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Review Article

# PREPARATION AND EVALUATION OF NILVADIPNE LIQUISOLID COMPACTS

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**ABSTRACT**

The purpose of the present study is to develop a novel liquid solid technique which enhances the dissolution rate of water insoluble or poorly water soluble drugs of Nilvadipine, which belong to class II of BCS. Generally the liquisolid technique is based upon the admixture of drug loaded with non volatile solutions (or) liquid drug incorporated with required carrier and coating materials in order to obtain a dry, non adherent, free flowing and compressible powder. Various non volatile solvents used were Propylene glycol, Poly ethylene glycol. The solubility of drug in the non volatile solvents plays an important role in this formulation Avicel PH 102 and aerosil were used as carrier and coating materials. Super disintegrants were used to increase the dissolution rate.Evaluation tests such as Disintegration time, Friability, Hardness and in-vitro dissolution studies were conducted. Amongst all the formulations F14 was considered to be the best in which Propylene glycol is used and the drug release was found to be 97% in 10 min.

**Keywords:** Nilvadipine, PEG, PG, Avicel PH 102, Aerosil, Super disintegrants.

## INTRODUCTION

Solubility is the major challenge in the pharmaceutical industry for the development of new pharmaceutical products. Poor dissolution characteristics of water insoluble drugs are a major challenge for pharmaceutical scientists. It is well known that the active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastro intestinal tract[1].Several studies with poorly soluble drugs have demonstrated that particle size reduction to the sub micron range can lead to an increase in dissolution rate and higher bio availability. Poorly water soluble drugs belong to BCS class II and IV[2]group of compounds.

There are several techniques for enhancing solubility rate of poorly water soluble drugs:

Some techniques are:

1) Solid Dispersion[3]
2) Particle size reduction by micronization[4]
3) Hot melt method (Fusion method)
4) Solvent Evaporation[5]
5) Complexation[6]
6) Eutectic Mixtures[7]
7) Nano systems[8]
8) High pressure homogenization
9) Cryogenic technique
10) Super critical fluid[9]
11) Ultra rapid freezing[10]

These are some of the techniques which are generally used to reduce the particle size and increase the solubility. Nilvadipine acts a calcium channel blocker &anti hypertensive agent. Nilvadipine inhibits the influx of extracellular calcium through myocardial and vascular membrane pores by physically plugging the channel. The decrease in intracellular calcium inhibits the contractile processes of smooth muscle cells, causing dilation of the coronary and systemic arteries, increased oxygen delivery to the myocardial tissue, decreased total peripheral resistance, decreased systemic blood pressure, and decreased after load.The rate of oral absorption is often controlled by the dissolution rate in the GI tract.

## MATERIALS AND METHODS

Nilvadipine was obtained from TCI Chemicals, Chennai, India. MCC, PEG and PG was obtained from SD fine chemicals Mumbai, India. Aerosil was obtained from Fischer Scientific pvt ltd. Super disintegrants like crospovidone, croscarmellose, sodium starch glycolate were bought from Yarrow chemicals Mumbai, India.

### Solubility studies

In order to select the best and compatible non volatile solvent, solubility studies[11] were performed by dissolving the minimum dose of drug 4 mg in 0.1, 0.2, 0.3,.. ml of the non volatile solvents like PEG,PG & tween 80 and subjected for solubility. The solvent which utilizes the less amount of liquid to dissolve the drug is selected as the best solvent. In this present study PEG & PG utilized minimum quantities of the solvents to dissolve the drug.

### Preparation of Liqui-solid Tablets [12]

### Preparation of Liquid Medication

From the results of solubility studies, various types of non-volatile solvents are chosen for dissolving the drug. AvicelpH 102 as carrier and Aerosil as the coating material[13] is selected for the preparation of liquisolid compacts. Various ratios of carrier to coating materials are selected. Based on solubility of Nilvadipine desired quantities of drug and a non-volatile solvents were accurately weighed in a beaker and then stirred continuously, until a homogenous drug solution/suspension was obtained. Selected amounts (W) of the resultant liquid medication were incorporated into calculated quantities of carrier contained in a mortar.

### Mixing

The mixing procedure was conducted in three stages. During the first stage, the system was subjected to sonication for approximately one minute in order to evenly distribute the drug with the non-volatile liquid. In the second stage, calculated quantities of carrier material was added to the liquid medicament and evenly spread as a uniform layer on the surfaces of the mortar and left standing for approximately 5min to allow the drug solution to be absorbed in interior of the powder particles. In the third stage, the coating material was added and triturated. After triturating calculated quantity of super-disintegrant was added and mixed together, producing the final liquisolid formulation for compression.

### Preparation of Nilvadipine conventional tablets

Nilvadipine conventional tablets were produced by mixing the drug with microcrystalline cellulose, silica for a period of 10 min in a mortar. The mixture was mixed with disintegrant for 10 min. The mixture was compressed into tablets using a tablet press. Sufficient

compression load was applied in order to produce tablets with sufficient hardness. This formulation was denoted as directly compressed tablets.

**CALCULATION OF LIQUID LOADING FACTOR [14]**

Loading factor is calculated by dissolving the drug in the suitable non volatile solvents. Such liquid medication is incorporated to the carrier and coating materials and blended. Using the equation Lf = W/Q, the drug loading factors are determined and also used for calculating the amounts of carrier and coating materials in each formulation. Excipient ratio {R}: Defined as carrier to coating ratio quoted as:

$$R=Q/q$$

Q = Carrier material,

q = Coating material.

Liquid loading factor($L_f$): Defined as weight of liquid medicament (W) to weight of carrier (Q).

$$L_f = W/Q$$

$$Q = W/L_f$$

$$L_f = \Phi_{CA}+\Phi_{CO}.1/R$$

$$Lf= \Psi + \psi. 1/R$$

R is the ratio between the quantities of carrier (Q) and coating materials (q) present in the formulation.

The Φ – value of a powder represents the maximum amount of a given non volatile liquid that can be retained inside its bulk [w/w] while maintaining acceptable flowability.

The ψ – number of a powder is defined as the maximum amount of liquid the powder can retain inside its bulk [w/w] while maintaining acceptable compact-ability resulting in compacts of sufficient hardness with no liquid leaking out during compression.

**Pre Compression Studies**

**Characterization of powder mixture**

The quality of tablet, once formulated by rule is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced.

**Angle of Repose [15]**

The frictional force of a loose powder can be measured by the angle of repose (θ). It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles produces a surface angle θ, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured.

**Table 1: Examples of liqui-solid formulation parameters of various powder excipients with commonly used liquid vehicles.**

| Powder Excipient or system | Propylene Glycol Φ value | PEG 400 Φ value | Propylene Glycol Ψnumber | PEG 400 Ψnumber |
|---|---|---|---|---|
| Avicel pH 102 | 0.16 | 0.005 | 0.224 | 0.242 |
| Avicel pH 200 | 0.26 | 0.02 | 0.209 | 0.232 |
| Cab o sil | 3.31 | 3.26 | 0.560 | 0.653 |
| With Avicel pH102 | | | | |
| Cab o sil with Avicel pH 200 | 2.57 | 2.44 | 0.712 | 0.717 |

**Table 2: Formulation of liquisolid compacts**

| Formulation code | Lf | R (Value) | PEG | PG | Avicel (mg) | Aerosil (mg) | CP (mg) | Ccs (mg) | Ssg (mg) | Drug (mg) | Mg. Stearate(mg) | Total Weight (mg) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **F1** | 1.635 | 2 | 229 | - | 140.06 | 70.03 | - | - | - | 4 | 6.71 | 445.7 |
| **F2** | 1.635 | 2 | 229 | - | 140.06 | 70.03 | 8.78 | - | - | 4 | 6.71 | 454.5 |
| **F3** | 1.635 | 2 | 229 | - | 140.06 | 70.03 | - | 8.78 | - | 4 | 6.71 | 454.5 |
| **F4** | 1.635 | 2 | 229 | - | 140.06 | 70.03 | - | - | 8.78 | 4 | 6.71 | 454.5 |
| **F5** | 1.088 | 3 | 229 | - | 210.47 | 70.15 | - | - | - | 4 | 7.7 | 515.9 |
| **F6** | 1.088 | 3 | 229 | - | 210.47 | 70.15 | 10.1 | - | - | 4 | 7.7 | 526 |
| **F7** | 1.088 | 3 | 229 | - | 210.47 | 70.15 | - | 10.1 | - | 4 | 7.7 | 526 |
| **F8** | 1.088 | 3 | 229 | - | 210.47 | 70.15 | - | - | 10.1 | 4 | 7.7 | 526 |
| **F9** | 1.815 | 2 | - | 107.5 | 59.22 | 29.61 | - | - | - | 4 | 3.01 | 200.07 |
| **F10** | 1.815 | 2 | - | 107.5 | 59.22 | 29.61 | 3.93 | - | - | 4 | 3.01 | 204 |
| **F11** | 1.815 | 2 | - | 107.5 | 59.22 | 29.61 | - | 3.93 | - | 4 | 3.01 | 204 |
| **F12** | 1.815 | 2 | - | 107.5 | 59.22 | 29.61 | - | - | 3.93 | 4 | 3.01 | 204 |
| **F13** | 1.263 | 3 | - | 107.5 | 85.11 | 28.37 | - | - | - | 4 | 3.37 | 223.5 |
| **F14** | 1.263 | 3 | - | 107.5 | 85.11 | 28.37 | 4.41 | - | - | 4 | 3.37 | 228 |
| **F15** | 1.263 | 3 | - | 107.5 | 85.11 | 28.37 | - | 4.41 | - | 4 | 3.37 | 228 |
| **F16** | 1.263 | 3 | - | 107.5 | 85.11 | 28.37 | - | - | 4.41 | 4 | 3.37 | 228 |

The angle of repose (θ) was calculated using the following formula:

**Tan θ = h/r**

Where; θ = Angle of repose

h = Height of the cone in cms

r = Radius of the cone base in cms

**Bulk Density [15]**

Density is defined as weight per unit volume. Bulk density ($D_b$), is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm$^3$.

The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together.

Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.

The loose bulk density and tapped density were determined by using bulk density apparatus. Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume ($V_b$) and weight of the powder (M) was determined. The bulk density was calculated using the formula.

$D_b = M/V_b$

Where, M is the mass of powder, $V_b$is bulk volume of powder

**Tapped Density [16]**

The measuring cylinder containingknown mass of blend was tapped for a fixed time. The minimum volume ($V_t$) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the formula.

$D_t = M/V_t$

Where, M is the mass of powder, $V_t$is the tapped volume of powder

**Carr's Index (%) [17]**

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it measures the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant and the bulk and tapped densities will be closer in value.

For poor flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

CI (%) = [(Tapped density – Bulk density) / Tapped density] x100

The value below 15% indicates a powder which usually gives rise to good flow characteristics, where as above 25% indicates poor flowability, 1-10 showing excellent flow properties, 11-15 showing good flow properties 16-20 showing fair to passable, 21-25 showing passable.

**Table 3: Compressibility index**

| S. No. | Compressibility index | Flow |
|---|---|---|
| 1 | 5-12 | Free flow |
| 2 | 12-16 | Good flow |
| 3 | 18-21 | Fair |
| 4 | 23-25 | Poor |
| 5 | 33-38 | Verypoor |
| 6 | >40 | Extremelypoor |

**Hausner's Ratio [17]**

Hausner's ratio is an indirect index ease of powder flow. It is calculated by the following formula.

Hausner's Ratio=Tapped density ($\rho_t$) / Bulk density ($\rho_b$)

Where $\rho_t$ is the tapped density and $\rho_b$ is the bulk density.

**Table 4: Hausner' ratio**

| S. No. | Hausner' ratio | Flow |
|---|---|---|
| 1 | 1-1.11 | Free flowing |
| 2 | 1.12-1.18 | Good |
| 3 | 1.19-1.25 | Fair |
| 4 | 1.26-1.34 | Passable |
| 5 | 1.35-1.60 | Poor |

**FT-IR Studies**

The Compatibility studies were performed using FT-IR spectrophotometer. The FTIR spectrum of pure drug and physical mixture of drug and different excipients were studied. Drug-excipient interactions play a vital role with respect to release of drug from the formulation amongst others.

FT-IR techniques have been used here to study the physical and chemical interaction between drug and excipients used. In the present study, it has been observed that there is no chemical interaction between drug and the excipients used. It wasobserved that there were no changes in these main peaks in FT-IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and excipients. The peaks obtained in the spectra's of each excipients correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components.

**POST COMPRESSION PARAMETERS**

**Physicochemical characterization of tablets**

The designed liquisolid tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

**Weight Variation [17]**

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method for determining the drug content uniformity. The percentage deviation was calculated using the following formula.

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

**Tablet hardness [18];** Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined by using Monsanto hardness tester and the average is calculated and presented with standard deviation.

**Tablet thickness [18]:** Tablet thickness is an important characteristic in reproducing appearance. Six tablets were taken and their thickness was recorded using screw gauge. The average thickness is calculated and presented with standard deviation.

**Friability [17]:** It is to measure the mechanical strength of tablets. Roche friabilator (Electrolab, Mumbai, India) was used to determine the friability by following procedure. Preweighed tablets (10 tablets) were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re-weighed andloss in the weight of tablets is measured and is expressed in percentage as,

**% Friability = $[(W_1 - W_2) / W_1] \times 100$**

Where, $W_1$ = Initial weight of 20 tablets

$W_2$ = Weight of the 20 tablets after testing

**Determination of drug content [17]**

Ten tablets from each formulation were taken, crushed and mixed. From the mixture 100 mg of Nilvadipine equivalent of 1 tablet weight was extracted thoroughly with 100 ml of 1.2 pH phosphate buffer.

The amount of drug present in each extract was determined using UV spectrophotometer at 264nm. This procedure was repeated thrice and the average was taken.

**Table 5: Pharmacopoeial specifications for tablet weight variation**

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

**Disintegration Test [19]**

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 10 minutes and the basket was lifted from the fluid, and observed whether all the tablets have disintegrated.

**Dissolution Test of NilvadipineLiquisolid Tablets [18], [19]**

The in-vitro dissolution study was conducted as per the United States Pharmacopoeia (USP). The rotating paddle method was used to study the drug release from the tablets. The dissolution medium consisted of 900 ml of phosphate buffer (1.2pH). The release was performed at $37^0C \pm 0.5^0C$, at a rotation of speed of 50 rpm. 5 ml samples were withdrawn at predetermined time intervals (2,4,6,....32 mins) and the volume was replaced with fresh medium.

The samples were filtered through whatman filter paper and analyzed for Nilvadipine after appropriate dilution by UV spectrophotometer at 264 nm. The % drug release was calculated using the calibration curve of the drug in phosphate buffer 1.2 pH

**Table 6: Evaluation of Pre compression parameters**

| Batch code | Bulk density ($gm/cm^3$) | Tapped density ($gm/cm^3$) | Carr's index (%) | Hausner's ratio | Angle of repose |
|---|---|---|---|---|---|
| F1 | 0.336±0.003 | 0.394±0.012 | 14.81±0.65 | 1.17±0.021 | 29.3±1.04 |
| F2 | 0.292±0.002 | 0.363±0.011 | 19.35±0.37 | 1.24±0.012 | 30.9±0.93 |
| F3 | 0.313±0.007 | 0.378±0.009 | 17.24±0.98 | 1.20±0.039 | 27.1±0.48 |
| F4 | 0.324±0.004 | 0.412±0.008 | 21.42±0.49 | 1.27±0.093 | 32.5±1.06 |
| F5 | 0.318±0.002 | 0.404±0.018 | 21.21±1.02 | 1.26±0.062 | 32.9±1.25 |
| F6 | 0.362±0.006 | 0.438±0.006 | 17.24±0.93 | 1.20±0.038 | 30.9±0.99 |
| F7 | 0.389±0.002 | 0.478±0.004 | 18.5± 10.83 | 1.22±0.075 | 27.8±0.83 |
| F8 | 0.375±0.003 | 0.438±0.012 | 14.20±1.14 | 1.16±0.05 | 28.7±0.45 |
| F9 | 0.340±0.006 | 0.453±0.011 | 25±0.92 | 1.33±0.093 | 29.5±0.56 |
| F10 | 0.313±0.005 | 0.408±0.008 | 23±0.46 | 1.30±0.039 | 28.2±1.34 |
| F11 | 0.370±0.005 | 0.510±0.009 | 27.27±0.69 | 1.37±0.013 | 32.6±0.57 |
| F12 | 0.340±0.008 | 0.453±0.014 | 25±0.73 | 1.33±0.041 | 28.9±0.82 |
| F13 | 0.383±0.006 | 0.511±0.007 | 26.42±0.80 | 1.33±0.053 | 26.8±1.15 |
| F14 | 0.353±0.003 | 0.460±0.017 | 23.07±1.09 | 1.30±0.066 | 27.5±1.07 |
| F15 | 0.418±0.003 | 0.511±0.015 | 18.18±0.61 | 1.22±0.011 | 31.4±0.075 |
| F16 | 0.383±0.002 | 0.460±0.009 | 17.21±0.78 | 1.20±0.039 | 26.97±0.69 |

**Table 7: Evaluation of post-compressional parameters**

| Formulation code | Weight Variation(mg) | Hardness ($Kg/cm^2$) | Friability (%) |
|---|---|---|---|
| F1 | 448.71±1.15 | 3.8±0.15 | 0.48 |
| F2 | 455.57±1.09 | 4.1±0.13 | 0.29 |
| F3 | 454.55±1.10 | 3.9±.17 | 0.15 |
| F4 | 454.92±1.08 | 4.0±0.19 | 0.19 |
| F5 | 526.14±1.90 | 4.3±0.24 | 0.23 |
| F6 | 519.65±1.76 | 4.2±0.152 | 0.26 |
| F7 | 527.33±1.85 | 3.7±0.161 | 0.15 |
| F8 | 528.36±1.95 | 4.3±0.164 | 0.34 |
| F9 | 204.43±1.25 | 3.9±0.172 | 0.58 |
| F10 | 203.52±1.19 | 4.0±0.098 | 0.47 |
| F11 | 206.11±1.28 | 3.8±0.103 | 0.20 |
| F12 | 205.55±1.08 | 4.3±0.091 | 0,45 |
| F13 | 226.41±1.27 | 3.7±0.087 | 0.30 |
| F14 | 230.08±2.15 | 3.8±0.16 | 0.44 |
| F15 | 232.02±1.93 | 3.9±0.175 | 0.34 |
| F16 | 229.50±2.07 | 4.2±0.194 | 0.47 |

**Table 8: Evaluation of pre-compressional parameters**

| Formulation code | Thickness (mm) | Drug content (%) | Disintegration(min) |
|---|---|---|---|
| F1 | 4.14±0.032 | 95.8±1.174 | 0.94±0.045 |
| F2 | 4.07±0.012 | 92.1±1.147 | 1.60±0.025 |
| F3 | 4.01±0.041 | 90.3±1.126 | 2.10±0.283 |
| F4 | 4.09±0.025 | 88.5±1.331 | 3.25±0.356 |
| F5 | 4.56±0.036 | 93.9±1.296 | 2.45±0.312 |
| F6 | 4.43±0.028 | 87.5±1.103 | 3.10±0.296 |
| F7 | 4.48±0.032 | 88.3±1.112 | 4.15±0.217 |
| F8 | 4.49±0.035 | 84.5±2.095 | 3.26±0.237 |
| F9 | 3.03±0.009 | 85.6±1.961 | 1.55±0.103 |
| F10 | 3.27±0.015 | 89.0±1.984 | 0.85±0.039 |
| F11 | 3.23±0.012 | 91.9±1.543 | 4.13±0.236 |
| F12 | 3.14±0.017 | 96.1±1.178 | 1.29±0.074 |
| F13 | 3.65±0.016 | 98.2±1.098 | 2.50±0.307 |
| F14 | 3.76±0.023 | 92.5±1.103 | 3.19±0.274 |
| F15 | 3.69±0.022 | 93.7±1.109 | 2.36±0.283 |
| F16 | 3.78±0.034 | 88.3±1.431 | 3.35±0.257 |

### *In Vitro* drug release studies

*In Vitro* drug release experiments were performed at 37±0.5$^0$C in U.S.P II dissolution apparatus. The results showed that all the formulations release the drug within 2 to 32 min. All the 16 formulations of Nilvadipine Liquid Solid Compacts are subjected to dissolution studies. Dissolution was carried out at 50 rpm in the volume of 900ml dissolution media (1.2pH Phosphate Buffer) for 32 min. For all the F1 to F16 formulations done by wet granulation method by using Avicel used as carrier material and Aerosol used as coating material. The highly hydrophilic characteristic of Avicel could increase the wetting of drug and enhance its dissolution.

In the prescribed dissolution data F1, F5, F9, F13 are the formulations done without using super-disintegrants in which only the carrier and coating materials were used and the time taken for the percentage drug release was more when compared to that of formulations done by using super-disintegrants.

Whereas, F2, F6, F10, F14 are the formulations done by using crospovidone as super-disintegrants. In similar way F3, F7, F11, F15 are done by using croscaramellose.F4, F8, F12, F16 are done by using sodium starch glycolate.

By using crospovidone the time taken for the % drug release was very less when compared to that of croscarmellose and sodium starch glycolate. Out of the all three super disintegrants sodium starch glycolate took more time to release the maximum amount of drug this is because of poor surface area when compared to crospovidone, which has high interfacial activity.

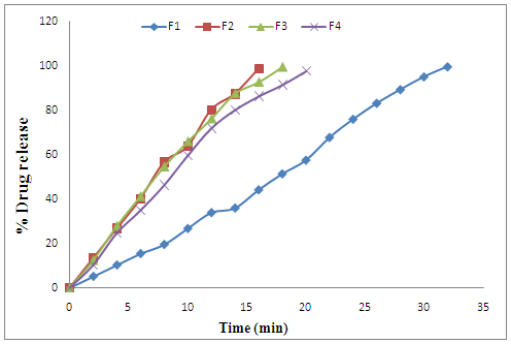


**Fig. 2: Comparison of dissolution profiles of F1 to F4**

In case of Nilvadipineliquisolid compacts, out of all the formulations propylene glycol has shown greater drug release than the PEG. This might be due to the greater solubility of the drug in the respective solvent. Formulation F14 containing propylene glycol as solvent, which is hygroscopic liquid containing an asymmetrical carbon atom, it exists in two stereoisomers.

Avicel and Aerosil as carrier and coating materials and crospovidone as super disintegrant, which is a water-insoluble synthetic cross linked homopolymer of N-vinyl-2-pyrrolidine which contains not less than 11.0% and not more than 12.8% of nitrogen, calculated on anhydrous basis has shown greater drug release than the remaining super-disintegrants.

The F14 formulation was taken as optimized formulation and maximum percentage drug release of 97.14 was obtained within 10 min. A single graph was plotted for four formulations by taking % drug release on y-axis and time on x- axis.

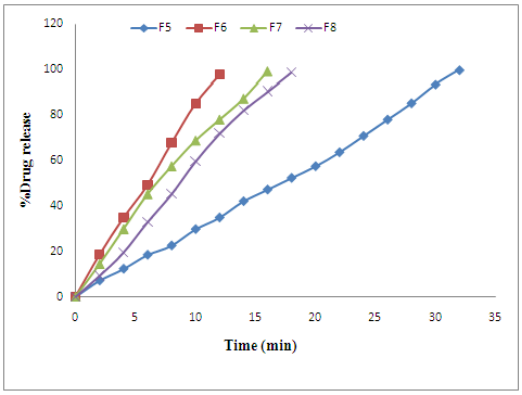


**Fig. 3: Comparison of dissolution profiles of F5 to F8**

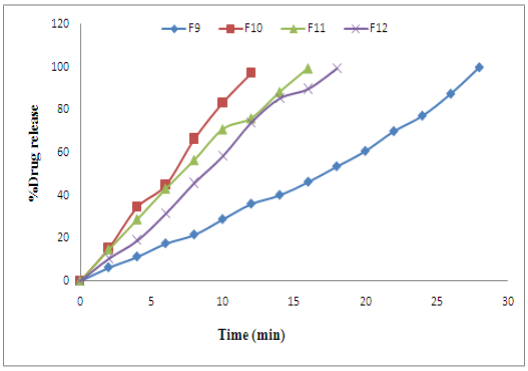


**Fig. 4: Comparison of dissolution profiles of F9 to F12**

**Table 9: *in-vitro* drug release of profiles of formulations F1 to F4**

| Time (min) | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| **0** | **0** | **0** | **0** | **0** |
| 2 | 5.14±0.43 | 13.36±0.589 | 12.34±0.487 | 10.28±0.39 |
| 4 | 10.28±1.25 | 26.73±0.703 | 27.76±0.521 | 24.68±0.47 |
| 6 | 15.42±0.431 | 40.10±0.63 | 41.13±0.31 | 34.96±0.24 |
| 8 | 19.53±1.19 | 56.56±1.07 | 54.50±0.97 | 46.27±0.631 |
| 10 | 26.73±0.799 | 63.7±0.655 | 65.81±0.71 | 59.64±0.901 |
| 12 | 33.93±0.891 | 80.21±0.713 | 76.10±1.15 | 71.89±0.616 |
| 14 | 35.99±1.28 | 87.41±0.620 | 87.41±0.216 | 80.21±0.41 |
| 16 | 44.22±0.81 | 98.72±1.07 | 92.55±0.523 | 86.38±0.502 |
| 18 | 51.42±1.39 | | 99.34±1.23 | 91.52±1.08 |
| 20 | 57.59±1.13 | | | 97.69±0.86 |
| 22 | 67.87±0.98 | | | |
| 24 | 76.10±0.37 | | | |
| 26 | 83.30±0.76 | | | |
| 28 | 89.47±1.06 | | | |
| 30 | 95.23±1.00 | | | |
| 32 | 99.75±1.39 | | | |

**Table 10: *In-vitro* drug release of profiles of formulations F5 to F8**

| Time (min) | F5 | F6 | F7 | F8 |
|---|---|---|---|---|
| **0** | **0** | **0** | **0** | **0** |
| 2 | 7.19±0.25 | 18.51±0.767 | 14.39±0.834 | 9.25±0.331 |
| 4 | 12.34±0.90 | 34.96±1.25 | 29.82±0.291 | 19.53±0.414 |
| 6 | 18.51±0.79 | 49.36±1.04 | 45.25±0.486 | 32.90±0.402 |
| 8 | 22.62±0.503 | 67.87±0.96 | 57.59±0.312 | 45.25±0.517 |
| 10 | 29.82±0.331 | 85.35±1.27 | 68.90±0.218 | 59.64±0.304 |
| 12 | 34.96±0.207 | 97.69±0.870 | 78.15±0.305 | 71.98±1.116 |
| 14 | 42.16±1.723 | | 87.41±1.091 | 82.27±1.103 |
| 16 | 47.30±0.491 | | 99.03±0.798 | 90.50±1.03 |
| 18 | 52.44±0.39 | | | 98.80±0.538 |
| 20 | 57.59±0.476 | | | |
| 22 | 63.76±0.105 | | | |
| 24 | 70.96±1.52 | | | |
| 26 | 78.15±0.51 | | | |
| 28 | 85.35±0.340 | | | |
| 30 | 93.58±0.418 | | | |
| 32 | 99.96±0.513 | | | |

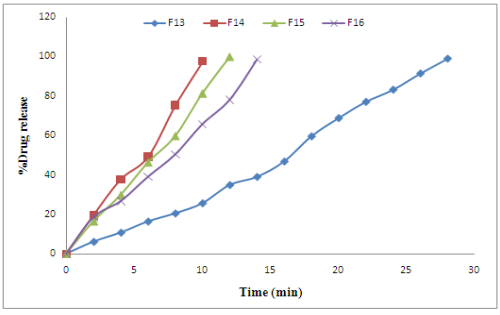


**Fig. 5: Comparison of dissolution profiles of F13 to F16**

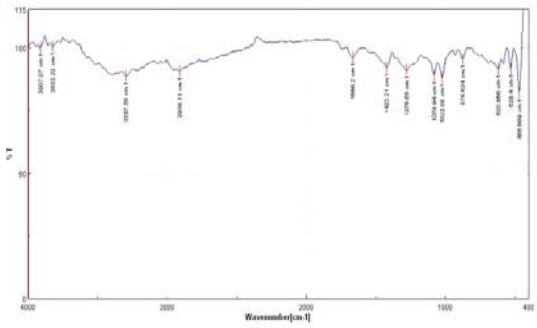

**Fig. 7: FTIR For Nilvadipine With PEG 400**

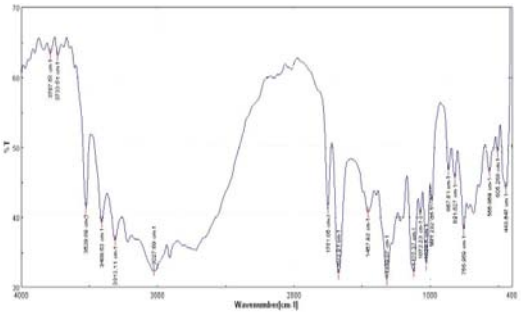

**Fig. 6: FT-IR of Nilvadipine Pure Drug**

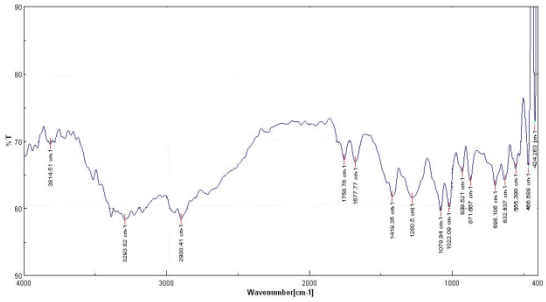

**Fig. 8: FT-IR of Nilvadipine best formulation**

**Fourier Transform Infrared (FTIR) spectroscopic studies**

Compatibility studies were performed using Fourier Transform Infrared (FTIR) spectrophotometer. The IR spectrum of pure drug (Nilvadipine) and physical mixture of drug and excipients were studied.

The peaks obtained in the spectrum of formulation correlated with the peak of drug spectrum and there were no significant extra peaks. This indicates that the drug was compatible with the formulation components. The spectra of pure drug and formulation are shown in Fig.6

**Table 11: In-vitro drug release of profiles of formulations F9 to F12**

| Time (min) | F9 | F10 | F11 | F12 |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 2 | 6.27±0.201 | 15.42±0.302 | 14.70±0.294 | 10.48±1.15 |
| 4 | 11.31±0.301 | 34.65±0.401 | 28.79±0.42 | 18.92±0.41 |
| 6 | 17.59±0.59 | 45.04±1.256 | 43.19±1.02 | 31.42±1.93 |
| 8 | 28.79±0.193 | 66.53±1.129 | 56.56±0.408 | 45.76±1.27 |
| 10 | 35.99±0.715 | 83.60±0.490 | 70.96±0.339 | 58.31±0.93 |
| 12 | 40.10±0.91 | 97.39±0.672 | 76.10±0.551 | 74.04±1.43 |
| 14 | 46.27±0.22 | | 88.44±1.16 | 85.35±0.84 |
| 16 | 53.47±1.05 | | 99.55±1.052 | 89.78±0.56 |
| 18 | 60.67±1.118 | | | 99.24±1.087 |
| 20 | 69.93±0.104 | | | |
| 22 | 77.13±1.099 | | | |
| 24 | 87.41±0.732 | | | |
| 26 | 99.75±0.69 | | | |
| 28 | | | | |
| 30 | | | | |
| 32 | | | | |

**Table 12: In-vitro drug release of profiles of formulations F13 to F6**

| Time (min) | F13 | F14 | F15 | F16 |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 2 | 6.17±0.82 | 19.53±0.72 | 16.45±0.471 | 18.57±0.417 |
| 4 | 10.79±0.73 | 37.74±0.413 | 29.82±1.03 | 26.73±0.279 |
| 6 | 16.45±0.65 | 49.15±0.639 | 46.27±0.732 | 39.07±0.624 |
| 8 | 20.56±1.17 | 75.27±1.001 | 59.64±0.213 | 50.39±1.18 |
| 10 | 25.71±0.304 | 97.49±0.582 | 81.24±1.051 | 65.81±1.045 |
| 12 | 34.07±0.592 | | 99.76±0.389 | 78.15±0.72 |
| 14 | 39.07±0.421 | | | 98.52±0.831 |
| 16 | 46.89±0.49 | | | |
| 18 | 59.64±0.732 | | | |
| 20 | 68.90±0.390 | | | |
| 22 | 77.13±0.473 | | | |
| 24 | 83.30±1.19 | | | |
| 26 | 91.52±0.721 | | | |
| 28 | 99.03±1.35 | | | |
| 30 | | | | |
| 32 | | | | |

**CONCLUSION**

This novel technique is found to be efficient method for formulation of water insoluble solid drugs and liquid lipophilic drugs. Rapid disintegration rates are observed compared to conventional tablets and therefore, they show improved release rates and hence greater bioavailability. The use of non-volatile solvent in the formulation causes increased wettability of water insoluble drugs and ensures molecular dispersion of drug in the formulation.

Modification of formulation by use of certain agents cause sustained release of drugs from the liquisolid tablets. Liquisolid Formulations shows better Flowability, Compressibility, improves solubility, dissolution and better absorption.

**CONFLICT OF INTERESTS**

Declared None

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