight of the drug and carrier used for the preparation of complex.

b) Drug content

About 10 mg drug equivalent were weighed accurately and transferred to 100 ml volumetric flask. From this stock solution (100µg/ml), 1 ml was withdrawn and further diluted upto 10 ml with methanol. This solution was used for the assay for drug content by UV spectrophotometer at 239 nm. Concentration of drug in stock solution was calculated by using calibration curve and from which percentage drug content in complex was calculated.

c) Fourier Transform Infrared Spectroscopy

Compatibility study was carried out by using Fourier transform infrared spectrophotometer. FTIR study was carried on pure drug and solid dispersion (SD). SD was prepared, and samples were stored at 400C for 1month. The infrared absorption spectrum of drug and SD of drug was recorded with a KBr disc over the wave number 4000 to 400 cm^{-1} [7, 10].

d) Differential Scanning Calrimetry (DSC)

Thermal analysis was performed using a differential scanning calorimeter equipped with a computerized data station. The sample of pure drug and SD of drug was weighed and heated at a scanning rate of 10 °C/min between 30 °C and 300 °C and 40ml/min of nitrogen flow. DSC analysis gives an idea about the interaction of various materials at different temperatures. It also allows detecting possibility degradation of the material.

e) X Ray Diffraction

For the structural, crystal, and physical state characterization of Nicardipine Hydrochloride, X-Ray diffraction studies were performed for pure drug, Nicardipine Hydrochloride. XRD study was carried out with Bruker AXS D8 Advance with Vertical, Theta/2 geometry using copper target, a voltage of 40 kv and a current of 35 mA. The scanning was done over 2θ range of 3° to 135°.

3.5 Evaluation of Tablets

a) Evaluation for Pre-Compressive Parameters [11-13]

1. Bulk density

Method

The powder blend sample equivalent to 25 g was accurately weighed and filled in a 100 ml graduated cylinder and the powder was leveled and the unsettled volume, Vo was noted. The bulk density was calculated by the formula

Bulk density (ρo) = M/Vo
Where, M = mass of powder taken
Vo = Apparent unstirred volume

2. Tapped density

Method

The weight of powder blend sample equivalent to 25g was filled in 100 ml graduated cylinder. The mechanical tapping of the cylinder was carried out using tapped density tester at a nominal rate of 300 drops per minute for 500 times initially and the tapped volume VO was noted. Tapping was proceeding further for an additional tapping for 750 times and tapped volume Vb was noted. The difference between two tapped volumes was less than 2%, so Vb was considered as a tapped volume Vf. The tapped density was calculated by the formula

Tapped density (ρt) = M / Vf
Where, M = weight of sample powder
Vf = Tapped volume

3. Compressibility Index

Method

The bulk volume and tapped volume was measured and compressibility index was calculated using the formula

Compressibility index =100 (Vo-Vf)/Vo
Where, Vo = Bulk density
Vf = Tapped Density

4. Hausner ratio

Method

Tapped volume and bulk volume were measured and the hausner ratio was calculated using the formula

Hausner ratio = Vo/Vf
Where, Vo = Bulk density
Vf = Tapped density

5. Angle of repose

It can be experimentally determined by allowing the powder to flow through funnel and fall freely onto surface. The height and diameter of resulting cone is measured and using following equation angle of repose is calculated.[8.11]

Tan Θ = h/ r
Where, r = Radius of powder cone
h = Height of powder.

b) Evaluation for Post-Compressive Parameters [13-15]

1. Thickness

For this test, Vernier caliper was used. Three tablets from each batch were used and an average value was calculated.

2. Hardness
Hardness of tablets was determined using Monsanto Hardness Tester. Three tablets from each batch were used and an average value was calculated.

3. Friability
Twenty tablets were weighed and placed in the Roche friabilator. After this the apparatus was rotated at 25 rpm for 4 min (100 times). After revolution the tablets remove any loose dust and weighed. A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 percent is acceptable for most tablets. The friability is given by the formula:

$F = (W_1\text{-}W_0/ W_0) \times 100$
Where, W_1 = Weight of the tablets before the test
W_0 = Weight of the tablets after the test

4. Uniformity of weight
Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of twenty tablets were calculated. The batch passes the test for weight variation if not more than two of the individual weight of tablet deviate from the average weight by more than the %.

5. Disintegration study
Disintegration test was carried out as described under procedure for uncoated tablets in USP. One tablet each was placed in each of six tubes of the basket of the assembly. Apparatus was operated using water, maintained at 37 ± 2^0 c as the immersion fluid.

6. Wetting time
A piece of tissue paper (12 cm × 10.75 cm) folded twice was placed in a Petri dish (10 cm diameter) containing 5 ml of water. A tablet was carefully placed on the surface of the tissue paper and allowed to wet completely. The time required for the water to reach the upper surface of the tablet was noted as the wetting time for that tablet. Three tablets from each batch were used and an average value was as shown in Table 6.

7. Water absorption ratio
A piece of tissue paper folded twice was placed in a small Petri dish (10 cm diameter) containing 6 ml of water. A weighed tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio (R) was calculated using following formula:
$R = 100 (W_a–W_b)/ W_a$
Where, W_a= weight of tablet after water absorption
W_b= weight of tablet before water absorption

8. Drug content
Three tablets were weighed individually and powdered. The blend equivalent to 10 mg of Nicardipine Hydrochloride was weighed and dissolved in phosphate buffer of pH 6.8. The volume was made upto 100 ml with the same solvent. Resultant stock solution was kept for sonication for 10 min. It was then filtered and dilutions were prepared of 100 µg/ml. The drug content was analyzed spectrophotometrically at 239 nm. Each sample was analyzed in triplicate.

9. *In- vitro* drug release
The in-vitro drug release study was performed in the USP Dissolution apparatus type II. Phosphate buffer pH 6.8 was used as dissolution medium. Temperature was maintained at $37^0C \pm 0.5^0C$ and paddle was rotated at the speed of 50 rpm. 10 ml of dissolution medium was withdrawn at the end of each 2 min. Fresh medium was added every time to maintain sink condition. Sample was filtered and absorbance of filtered solution was determined by UV spectroscopy at 239 nm. Dissolution rate was studied for all nine formulations and formulation batch with maximum drug release (F8); at the end of 5 min., was subjected for dissolution in triplicate to check reproducibility in drug release [12].

10. Drug release kinetic study
To study the kinetics of *in vitro* drug release, data was applied to kinetic models such as zero order, first order, Higuchi and Korsmeyer- Peppas.

11. Stability Study [16]
Stability study of optimized formulation was carried out to point out any visual physical or chemical changes made in the formulation after storing it at elevated temperature and humidity conditions. Chemical and physical stability of optimized Nicardipine Hydrochloride formulation was assessed at 40±2 ^{0}c/ 75±5% RH as per ICH Guidelines. Tablets were packed in aluminium foil and stored for 3 months. Samples were analyzed after 3 months for physical appearance, drug content, and *in vitro* dissolution profile.

4. Result and Discussion
4.1 Preformuation Study
The Drug selected Nicardipine Hydrochloride was characterized and analyzed for its physical appearance and solubility, which complies with the monograph as specified in United State Pharmacopoeia. UV and IR spectral analysis was done and the drug shows similar data as mentioned in different official publications. By FTIR analysis of pure Nicardipine showed characteristic peaks at $1521cm^{-1}$,$1490cm^{-1}$, $1347cm^{-1}$, $1271cm^{-1}$, $1204cm^{-1}$, $1734cm^{-1}$, $1409cm^{-1}$, $753cm^{-1}$. These are almost same as reported in the official publications for Nicardipine Hydrochloride. Drug-polymer interaction study by FTIR for pure drug, crospovidone, and Microcrystalline Cellulose showed that there were no significant changes in the position of the characteristic peaks of drug when mixed with superdisintegrants which indicated compatibility of polymers with the drug.

4.2 Characterization of prepared Solid Dispersions
The prepared SD was subjected for solubility study and optimized ratio was evaluated for further characterization.

4.2.1 Production yield
The production yield of Solid dispersion by Kneading method was found to be always in the range of 94.5 to 97.5%. Any loss in yield can be attributed to the product remaining adhered to the walls of the evaporating dish or the mortar which could not be retrieved.

4.2.2 Drug content estimation
Drug content analysis was performed in orders to study the % amount of drug incorporated in the SD. After drug content analysis studies it was found that almost 91.56 to 98.58% of drug was incorporated in the SD indicated uniform dispersion of drug.

4.2.3 Solubility Study

The solid dispersions were subjected for solubility studies to evaluate the effect of carrier (β-CD) and there different ratios on the aqueous solubility of Nicardipine Hydrochloride and results of solubility analysis as shown in table 3.

Table 3: Result of Saturation solubility study of various ratios Solid dispersion

S. No.	Drug	Polymer	Ratio	Solubiity (mg/ml)	Fold increase in solubility
1	Nicardipine Hydrochloride	-	-	0.00247	-
2	Nicardipine Hydrochloride	β –CD	1:1	0.1638	6.7
3	Nicardipine Hydrochloride	β –CD	1:2	0.0301	1.2
4	Nicardipine Hydrochloride	β –CD	1:3	0.083	3.4
5	Nicardipine Hydrochloride	β –CD	1:4	0.1042	4.27
6	Nicardipine Hydrochloride	β –CD	1:5	0.065	2.67

5. Evaluation of tablets

5.1 Precompressional evaluation

Table 4: Evaluation of Powder Blends

Batch No.	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Compressibility index (%)	Hausner's ratio	Angle of repose (ɵ)
F1	0.26±0.014	0.31±0.017	13.93±0.60	1.15±0.014	28.68±0.45
F2	0.25±0.02	0.29±0.01	13.48±0.25	1.15±0.007	30±0.00
F3	0.26±0.015	0.30±0.022	14.09±0.94	1.16±0.015	29.23±1.14
F4	0.27±0.01	0.32±0.017	15.30±0.26	1.17±0.007	29.36±1.14
F5	0.26±0.02	0.32±0.017	14.56±1.03	1.16±0.012	30.1±1.2
F6	0.28±0.007	0.33±0.003	14.43±0.046	1.16±0.00	29.65±2.44
F7	0.26±0.014	0.31±0.017	13.93±1.02	1.15±0.014	28.8±0.62
F8	0.26±0.014	0.31±0.017	13.93±1.02	1.15±0.014	29.66±1.8
F9	0.31±0.017	0.31±0.017	13.23±0.96	1.15±0.014	30.11±0.00

The above results predict that, the Carr's index is in the range of 11-15% which is considered as Good compression property. Angle of repose less than 30° gives the excellent flow property to the powder blend. Similarly, the bulk density and tapped density value was found to be less than one. Hence have good flow property. All these results indicate that, the powder blend possess satisfactory flow and compressibility properties.

5.2 Post compressional evaluation

Table 5: Evaluation of tablets parameter

Batch No.	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Average Weight	Disintegration Time (Sec)
F1	3.09±0.35	2.6±0.25	0.25±0.017	197.9±1.97	50
F2	3.43±0.023	2.8±0.07	0.35±0.015	199.3±2.01	54
F3	3.44±0.018	3.0±0.17	0.56±0.015	198.3±1.45	58
F4	3.44±0.018	3.3±0.15	0.64±0.007	197.8±1.98	42
F5	3.44±0.023	3.2±0.12	0.51±0.01	197.5±1.98	44
F6	3.45±0.022	2.6±0.14	0.55±0.012	198.1±1.65	43
F7	3.44±0.013	2.6±0.22	0.45±0.015	197.7±2.02	37
F8	3.44±0.013	2.6±0.15	0.25±0.014	198.1±1.54	35
F9	3.44±0.02	3.0±0.12	0.45±0.07	198.75±1.68	38

The percentage friability, as depicted in Table no. 2 was in the range of 0.25 – 0.56% to be well within approved range (<1%) which indicates the tablet had good mechanical resistance.

Some other important parameters tested viz Wetting time, Water absorption ratio; content uniformity and In-vitro release are enlisted in following table.

Table 6: Evaluation of Tablets Characteristic

Batch No.	Wetting time(sec)	Water absorption ratio (%)	Drug content (%)	In-vitro Drug release (%)
F1	91.0±2	42.6±0.3	96.13±0.75	76.05±1.84
F2	93.6±1.5	43.1±0.2	95.36±0.66	72.54±0.93
F3	86.6±4.07	42.5±0.17	94.53±0.82	69.12±1.25
F4	87.0±2.5	42.5±0.27	96.36±0.50	81.27±0.21
F5	93.3±1.03	43.6±0.1	97.31±0.33	79.49±1.13
F6	86.0±2.5	43.1±0.4	97.03±0.68	77.76±0.94
F7	90.0±1.2	42.9±0.17	96.32±0.48	95.04±1.13
F8	92.3±1.15	43.4±0.1	98.79±0.34	98.58±1.15
F9	94.0±1.58	42.8±0.2	97.99±0.15	93.33±0.83

Table 7: *In-vitro* % Drug Release of Formulation

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	18.90±0.90	8.55±1.22	6.84±0.90	24.12±0.81	22.42±1.06	22.42±1.71	37.98±1.07	43.11±1.40	36.27±1.19
2	27.54±0.81	17.19±0.94	13.77±2.35	32.72±1.53	31.65±1.53	29.34±2.35	58.77±1.85	69.12±2.38	55.36±1.83
3	55.26±1.40	24.12±0.79	20.61±1.08	48.33±0.89	44.91±0.81	50.04±0.87	74.34±2.24	81.12±1.13	72.54±2.44
4	70.88±1.25	58.33±1.21	50.04±3.43	74.34±1.39	72.54±0.96	69.12±1.25	88.11±1.50	91.62±0.87	86.40±2.35
5	76.05±1.84	72.54±0.93	69.12±1.25	81.27±0.21	79.49±1.13	77.76±0.94	95.04±1.13	98.58±1.15	93.33±0.83

Percent drug release data expressed in Table 7 and Fig. 1 Indicate *In-Vitro* release study was shown 98.58% release of Nicardipine Hydrochloride through F8 formulation in 5 minutes. Formulation F8 showed less disintegration time and percent cumulative drug release 98.58% so it was declared as an optimized formulation and was subjected for further evaluation and stability studies.

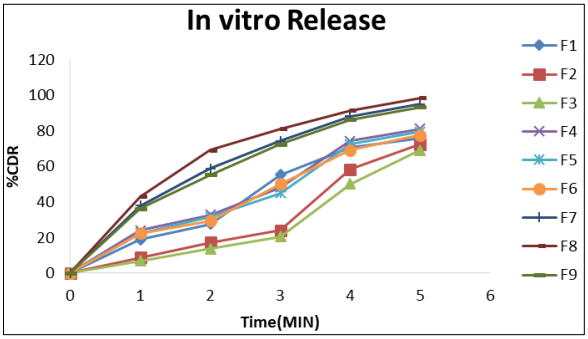

Fig 1: *In-vitro* % Drug Release of Formulation

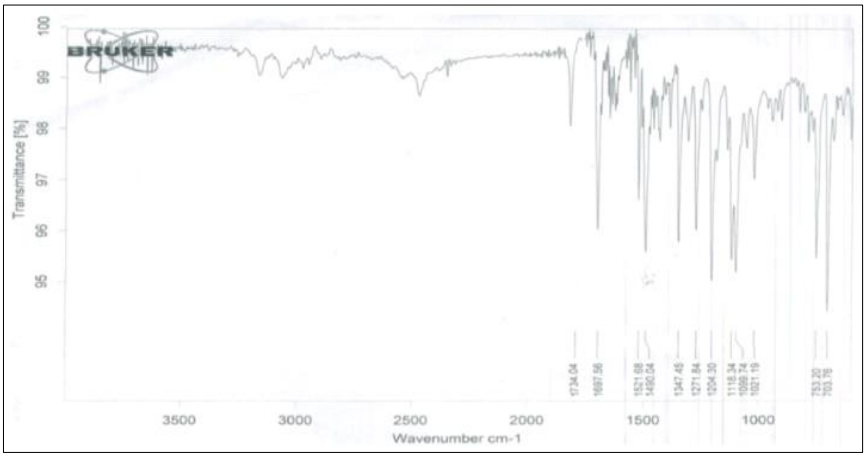

Fig 2: FTIR Spectra of Nicardipine Hydrochloride

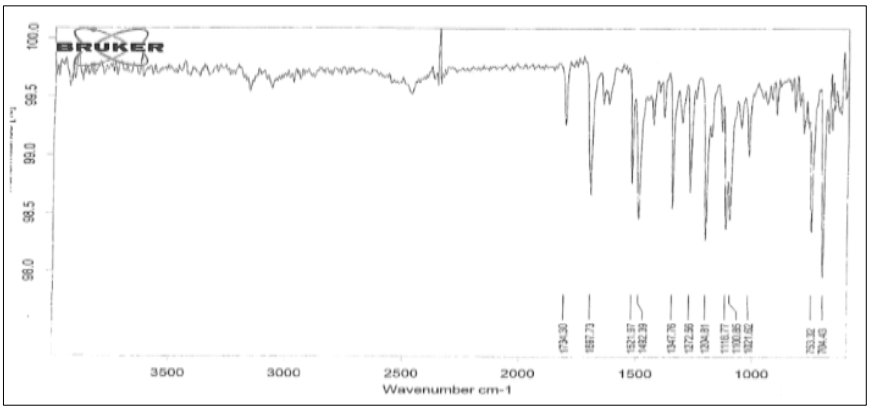

Fig 3: FTIR Spectra of Nicardipine Hydrochloride+ Physical Mixture

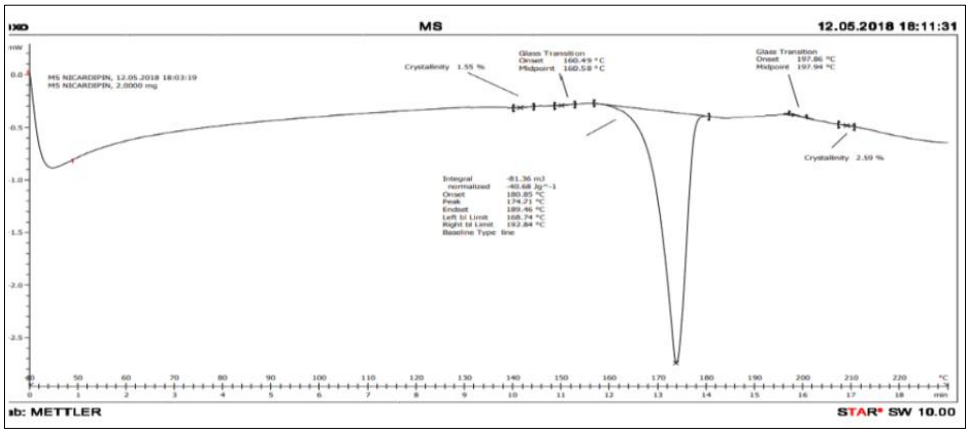

Fig 4: Differential Scanning Calorimetry (DSC) of Nicardipine Hydrochloride

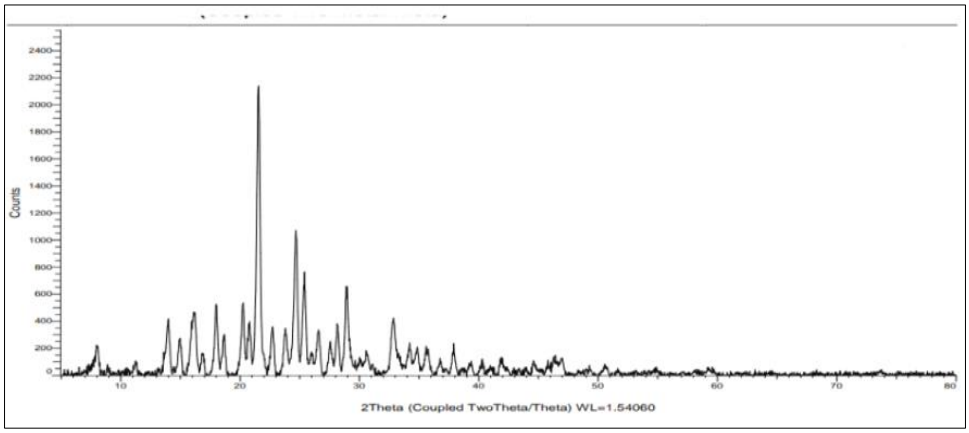

Fig 5: X ray Diffraction of Nicardipine Hydrochloride

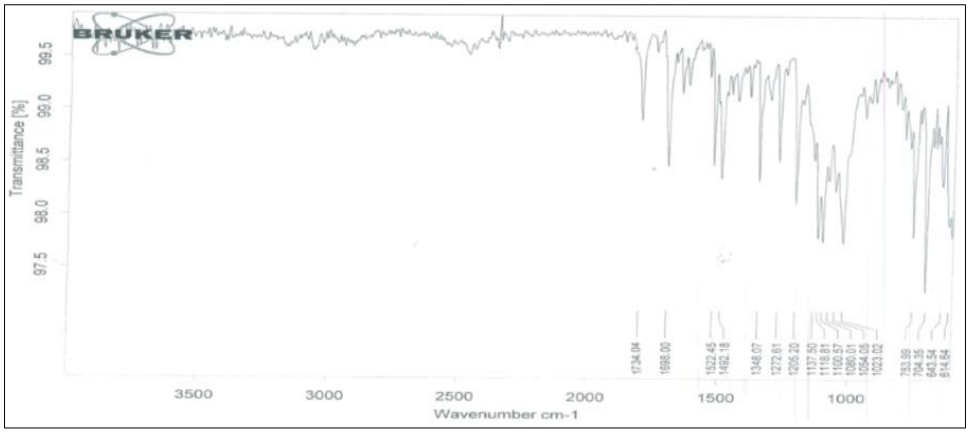

Fig 6: FTIR Spectra of Nicardipine Hydrochloride + β Cyclodextrin

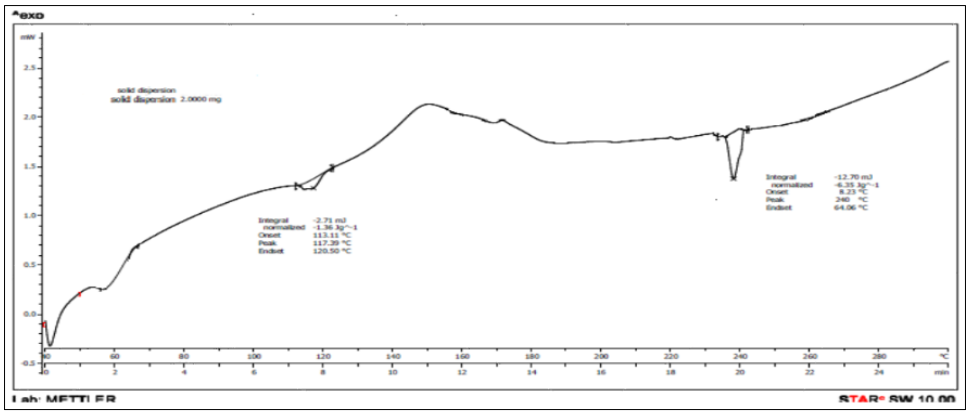

Fig 7: Differential Scanning Colorimetry of Solid Dispersion

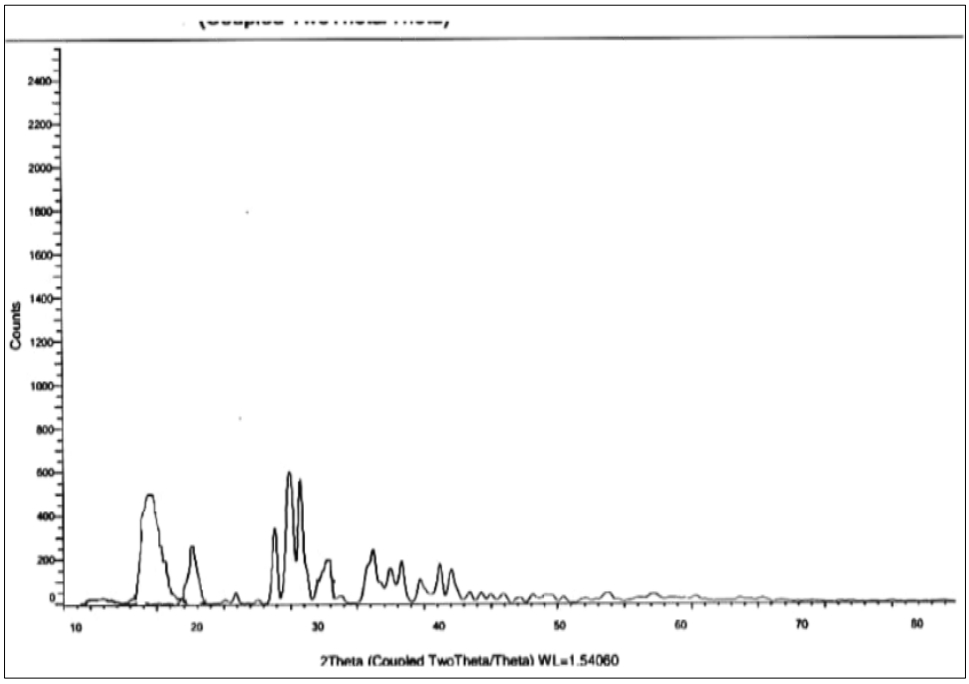

Fig 8: X ray Diffraction of Solid Dispersion

5.3 Dissolution Kinetics

5.3.1 Release kinetics studies

The dissolution kinetics of optimized batch was applied to various dissolution models such as Zero order, First order, Higuchi, Korsemayer- peppas. The best fitted model gives the highest R^2 value and least slope value. Thus, first order model fits best for the dissolution data of the optimized batch as it showed the highest value for R^2 and least slope value.

Table 8: R^2 values and slope values for optimized batch

Sr. No.	Models	R^2 values	Slope values
1	Zero order	0.903	1.931
2	First order	0.934	0.346
3	Higuchi	0.909	46.47
4	Korsemayer-peppas	0.523	1.864

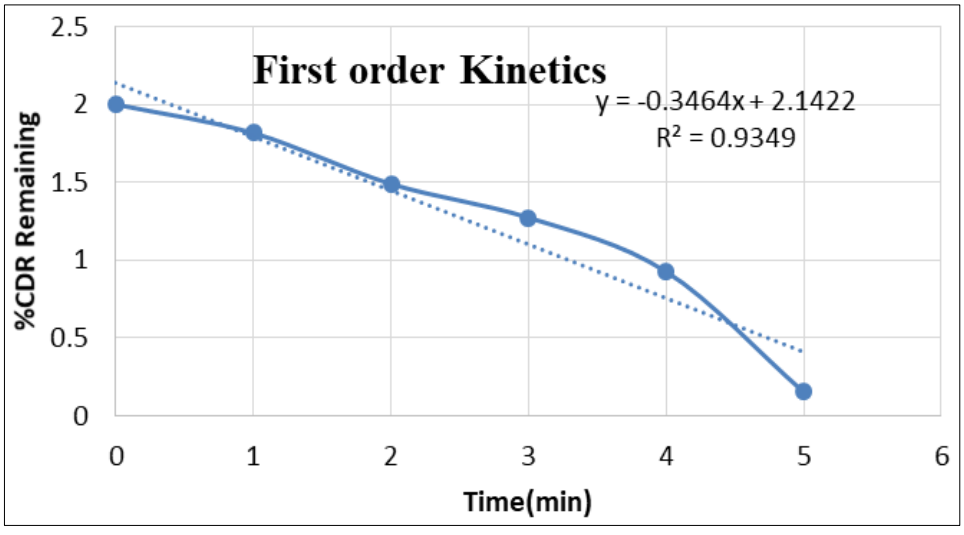

Fig 9: Model Graph for First Order Kinetics

5.4 Optimization Data Analysis

5.4.1 Model assessments for the dependent variables: %CDR in 5 min after putting the data in Design Expert (version 11.0), fit summary applied to data in that, linear model had been suggested by the software so as per this model the equations are as follows.

Final Equation in Terms of Actual Factors:

% CDR = (+82.57-2.03A+11.53B)

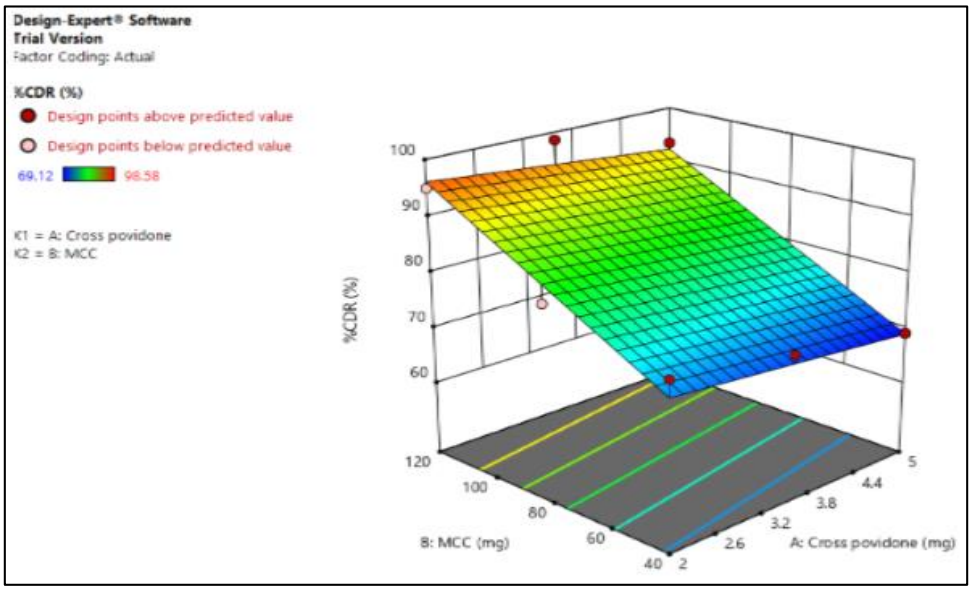

Fig 10: 3D Response curve of % cumulative drug release for 5 min

5.4.2 Model assessment for the dependent variable: DT
After putting the data in Design Expert (version 11.0), fit summary applied to data in that, linear model had been suggested by the software so as per this model the equations are as follows.

Final Equation in Terms of Actual Factors
DT = (+44.56+1.67A-8.67 B)

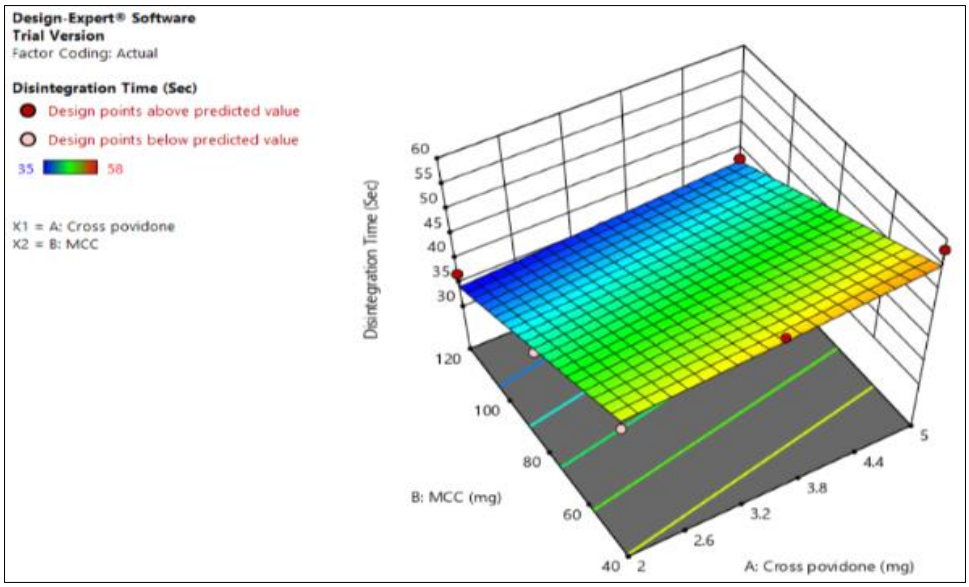

Fig 11: 3D Response curve of Disintegration time

5.5 Stability Study: At the end of 90 days, Accelerated stability studies (AST) was carried out for optimized batch F8 by exposing it to 45 °C/75% RH the tablets was analyzed for Hardness, friability, disintegration time, drug content and % drug release. The results observed are reported in the Table 9.

Table 9: Results of Stability Study

Parameters	Months			
	0	1	2	3
Hardness (kg/cm^2)	2.60	2.62	2.65	2.70
Friability (%)	0.25	0.27	0.24	0.26
Disintegration Time (sec)	35	34	35	37
Drug Content (%)	98.79	98.01	98.81	97.99
% Drug release	98.58	98.61	97.84	98.55

6. Conclusion
In the present research a successful attempt was made to formulate fast dissolving tablets of Nicardipine Hydrochloride by using solid dispersion Technique and compressed by direct compression method to improve solubility, bioavailabity and patient compliance especially for the pediatric and geriatric

patients. Nicardipine Hydrochloride has poor solubility in water. It is a BCS Class II drug. The present study has shown that it is possible to increase the dissolution rate of poorly soluble drug Nicardipine Hydrochloride by preparing it as solid dispersions with carrier β Cyclodextrin. Solid dispersions prepared by Kneading method in the ratio of 1:1 for drug and carrier exhibit rapid dissolution rate when compared with pure drug. Fast dissolving tablets of Nicardipine Hydrochloride prepared by using Crosspovidone superdisintegrant showed rapid dissolution. Based on the study, it may be concluded that Nicardipine Hydrochloride tablets prepared by using solid dispersions with crospovidone as superdisintegrant was found to be ideal for rapid disintegration and for improving dissolution rate, which in turn increased the bioavailability. Crospovidone was the best superdisintegrant showing the shortest disintegration time. Crospovidone quickly wicks saliva to generate the volume of expansion and hydrostatic pressure, this is necessary to provide the rapid disintegration in the mouth. This study indicates the possibility of utilizing the selected best formulation F8 in the preparation of Nicardipine Hydrochloride fast dissolving tablet as a new dosage form for oral administration having increased solubility, improved bioavailability, rapid dissolution and more patient compliance.

7. References

1. Kumar S, Kumar S, Kumar P. A Review on Recent Trends in Oral Drug Delivery –Fast Dissolving Formulation Technology Advances in Biological Research. 2012; 6(1):6-13.
2. Aher SB, Gahide KS. Fast dissolving tablets: Review Study- Advantages and Limitations for Fast Dissolving Tablet Research Journal of Pharmaceutical Dosage form and Technology. 2015; 7(3):215-225.
3. Patil MS, Godse SZ, Saudagar RB. Solubility Enhancement by various Techniques: An Overview World Journal of Pharmacy and Pharmaceutical Sciences. 2015; 2(6):4558-4572.
4. United State Pharmacopoeia 38 National Formulary 33, Global Trusted Standards Improved Health. 3:45-48.
5. Kharat R, Bathe R. A Review on: Nicardipine HCl International Journal of Pharmaceutical Science and Research. 2016; 1(3):33-37.
6. http://www.drugbank.ca/salts/DBSALT000499.17th August, 2017
7. Sharma YR. Elementary Organic Spectroscopy Principles and Chemical Applications. 4th ed. New Delhi: S. Chand and Company Ltd Multicolour Edition, 69-148.
8. Leon Lachman, Herbert A. Liberman The Theory And Practice of Industrial Pharmacy 3rd Edition, Varghese Publication House, 293-308.
9. Aulton Machael E. Aulton's Pharmaceutics, The Design and Manufacture of Medicines 3rd Edition, 2001, 441-472.
10. Pavia DL, Lampman GM, Kriz GS. Introduction to Spectroscopy A Guide for student of organic chemistry. 4th ed. Cennage Learning Pvt. Ltd, 2007, 26-90.
11. Liberman H, Lachman L, Schwartz J. Pharmaceutical Dosage forms: Tablets, 2nd Edition, Churchill Livingstone, 336-360.
12. Sandhyarani GK, Kumar P. Formulation And Evaluation of Fast Dissolving Tablet of Imidapril International Journal Pharmaceutical Science and Research. 2014; 4(3):147-150.
13. The Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare, 7th Edition. The controller of publications, New Delhi. 2014; II:959-961.
14. Bhise SB, Dias RJ, Dhawale SC, Mali KK. Laboratory Manual of Biopharmaceutics and Pharmacokinetics, Trinity Publishing House, 2010, 64-65.
15. Subramanyam S. Biostatistics Career Publications, 1st Edition 2005:145-159.
16. ICH Harmonized Tripartite Guideline, International Conference on Harmonization. Stability testing of new drug substances and products Q1A (R_2) and Evaluation for stability data Q1E. Current step version, 6 February, 2003.