

Preparation and Evaluation of Melt in Mouth Tablets of Nicardipine by Using Liquisolid Technique

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ABSTRACT: This study will be conducting a liquisolid technique to develop melt in mouth tablets of Nicardipine to improve the dissolution and bioavailability of Nicardipine drug. Nicardipine liquisolid melt in mouth tablets was prepared using Avicel pH -102(as carrier), Aerosil-200(as coating) sodium starch glycolate and croscarmellose sodium in different ratios, propylene glycol as liquid medium and other excipients. We tested the ratio of carrier and coating material 10:1, 15:1 and 20:1. The 15:1 gave the best results compared to the others.

With results FTIR analysis shows that the polymer and Nicardipine drug do not interact. XRD diffractogram analysis shows that the diffraction peaks of Avicel pH 102 remains in crystalline state and absence of characteristics peaks of Nicardipine. Liquisolid melt in mouth tablets have acceptable tableting properties. When comparing 1:1, 1:2 and 1:3 ratios of superdisintegrants the 1:1ratio has the best disintegration time. We prepared optimized formulation F4 using SSG: CS (1:1), Avicel pH 102: Aerosil-200(15:1), liquid medication (drug: PG%W/W) by direct compression, we see the shortest disintegration time (23sec), superior cumulative % drug release (99.3%±0.529). In addition, it showed highest R² value of Higuchi's model release kinetic (R²= 0.999) acceptable friability and hardness (3±0.2) so it selected as best formulation.

KEYWORDS: Nicardipine, Liquisolid Technique, Avicel pH-102, Aerosil -200, Propylene glycol.

I. INTRODUCTION

The concept of melt in mouth tablets to improve drug molecule safety & efficacy by developing a convenient dose form for administration & improving better patient's compliance [1]. Melt in mouth tablets results in

quick dissolution & rapid absorption which provide rapid onset of action. The disintegration time for good melt in mouth tablets is beneficial, especially for children, the elderly who have difficulties swallowing conventional tablets & capsules. As well as patients travelling with the little or no access to water [2]. Higher bioavailability, especially for insoluble and hydrophobic medicines, due to fast disintegration and dissolution after tablet [3].

1.1 Challenges in formulation of melt in mouth tablets [4]:

- Mechanical strength & disintegration time: MMTs are designed to have a disintegration time of less than one minute.
- Tastes masking: Many medications have a bitter taste, therefore a bitter drug tablet dissolving/ disintegrating in the mouth will have a significant impact on patient compliance and acceptance of the dosage form.
- Size of tablet: The ease with which you can take medications is determined by their size. The easiest size of pill to swallow is 7-8 mm, whereas the easiest size to handle is one larger than 8 mm, according to research. As a result, finding a tablet size that is both easy to take and easy to hold is tough.
- Amount of drug: The amount of medicine that can be included into each unit dose limits the application of MMT technologies. The weight of an ODT pill should not exceed 500 mg, according to USP guidelines.
- Mouthfeel: In the oral cavity, MMTs should not break into larger particles. The particles produced after the MMTs disintegrate should be as tiny as feasible.
- Good packaging design: The packaging design should be addressed for the protection of

MMTs from moisture and other environmental dangers.

1.2 Benefits of melt in mouth tablets:

- Can be given anywhere, at any time, without the use of water.
- Useful in situations where an ultra-rapid commencement of action is required, such as motion sickness or an allergic response.
- Suitability for geriatrics, paediatric patients with swallowing difficulties, and other groups who may have difficulty using conventional oral dose forms due to mental illness, patients who are uncooperative, on decreased liquid intake regimens, or who are queasy.
- Higher bioavailability, especially for insoluble and hydrophobic medicines, due to fast disintegration and dissolution after tablets.

1.3 Advantages of melt in mouth tablets [5, 6]:

- Easy to provide to patients who are unable to swallow, such as children, the elderly, the bedridden, stroke victims, and institutionalized patients. Melt in mouth dissolving tablets combine the benefits of solid and liquid dose forms.
- When compared to liquids, it's easier to administer and dosing is more precise. Melt pills results in rapid dissolve and absorption, potentially slowing the beginning of effect.
- No water needed.
- Better taste.
- Improved stability.
- Allows high drug loading.
- Cost effective.
- Have acceptable taste & pleasant mouth feeling.

1.4 An overview of liquisolid technique [7]:

- Before preparing melt in mouth tablets an efforts to increase solubility of drug is often needed. Among the various techniques available liquisolid technique is most promising method.
- To enhance solubility & dissolution rate of poorly water soluble drugs. To improve efficiency of tablet manufacturing.
- For poorly flowable powder admixtures. To aid of direct compression.
- The concept of liquisolid compacts can be used to formulate liquid medication such as liquid drug and solutions or suspension of water-insoluble solid drugs in non-volatile vehicles, into acceptably and compressible powder

1.5 Important terms in liquisolid technique:

- Non-volatile solvents.
- Liquid medication.
- Liquisolid system.
- Carrier material (Q).
- Coating material (q).
- Loading factor (Lf).
- Ratio of excipients (R).

1.6 Theory of liquisolid system [8, 9, 10]:

Spireas developed a mathematical approach for the formulation of liquisolid system to calculate the required amounts of powder excipients (carrier & coating material).

$$Lf = W/Q, R = Q/q$$

Mechanism of enhanced drug release from liquisolid system:

- Increased surface area.
- Increased aqueous solubility of drug.
- Improved wetting properties.

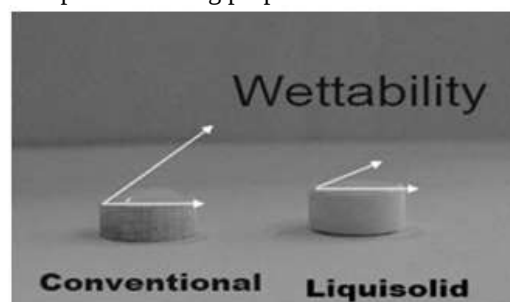


Fig. 1

1.7 Classification of liquisolid technique [11]:

Liquisolid systems can be divided into three groupings based on the sort of liquid medication they include.

- Powdered drug solubility.
- Powdered drug suspension.
- Powdered liquid drugs.

The first two may be produced from the conversion of drug solutions or drug suspension [Nicardipine in PG] & the latter from the formulation of liquid drugs into liquisolid systems.

Liquisolid systems can be divided into two types based on the formulation technique used.

- Liquisolid compacts.
- Liquisolid Microsystem.

Liquisolid compacts are made using a previously developed process for making tablets or capsules, whereas Liquisolid microsystems are based on a new concept that uses a similar technology with the addition of PVP. In the liquid

medication that is mixed with the carrier and coating components to make the admixtures for encapsulation that flow well. Liquisolid compacts have a five-fold advantage over microsystems.

1.8 Liquisolid technology applications [12]:

- Improving solubility and dissolution.
- Effective for solid medicines that are insoluble in water or liquid lipophilic medications.
- Rates of rapid release.
- Designed for tablets with a controlled release designed to deliver water-soluble medications

II. AIMS AND OBJECTIVES

Nicardipine has an extensive hepatic first pass metabolism following oral administration with systemic bioavailability is about 35%. Because of its poor aqueous solubility in biological fluids having pH of 5 to 8, the drug has to be given frequently (30mg, 3 times daily)[13,14]. So, there is a necessity to enhance the dissolution of the drug and convert into melt in mouth tablet to ensure maximum therapeutic utility of the drug. As a result, the current study aims to use liquisolid technology to improve Nicardipine solubility and dissolution characteristics, as well as to make Nicardipine melt in mouth tablets utilizing the direct compression method.

2.1 The specific objectives of the present study are detailed below:

- To study the solubility of drug in different non-volatile solvents.
- To enhance solubility and dissolution of the drug by liquisolid technique.
- To study the Drug polymer compatibility by FTIR Spectroscopy.
- To formulate melt in mouth tablets of Nicardipine by using liquisolid powder blend,

like Propranolol HCL over a long period of time.

- Applications in probiotic.

Nicardipine is potent calcium channel blocker marked vasodilator action. It has antihypertensive properties and is effective in the treatment of angina and coronary spasm without showing cardio depressant effects. It has also been used in the treatment of asthma and enhances the action of specific antineoplastic agents with systemic bioavailability is about 35%.

superdisintegrants and other additives by direct compression method.

- To study the pre-compression and post-compression parameters for prepared tablet formulations.
- The in vitro dissolution studies of the tablets will be studied to derive dissolution profile of the drug.
- Further, Stability of the dosage forms according to ICH guidelines shall be undertaken.

III. MATERIALS AND METHODS

- Drug: Nicardipine.
- Ingredients: Avicel pH 102 (Carrier material), Aerosil 200 (Coating material), Propylene glycol, Polyethylene glycol 400, Tween80 (were used as Solvent system), Croscarmellose sodium and Sodium starch glycolate (Superdisintegrant), magnesium stearate (Lubricant).

3.1 Calibration curve of Nicardipine:

- Solutions of Nicardipine (5,10,15,20,25 µg/ml) was prepared using methanol and absorbance measured using UV-Visible Spectrophotometer (shimadzu 1800) at 237nm [Fig 2].

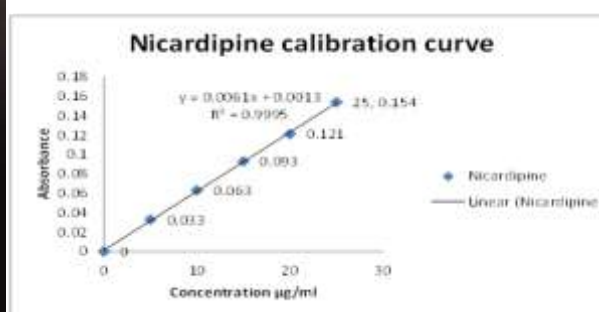
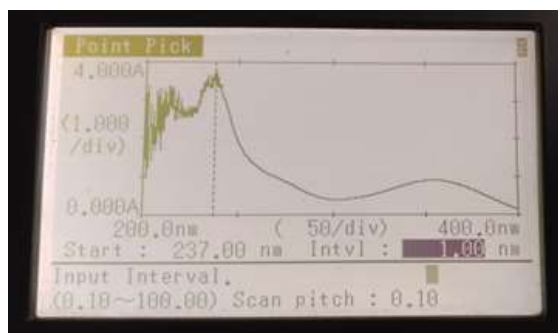


Fig:2 Nicardipine UV- absorbance at 237nm

3.2 Solubility Studies For Selection of Non-Volatile Solvent [15]:

The solubility of the Nicardipine was determined in various non-volatile solvents like PG, PEG-400 and Tween -80 according to the method proposed by Egla M.et.al., triplicate reading were taken and average was calculated [table 3].

3.3 Preparation of liquisolid system of Nicardipine [16]:

Liquisolid formulations were prepared by using drug and carrier –coating powder materials according to mathematical modelling.

Step 1: Nicardipine drug was initially dispersed in non-volatile solvent in porcelain

mortar at an approximate mixing rate of one rotation per second for one minute in order to equally distribute the drug in non-volatile solvent (PG) system termed as liquid vehicle or liquid medication.

Step 2: Then added the calculated quantity (Q) of carrier material (Avicel pH 102) to the above liquid medication by continuously mixing in mortar and was left standing for approximately 10 minutes to allow the drug solution to be absorbed into the carrier material.

Step 3: To the above mixture the calculated quantity (q) of coating material (Aerosil 200) was added with approximate mixing rate one rotation per second for 1 minute.



Fig. 3. Steps involved in the formulation of liquisolid system

3.4 Preparation of Melt in Mouth Tablets of Nicardipine:

To the above liquisolid powder blend different ratio of sodium starch glycolate and croscarmellose sodium as superdisintegrants and mannitol as bulking agents were mixed.

After adding talc as glidant and magnesium stearate as a lubricant to the above

liquisolid powder blend, the prepared powder blend of all the formulations as shown in table no. 1 were evaluated for various rheological properties like percentage yield, tapped density, bulk density, angle of repose, Carr's index and Hausner's ratio and compressed into tablets by direct compression method (PP1D, Rimek RSB-4 mini press, India) by using 8mm diameter, flat punches.

Table: 1. List of ingredients used in formulae of different Melt in mouth tablet of Nicardipine:

INGREDIENTS(mg)		F1	F2	F3	F4	F5	F6	F7	F8	F9
Nicardipine		20	20	20	20	20	20	20	20	20
Propylene glycol		20	20	20	20	20	20	20	20	20
R		10	10	10	15	15	15	20	20	20
Lf		0.270	0.270	0.270	0.261	0.261	0.261	0.258	0.258	0.258
Avicel Ph102		148	148	148	153.2	153.2	153.2	155	155	155
Aerosil 200		14.8	14.8	14.8	10.22	10.22	10.22	7.75	7.75	7.75
Superdisintegrants	1:1	10			10			10		

Sodium starch glycolate : croscarmellose sodium	1:2		10			10			10	
	1:3			10			10			10
Mannitol		8.2	8.2	8.2	7.53	7.53	7.53	8.25	8.25	8.25
Magnesium stearate		2	2	2	2	2	2	2	2	2
Talc		2	2	2	2	2	2	2	2	2
Total weight of tablet		225	225	225	225	225	225	225	225	225

R=excipient ratio; Lf=loading factor

3.5 Evaluation of Prepared Nicardipine Melt in Mouth Tablets:

- Weight variation test: 10 tablets were randomly selected from each formulation and weighed using an electronic balance. The mean SD values were calculated.
- Thickness test: 3 tablets pick randomly from each batch and their thickness was determined using Vernier caliper. The mean SD values were calculated.
- Friability test: The test was performed using Roche friabilator. 5 tablets were randomly weighted and placed in the friabilator. The apparatus was rotated at 25 rpm for 100 revolutions (4min). after revolution the tablets were weighed. The friability was calculated by using following equation.

$$F = (W1 - W0) / W0 \times 100.$$

Where, W1=weight of tablet before test and W0=weight of the tablet after test.

- Hardness test: Hardness indicates the ability of tablet to withstand mechanical shocks while handling. Hardness of tablets was determined using Monsanto Hardness Tester. Three tablets pick randomly from each batch were used and the mean SD values were calculated.
- Drug content uniformity or Assay: From each batch three randomly selected tablets were weighed accurately and powdered in a glass mortar with pestle. Powder equivalent to 20 mg of drug was transferred into 100 ml volumetric flask containing 10 ml of methanol and sonicate for 10 minutes the remaining volume was made up to 100 ml with phosphate buffer pH 7.4. Shake it and filter the solution, make up desired dilutions and analysed for drug content at λ_{max} 237nm, against a blank tablet prepared in the similar manner excluding drug.
- Disintegration time: Disintegration test was performed by using distilled water at 37°C by introducing one tablet into each tube, add a

disc to each tube, suspend assembly in beaker containing specified liquid (6.8PH) and operated for specified time.

- In-vitro drug release dissolution studies: The drug release profile from melt in mouth tablet dosage form was studied using USP 24 dissolution testing apparatus; with the aid of USP type 2 (paddle) apparatus. The tablet was put in the jars containing 900 mL of phosphate buffer pH 7.4 dissolution medium; the medium was stirred at 50 rpm upto 45 minutes. The temperature of the medium was maintained at 37 ± 0.5 °C. Samples of 2 mL were collected at predetermined time intervals for 45 minutes. A drug free tablet was taken as blank. Absorbance was measured at λ_{max} 237 nm and from which percentage of nicardipine was calculated using calibration curve. All the studies were carried out in triplicate, n = 3.
- Kinetic study for drug release: Data was applied to kinetic models such as zero order, first order, Higuchi, and Korsmeyer-Peppas to study in vitro drug release.
- Fourier Transform Infrared Spectroscopy (FTIR): Compatibility study was determined by using FTIR. Fourier Transform Spectroscopy study was carried on pure Nicardipine HCL drug, pure Avicel pH102, Aerosil 200, liquisolid system and F7 formulation.
- Powder X-Ray diffraction: For structural, Physical state characterization of Nicardipine and liquisolid compact, XRD studies were carried out on pure Nicardipine and liquisolid compact.
- Statistics: The in vitro data was subjected to regression analysis by least squares method. The standard deviation was calculated and reported. In vitro data was analysed by ANOVA, a value of $p < 0.05$ was considered to be statically significant.

IV.RESULTS

Table: 2. Melting point determination:

SI NO	MELTING POINT	AVERAGE
1	138 °C	136°C
2	137° C	
3	136 °C	

Table:3.Solubility determination:

NON –VOLATILE SOLVENTS	SOLUBILITY MG/ML
PG	3.9
PEG-400	2.9
Tween-80	2.5

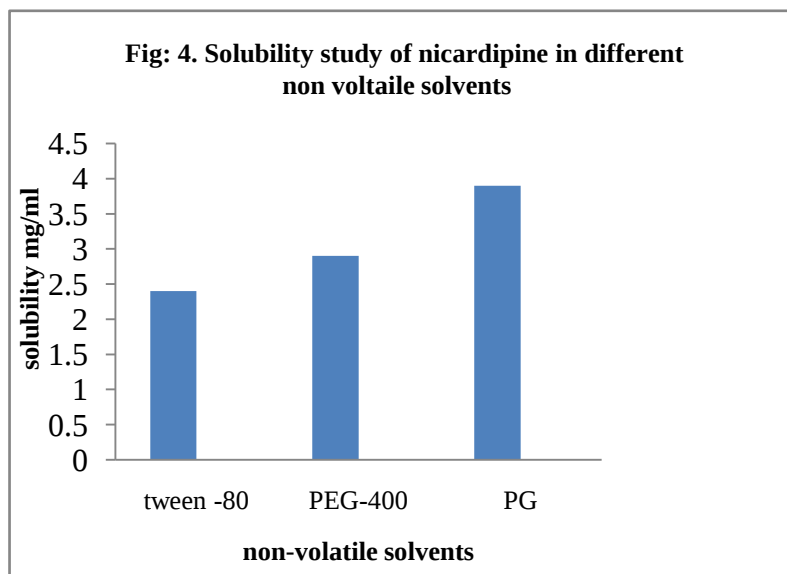


Table: 4. Percentage yield:

BATCHES	F1	F2	F3	F4	F5	F6	F7	F8	F9
Percentage yield	96	97	91	99.9	96	94	98	98	98

Fig. 5. FTIR Spectra of pure Nicardipine:

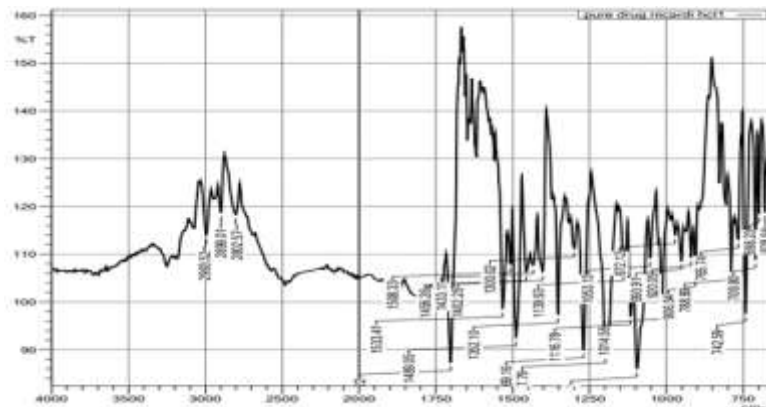


Table: 5. FTIR data of pure Nicardipine:

SI. NO	WAVE NUMBER OBSERVED PEAK IN CM ⁻¹	SUBSTITUTED FUNCTIONAL GROUPS
1	3190	-NH Tertiary amine Stretching
2	2993	Aromatic Stretching
3	2899	Aromatic Stretching
4	1690	-C=O Carbonyl Stretching
5	1489	-NO ₂ Stretching
6	116	-CH ₃ Stretching

Fig. 6. FTIR Spectra of Pure Aerosil-200:

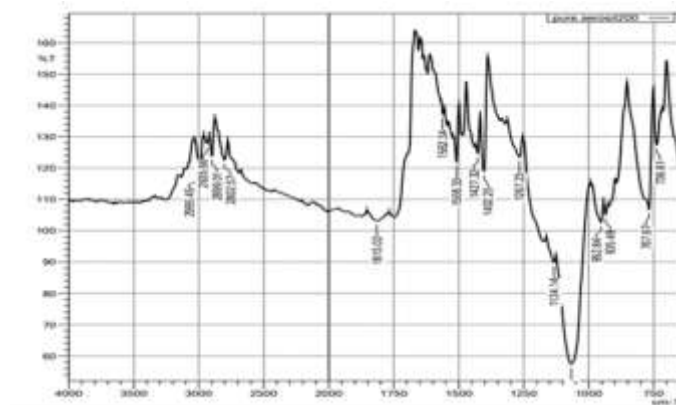


Table: 6. FTIR data of pure Aerosil-200:

SI.NO	WAVE NUMBER OBSERVED PEAK IN CM ⁻¹	SUBSTITUTED FUNCTIONAL GROUPS
1	1815	Carbonyl stretching
2	1267	Si (silicon) stretching

Fig. 7.FTIR data of pure Avicel pH 102:

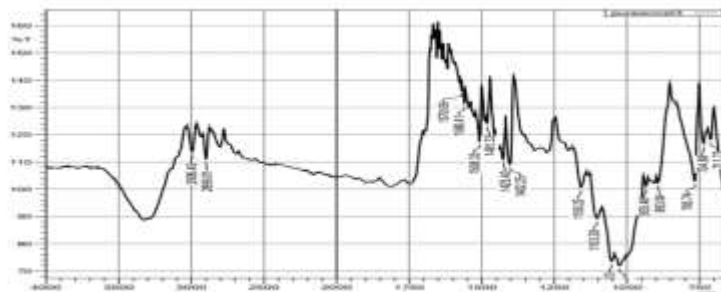


Table: 7. FTIR data of pure Avicel pH 102:

SL.NO	WAVE NUMBER OBSERVED PEAK IN CM ⁻¹	SUBSTITUTED FUNCTIONAL GROUPS
1	3350	-OH Stretching
2	2995	Aliphatic Stretching
3	1560	Carbonyl Stretching

Fig. 8. FTIR Spectra of formulation – 4:

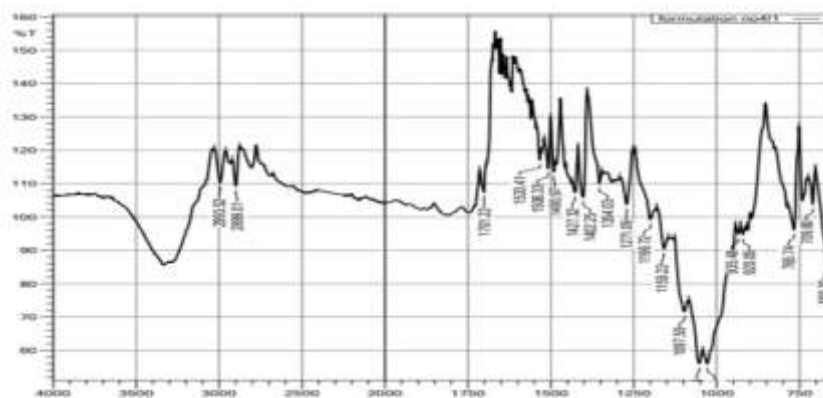


Table: 8.FTIR data of formulation-4:

SL.NO	WAVE NUMBER OBSERVED PEAK IN CM ⁻¹	SUBSTITUTED FUNCTIONAL GROUPS
1	3310	-OH Stretching
2	2993	-N-H Tertiary amine Stretching
3	2899	Aromatic Stretching
4	2800	Aliphatic Stretching
5	1701	-NO ₂ Stretching
6	1533	HO-C=O Carbonyl Stretching
7	1097	CH ₃ Alkane Stretching

Fig: 9. XRD of pure Nicardipine:

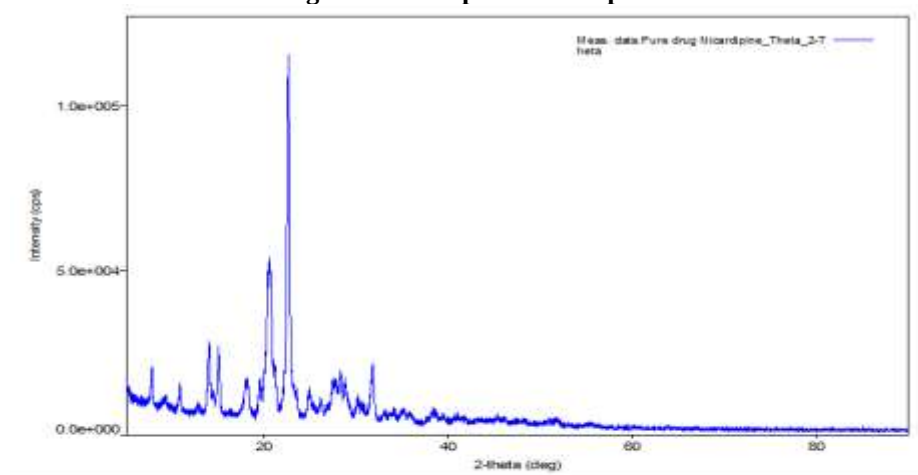


Fig:10. XRD of formulation -4 :

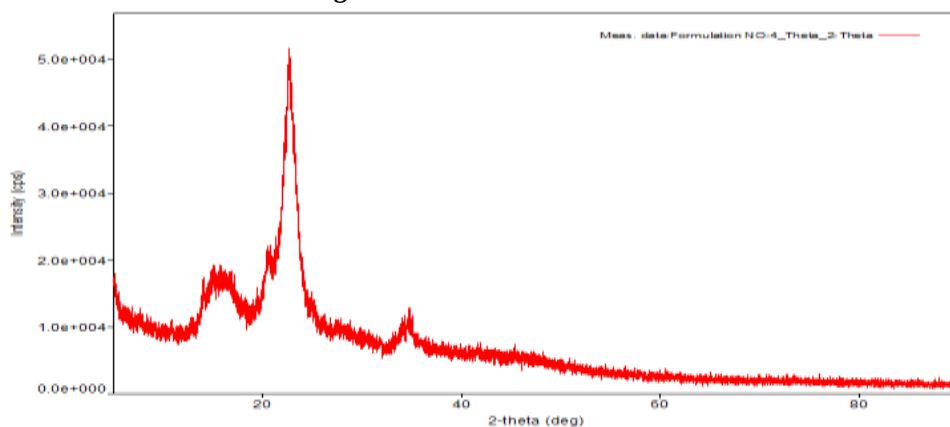


Table: 9. Flow properties:

FORM ULATI ON	TAPPED DENSITY(MG /CM ³) MEAN ± SD	BULK DENSITY(M G/CM ³) MEAN ± SD	CARR'S INDEX (%) MEAN ± SD	HAUSNER 'S RATIO MEAN±SD	ANGLE OF REPOSE(Θ) MEAN±SD
F1	0.324±0.003	0.290±	10.7±0.152	1.12±0.02	23.33±1.52
F2	0.347±0.002	0.301±0.001	13±3	1.15±0.02	25±1
F3	0.313±0.002	0.270±0.007	13.7±0.25	1.15±0.04	24.33±1.48
F4	0.315±0.003	0.292±0.002	7.30±0.513	1.07±0.030	21.3±1
F5	0.321±0.003	0.288±0.020	10.28±1.40	1.11±0.03	23.8±1.59
F6	0.309±0.002	0.275±0.0025	11±4	1.123±0.00	24±3.6
F7	0.317±0.003	0.288±0.003	9±3	1.10±	23±2.203
F8	0.306±0.004	0.267±0.002	12.74±6.2	1.146±0.00	23.2±2.08
F9	0.333±0.003	0.310±0.001	8±2.64	1.09±0.05	24.2±0.9

Post Compression parameters:

Table: 10. Post compression parameters:

FORMULATIONS	FRIABILITY (%) MEAN $\pm$ SD	HARDNESS(KG/CM ²) MEAN $\pm$ SD	THICKNESS (MM)MEAN $\pm$ SD	AVERAGE WEIGHT OF TABLETS(G) MEAN $\pm$ SD
F1	0.943 $\pm$ 0.0051	3 $\pm$ 0.152	3.89 $\pm$ 0.0152	4.074 $\pm$ 0.657
F2	0.943 $\pm$ 0.0051	2.2 $\pm$ 0.0577	3.91 $\pm$ 0.0577	3.437 $\pm$ 10.125
F3	0.943 $\pm$ 0.0051	2.7 $\pm$ 0.251	3.94 $\pm$ 0.01	4.357 $\pm$ 5.744
F4	0.90 $\pm$ 0.005	3 $\pm$ 0.2	3.81 $\pm$ 0.115	4.37 $\pm$ 2.221
F5	0.92 $\pm$ 0.0132	2.5 $\pm$ 0.450	3.93 $\pm$ 0.020	4.361 $\pm$ 2.964
F6	0.943 $\pm$ 0.0057	2.7 $\pm$ 0.264	3.86 $\pm$ 0.03	4.37 $\pm$ 3.117
F7	0.91 $\pm$ 0.0225	3 $\pm$ 0.577	3.87 $\pm$ 0.0611	4.37 $\pm$ 3.733
F8	0.943 $\pm$ 0.00051	2.5 $\pm$ 0.503	3.89 $\pm$ 0.0115	4.361 $\pm$ 3.203
F9	0.91 $\pm$ 0.0190	2.5 $\pm$ 0.0577	3.88 $\pm$ 0.02	4.352 $\pm$ 2.435

Table: 11. Drug content performed using media methanol + Phosphate buffer 7.4 pH :

FORMULATION CODE	DRUG CONTENT (%) MEAN $\pm$ SD
F1	90 $\pm$ 0.281
F2	91 $\pm$ 0.529
F3	95 $\pm$ 1
F4	98 $\pm$ 0.529
F5	95 $\pm$ 0.1
F6	94.5 $\pm$ 0.1
F7	97 $\pm$ 0.2
F8	93 $\pm$ 0.23
F9	93.1 $\pm$ 0.264

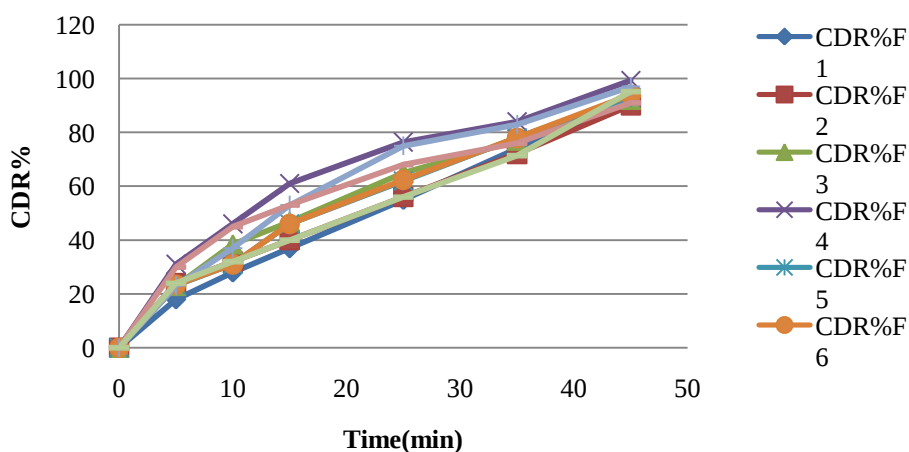
Table: 12 In-vitro Disintegration test:

FORMULATION CODE	DISINTEGRATION TIME (SEC)
F1	29
F2	30
F3	28
F4	23
F5	35
F6	36
F7	27
F8	35
F9	34

Table: 13. In vitro release data of nicardipine drug from the formulation F2 (n=3):

TIME(MIN)	CUMULATIVE %DRUG RELEASE (MEAN $\pm$ SD)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	18 $\pm$ 0.3	24 $\pm$ 2.1	23 $\pm$ 0.75	31 $\pm$ 1.13	23.2 $\pm$ 0.5	23.4 $\pm$ 0.32	23 $\pm$ 0.7	30 $\pm$ 0.87	24 $\pm$ 0.6
10	28 $\pm$ 1.9	32 $\pm$ 1.5	38.42 $\pm$ 1.2	46 $\pm$ 1.77	31 $\pm$ 1.92	31 $\pm$ 0.41	37 $\pm$ 0.49	45 $\pm$ 0.26	32 $\pm$ 4.16
15	37 $\pm$ 1.2	40 $\pm$ 0.7	46.10 $\pm$ 1.5	61 $\pm$ 0.3	46 $\pm$ 1.05	46 $\pm$ 1.56	53 $\pm$ 0.75	53 $\pm$ 0.34	40 $\pm$ 0.2
25	55 $\pm$ 2.4	56 $\pm$ 1.6	65 $\pm$ 2	76.4 $\pm$ 0.88	62 $\pm$ 2	62.4 $\pm$ 0.94	75 $\pm$ 0.41	68 $\pm$ 0.43	56 $\pm$ 0.6
35	74 $\pm$ 1	72 $\pm$ 0.1	77 $\pm$ 1.02	84 $\pm$ 0.69	78 $\pm$ 1.02	78 $\pm$ 2.84	83 $\pm$ 1	76 $\pm$ 0.2	71.4 $\pm$ 0.87
45	92 $\pm$ 0.6	90 $\pm$ 2	92.21 $\pm$ 1.9	99.3 $\pm$ 0.35	93 $\pm$ 1.89	94 $\pm$ 1.19	97 $\pm$ 0.79	91 $\pm$ 0.75	95.2 $\pm$ 0.3

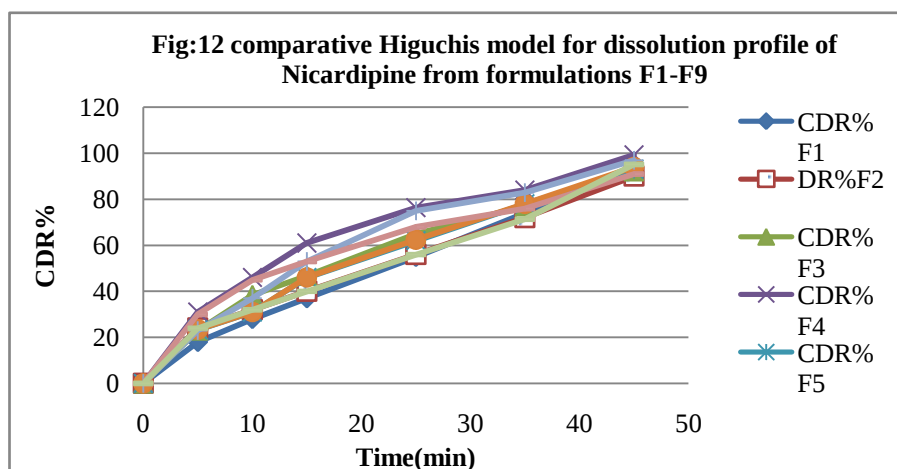
Fig:11.comparative dissolution profile of Nicardipine drug formulations F1-F9



Kinetic study for drug release:

Table: 14. Higuchi's Square root of time data of Nicardipine melt in mouth tablets:

TIME (MIN)	% CUMULATIVE DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	18	24	23	31	16	23.4	23	30	24
10	28	32	38	46	24	31	37	45	32
15	37	40	46	61	40	46	53	53	40
25	55	56	61.4	76.4	63	62.4	75	68	56
35	74	72	77	84	72	78	82	76	71
45	92	90	92	99.3	95	94	93	91	95



Regression coefficient (r^2) values of different kinetic models for Nicardipine melt in mouth tablets:

FORMULATION CODE	ZERO ORDER	FIRST ORDER	HIGUCHI MODEL	PEPPAS MODEL
F1	0.9915	0.619	0.9535	0.9458
F2	0.9725	0.5576	0.9734	0.908
F3	0.9567	0.543	0.9891	0.9088
F4	0.8957	0.4851	0.9994	0.874
F5	0.9828	0.6422	0.945	0.9601
F6	0.9707	0.5665	0.9785	0.9186
F7	0.9232	0.9232	0.9838	0.9453
F8	0.8956	0.8956	0.996	0.977
F9	0.9742	0.9742	0.9591	0.8765

V.DISCUSSION

Nicardipine was characterized by studying its absorbance, melting point and solubility in various non-volatile solvents. Further the liquisolid powder compact was characterized by FTIR and powder XRD. The liquisolid compacts were optimized for the amount carrier coating material was studied. In vitro dissolution studies were conducted in USP type-2 dissolution apparatus. The data was statistically analysed and mechanism of release kinetics was studied. All the studies were conducted at least 3 times and average was computed and tabulated. (n=3).

- The value of absorbance maxima 237 nm obtained during this study corroborates with the literature value 237 nm [17].
- Melting point of nicardipine was found to be 137 °C which was within the range of literature value 138-139 °C [18].
- The solubility of nicardipine was found to be 2.5mg/ml in Tween-80, 2.9 mg/ml in polyethylene glycol and 3.9 mg/ml in propylene glycol.

- The compatibility of nicardipine with Avicel pH 102 and Aerosol 200 was confirmed by FTIR and XRD.
- The FTIR spectra and X-ray diffraction patterns indicated that, no significant interaction between nicardipine and Avicel pH 102 and Aerosol 200 in solid state.
- Bulk density of liquisolid powder blend for all the formulations were in the range 0.267 to 0.310 which was found to be less than one for all formulations.
- Tapped density of liquisolid powder blend for all the formulations were in the range 0.306 to 0.347 which was found to be less than one for all formulations.
- The compressibility index of liquisolid was in the range of 7.3 to 14 which was found to be < 15 % indicating that the powder blend can be compressed into a compact mass of tablet.
- Repose of angle (θ^0) was found to be in the range of 25.530 to 33.500 for all formulations containing talc: magnesium stearate ratio at 2:2.

- As the amount of talc and magnesium stearate was added, Repose of angle (00°) was found to be good indicating free flowability.
- Liquisolid powder blend were compressed in 10 station rotary mini press by using 8 mm flat faced punches.
- Weight of the tablets of all the formulations was found to be in the range of 210 ± 2.128 mg to 241 ± 2.65 mg, which was within the limit of theoretical weight 225 mg of the tablets.
- Hardness of the tablets for all the formulations was found to be in the range 2.2 ± 0.057 kg/cm² and 3 ± 0.2 kg/cm².
- Thicknesses of the tablets for all the formulation were found to be in the range 3.81 ± 0.115 and 3.94 ± 0.01 mm.
- Drug content of all formulations was found to be in the range 16.2 mg to 19.6 mg (90 % to 98 %).
- The Avicel pH 102(carrier) and aerosol 200 (coating) materials were optimized for R value and liquid loading factor.
- In vitro release was studied by using USP-2 type paddle dissolution apparatus in phosphate buffer pH 7.4 at constant temperature of $37 \pm 0.05^\circ\text{C}$ stirred at 50 rpm for a period of 45 minutes. In vitro release data was statistically analysed by ANOVA and a value of $p < 0.05$ was considered as statistically significant. Also regression analysis by least squares method (r) was performed on the raw data to assess the linearity of the curve.
- According to Higuchi's model equation the tablet formulations F1 to F9 were found to be following fickian diffusion.
- The study has indicated that, melt in mouth tablets of Nicardipine using liquisolid technique can be tailored to release nicardipine by Higuchi's model release kinetics. Thus, study of pre-compression and compression characteristics and in vitro release studies concluded the objectives of the investigation.

VI. CONCLUSION

The overall study it was concluded that formulation F4 using SSG: CS (1:1), Avicel pH 102: Aerosil-200(15:1), Liquid medication (Drug: PG 20%W/W) explained superior disintegration time and dissolution rate. The loading factor 0.261 demonstrated the best release in preparation of Nicardipine liquisolid melt-in-mouth tablets. This may be attributed to the high Avicel pH 102 concentration where Avicel pH 102 functions as swellable disintegrant; In addition, the hydrophilic

characteristics of Avicel pH 102 could increase the wetting of nicardipine and enhance its dissolution.

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