AMERICAN JOURNAL OF PHARMTECH RESEARCH
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# Preparation and In Vivo Evaluation of Nimodipine Solid Dispersions

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## ABSTRACT

Nimodipine, a poorly soluble drug, was considered to be fit for solid dispersions to improve its solubility and bioavailability. Our study intended to prepare Nimodipine solid dispersions by solvent evaporation method using various novel polymers. Solubility and dissolution studies indicate that Kolliwax RH 40 and SLS is the most suitable polymer. The solubility studies were corresponded with dissolution data and the formulation SD15 was found to be having highest drug release of about 98.96±5.15% in about 90 minutes. *In-vitro* release data from several formulations containing XRD and SEM studies indicate no crystallinity in the optimized formulation SD15. FTIR studies suggested good drug excipient compatibility between all components of prepared formulation. From in vivo bioavailability studies, $C_{max}$ of the optimized formulation SD15 was 4.34±0.08ng /ml, was significantly higher as compared to pure drug suspension, i.e., 2.78±0.35ng/ml. $T_{max}$ of optimized formulation was decreased significantly when compared with pure drug (1.00±0.05hr, 2.00±0.01hr), $AUC_{0-\alpha}$ and $AUC_{0-t}$ for optimized solid dispersion formulation was significantly higher ($p<0.05$) as compared to pure drug suspension. The present study demonstrated that formulation of Nimodipine solid dispersion by solvent evaporation technique is a highly effective strategy for enhancing the bioavailability of poorly water soluble Nimodipine.

**Keywords:** Nimodipine, Solid dispersions, Hypertension, Kolliwax, Solvent evaporation, Bioavailability studies.

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Received 11 July 2018, Accepted 23 July 2018

Please cite this article as: Bhikshapathi DVRN *et al*., Preparation and In Vivo Evaluation of Nimodipine Solid Dispersions. American Journal of PharmTech Research 2018.

## INTRODUCTION

Today, there is a great increase in the number of poorly soluble drugs. Hence it is important to develop techniques to increase the solubility and bioavailability of poorly soluble drugs. The formulation of poorly soluble drugs to oral formulations is a great challenge to the formulation scientists [1]. Solid dispersions are the dosage forms where the drug is distributed in a biologically inert matrix. Solid dispersions are used to increase the dissolution rate of drugs with poor aqueous solubility, thereby increasing its oral bioavailability. Optimizing wetting characteristics and increasing the interfacial area are important to increase the drug dissolution rate [2]. Interfacial area can be increased by micronization but then it also leads to agglomeration. Hence, it is preferable to introduce the drug in the form of molecular dispersions like solid dispersion [3]. Multicomponent dispersion systems contain more than one hydrophilic polymer and this enhances the solubility and dissolution of poorly soluble drugs[4]. These also have higher dissolution rate than single or two component systems [5]. Nimodipine is a dihydropyridone calcium channel blocker originally developed to treat hypertension. It is used in the treatment of subarachnoid haemorrhage. The chemical name of Nimodipine is [2, 6-Dimethyl-4-(3'-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylic acid 3-beta-methoxyethyl ester 5-isopropyl ester]. It is used for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in patients with subarachnoid haemorrhage from ruptured congenital aneurysms [6]. It is a BCS class II (low solubility – high permeability) drug. Bioavailability is less of about (3-30%) following oral administration due to low water solubility and extensive first-pass metabolism through CYP 3A4 in the liver [7]. In the present work, solid dispersions of Nimodipine in Kolliwax are prepared and evaluated.

## MATERIALS AND METHOD

**Materials:**

Nimodipine pure drug was generous gift from MSN Laboratories Pvt. Ltd, Hyderabad, India. Kolliphor P 407 and Kolliphor P188 were obtained from BASF, Mumbai. Labrafac PG, Labrafil M 2125 CS, Kolliwax RH 40, Kolliwax GMS II were obtained from Signet Chemical Corp. Pvt. Ltd, Mumbai. Gelucire 44/14 was supplied by Gattefosse, France.Soluplus were gifted from BASF, Germany. Urea, PEG 4000 and PVP K-30 and were gifted from Dow Chemicals, USA. All other chemicals used were of analytical grade.

**Preliminary solubility studies of Nimodipine**

Solubility measurements of Nimodipine were performed according to a published method [8,9]. An excess amount of Nimodipine was added to 25ml of aqueous solution of water soluble carriers like Labrafac PG, Labrafil M 2125 CS, Kolliwax RH 40, Soluplus, Kolliwax GMS II, Kolliphor P 407, Kolliphor P188, Urea, Gelucire 44/14 and PVPK-30 in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with methanol. The diluted solution was analyzed for Nimodipine at 238 nm.

**Preparation of Nimodipine solid dispersion by the solvent evaporation method**

The calculated amount of Nimodipine and the employed polymers (Labrafac PG, Labrafil M 2125 CS, Kolliwax RH 40, Soluplus, Kolliphor P 407) in different drug-polymer-surfactant (SLS) ratios (1:1:1, 1:3:1.5 and 1:5:2) (as shown in table 1) were weighed and mixed together in a porcelain dish. Twenty different formulae were prepared by the solvent evaporation method. The mixture was dissolved in the least amount of methanol as a common solvent. Then the solvent was evaporated in oven at temperature 50ºC till complete evaporation. The solid dispersions prepared were pulverized in a mortar and sieved and the fraction of the powder that passed through 45 µm was stored in a desiccator and used for further investigations.

**Table 1: Composition of Nimodipine solid dispersions**

| Ingredients & formulation ratios | Nimodipine (mg) | Soluplus (mg) | Kolliphor P 407(mg) | Labrafac PG (mg) | Labrafil M 2125 CS | Kolliwax RH 40 | SLS (mg) | Methanol (mL) |
|---|---|---|---|---|---|---|---|---|
| SD1 1:1:1 | 30 | 30 | - | - | - | - | 30 | Qs |
| SD2 1:3:1.5 | 30 | 90 | - | - | - | - | 45 | Qs |
| SD3 1:3:2 | 30 | 150 | - | - | - | - | 60 | Qs |
| SD4 1:1:1 | 30 | - | 30 | - | - | - | 30 | Qs |
| SD5 1:3:1.5 | 30 | - | 90 | - | - | - | 45 | Qs |
| SD6 1:3:2 | 30 | - | 150 | - | - | - | 60 | Qs |
| SD7 1:1:1 | 30 | - | - | 30 | - | - | 30 | Qs |
| SD8 1:3:1.5 | 30 | - | - | 90 | - | - | 45 | Qs |
| SD9 1:3:2 | 30 | - | - | 150 | - | - | 60 | Qs |
| SD10 1:1:1 | 30 | - | - | - | 30 | - | 30 | Qs |
| SD11 1:3:1.5 | 30 | - | - | - | 90 | - | 45 | Qs |
| SD12 1:3:2 | 30 | - | - | - | 150 | - | 60 | Qs |
| SD13 1:1:1 | 30 | - | - | - | - | 30 | 30 | Qs |
| SD14 1:3:1.5 | 30 | - | - | - | - | 90 | 45 | Qs |
| SD15 1:3:2 | 30 | - | - | - | - | 150 | 60 | Qs |

**Evaluation of Nimodipine solid dispersions**

Solid dispersions obtained from the above method were tested for their % Practical yield, Drug content and in-vitro release studies.

**Percentage Practical Yield**

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production. SDs were collected and weighed to determine practical yield (PY) from the following equation [10].

$$\% \text{ Practical Yield} = \frac{\text{Practical Mass (Solid dispersion)}}{\text{Theoretical Mass (Drug + Polymer + Surfactant)}} \times 100$$

**Drug content estimation**

The percentage drug content in physical mixtures and solid dispersions was estimated by dissolving 20 mg quantities of physical mixtures and solid dispersions in methanol, mixed thoroughly by shaking and the volume was made-up to the mark with solvent (0.1N HCl) [11]. The solution was filtered and the filtrate was diluted suitably with 0.1N HCl (1.2) pH and absorbance was measured at 238 nm using UV/Visible spectrophotometer [4].

The actual drug content was calculated using the following equation.

Drug content (%) = Actual amount of Solid dispersion x 100 Theoretical amount of Solid dispersion.

**Dissolution studies**

Dissolution studies were performed using USP apparatus II [12]. Pure drug and all the other products prepared as described earlier were included in this study. Samples of each preparation equivalent to 20 mg of drug were spread over the surface of the dissolution medium (900 ml of phosphate buffer at pH (6.8) maintained at a temperature of 37±0.5 ºC, stirring at 50 rpm [13]. The samples were withdrawn at predetermined time intervals, filtered, diluted with methanol and analyzed using a UV spectrophotometer at 238 nm. Each test was performed in triplicate [14].

**Fourier Transformation Infrared spectroscopy (FTIR)**

The IR spectra were recorded using an FTIR spectrophotometer (Shimadzu, Japan) with diffuse reflectance principle [15]. The samples were scanned over the frequency range 4000–400-$^{1}$cm [16].

**X-ray diffraction (XRD) studies**

X-ray powder diffraction patterns were recorded on an X-ray powder diffraction system (Shimadzu, Japan) using copper target, a voltage of 40 Kv and a current of 30 ma [17]. The scanning was done over 2_ range of 5º to 60º [18].

**SEM (Scanning Electron microscope) studies**

The surface morphology of the layered sample was examined by using SEM (Hitachi, Japan). The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated

tape) adhered to an aluminum stub. These sample stubs were coated with a thin layer (30Å) of gold by employing POLARON-E 3000 sputter coater. The samples were examined by SEM and photographed under various magnifications with direct data capture of the images onto a computer.

**Stability studies**

Prepared solid dispersions were placed inside sealed 40cc HDPE container with child resistant cap under controlled temperature environment inside stability chamber (Thermo Lab, India) with relative humidity of 75%±5%RH and temperature of 40 $^0$C±2$^0$C for stability studies. Samples were removed after 1, 2 and 3 months and evaluated for percentage drug content and in vitro dissolution studies [19].

***In vivo* studies**

**Animal preparation**

Healthy male Wistar rats were (weighing approximately 250±25 g) selected for this study, all the animals were healthy during the period of the experiment. All efforts were made to maintain the animals under controlled environmental conditions (Temperature 25$^0$C±2$^0$C, Relative Humidity 45%±5%RH and 12 h alternate light and dark cycle) with 100 % fresh air exchange in animal rooms, uninterrupted power and water supply. Rats were fed with standard diet and watered libitum.

**Pharmacokinetic studies** [20]

The pharmacokinetic characteristics for Nimodipine pure drug suspension 30 mg, optimized preparation of solid dispersion 30 mg were evaluated using twelve healthy Male Wister rats weighing 250±25g. Rats were divided in to two groups at random, each group containing six animals. First group was administered Nimodipine (as such) suspension was prepared in 0.5% w/w of HPMC 2.5cPs, second group was administered optimized preparation of solid dispersion suspension was prepared in 0.5% w/w of HPMC 2.5cPs by oral route at an equivalent dose of 30 mg/kg body weight.

About 500 µl of blood was withdrawn from retro orbital plexus at different time intervals such as 0.25, 0.50, 1.00, 1.50, 2.00, 2.50, 3.00, 4.00, 5.00, 6.00, 8.00, 12.00, 16.00, 20.00 and 24.00h. Blood samples were transferred into Eppendorf tubes containing heparin in order to prevent blood clotting. The samples were centrifuged immediately at 4000 rpm and the plasma was stored in light-protected container at -20 $^0$C till analysis.

**Determination of Nimodipine in Rat plasma by HPLC method** [21]:

The chromatographic method was standardized using a HIQ sil C18 column (250×4.6 mm i.d, 5 µm particle size) with UV detection at 238 nm and flow rate of 1 ml/min. The mobile phase

consisting of Acetonitrile-Ammonium acetate 0.02 ml/L (80:20v/v). With addition of 0.1 percent 1-hexanesulfonic acid monohydrate sodium salt as an ion-pairing reagent was selected.

The retention times about 2.28 min for Nimodipine and 2.58 min for (dibucaine) IS.

**Pharmacokinetic data analysis for optimized preparation of solid dispersions and pure drug suspension:**

The area under the drug concentration-time curve from zero to 24h (AUC) was calculated using the trapezoidal rule. The maximum plasma concentration of the drug ($C_{max}$ and the time to reach $C_{max}$ ($T_{max}$) was obtained directly from the plasma profiles.

The pharmacokinetic parameters were performed by a non-compartmental analysis using Win Nonlin 3.3® pharmacokinetic software (Pharsight Mountain View, CA USA). All values are expressed as the mean±SD. Statistical analysis was performed with Graph Pad InStat software (version 3.00, Graph Pad Software, San Diego, CA, USA) using one-way analysis of variance (ANOVA) followed by Tukey–Kramer multiple comparison test. Difference with $p<0.05$ was considered statistically significant.

The bioavailability of the optimized preparation of solid dispersion was evaluated using rats.

## RESLUTS AND DISCUSSION

**Preliminary solubility studies of Nimodipine:**

Preliminary solubility analysis was carried out to select the appropriate water-soluble carriers for the preparation of solid dispersion in which pure drug solubility was found to be 0.012±0.001 mg/ml. From this study, drug and Kolliwax RH 40 along with SLS in the ratio of 1:3:2 showed highest drug solubility of 0.492±0.041 mg/ml, almost 5-fold increase compared to that of pure drug. Amongst all the water-soluble carriers used in preliminary solubility studies, PEG 4000, PVP K30, Mannitol and Urea showed low solubility when compared with others and hence were not included in the preparation of Nimodipine solid dispersions. The graphical representation of solubility studies of Nimodipine physical mixtures was shown in figure 1 and the same was tabulated in table 2.

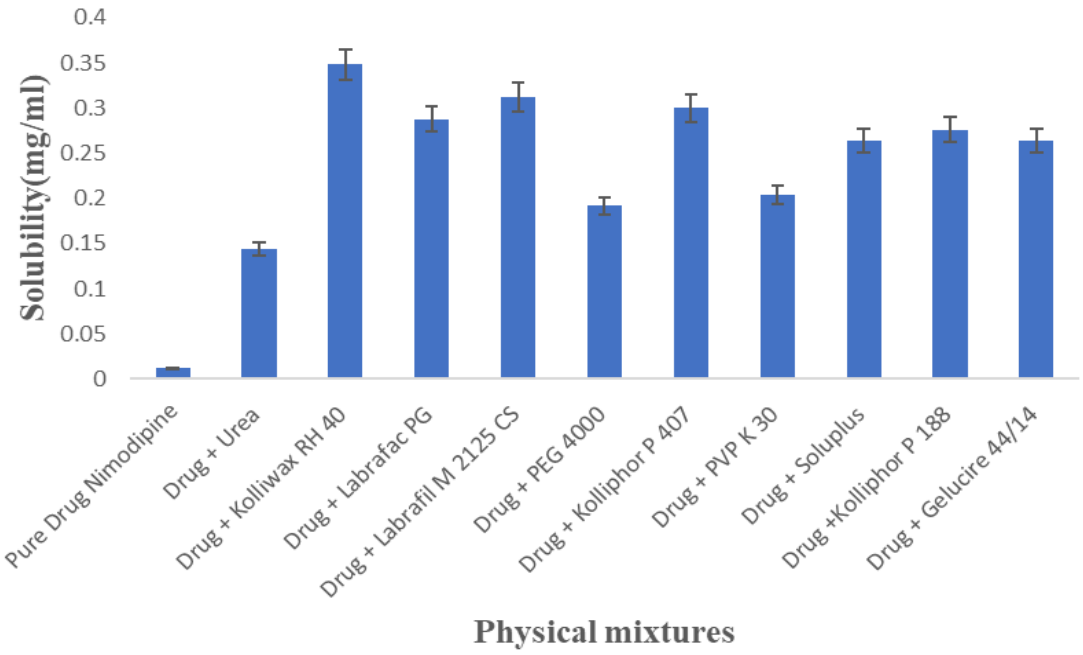


**Figure 1: Solubility studies of Nimodipine physical mixture**

**Table 2: Preliminary solubility studies of Nimodipine in different polymers**

| Physical Mixture | Solubility(mg/ml) * |
|---|---|
| Pure Drug Nimodipine | 0.012±0.001 |
| Drug + Urea | 0.144±0.003 |
| Drug + Kolliwax RH 40 | 0.348±0.113 |
| Drug + Labrafac PG | 0.288±0.002 |
| Drug + Labrafil M 2125 CS | 0.312±0.011 |
| Drug + PEG 4000 | 0.192±0.051 |
| Drug + Kolliphor P 407 | 0.30±0.002 |
| Drug + PVP K 30 | 0.204±0.112 |
| Drug + Soluplus | 0.264±0.031 |
| Drug +Kolliphor P 188 | 0.276±0.011 |
| Drug + Gelucire 44/14 | 0.264±0.001 |

***n=SD±3**

**Nimodipine solid dispersions**

All the solid dispersions prepared were found to be fine and free flowing powers.

**Evaluation parameters**

**Solubility studies of Nimodipine solid dispersions:**

Different formulations of Nimodipinesolid dispersions were prepared by solvent evaporation method with their respective carriers and solubility analysis was carried out. The results are tabulated in table 3 and graphical representation was shown in figure 2.

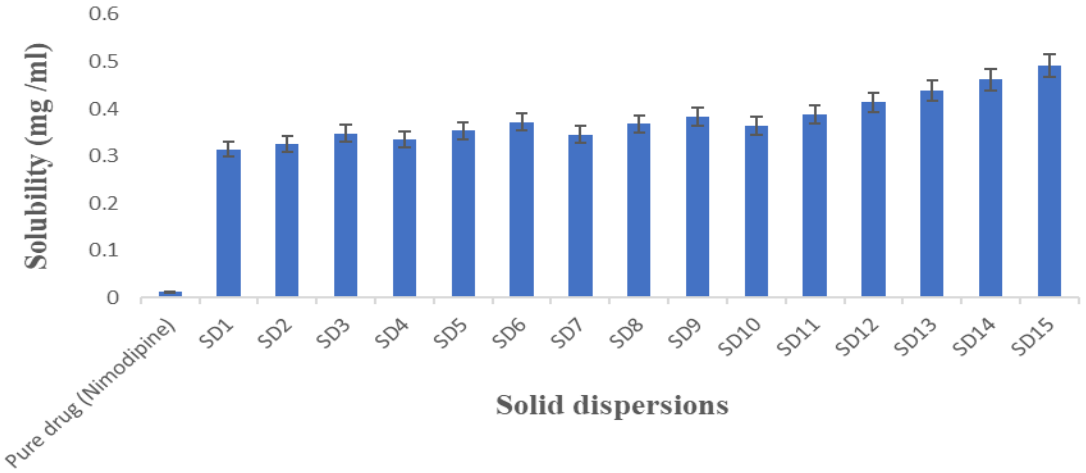


**Figure 2: Solubility studies of Nimodipine solid dispersion**

**Table 3: Solubility studies of Nimodipine solid dispersions prepared by solvent evaporation method**

| S. No. | Formulation code | Solubility (mg /ml) * |
|---|---|---|
| 1 | Pure drug (Nimodipine) | 0.012±0.001 |
| 2 | SD1 | 0.314±0.017 |
| 3 | SD2 | 0.326 ±0.103 |
| 4 | SD3 | 0.348±0.221 |
| 5 | SD4 | 0.336±0.018 |
| 6 | SD5 | 0.354±0.002 |
| 7 | SD6 | 0.372±0.031 |
| 8 | SD7 | 0.346±0.021 |
| 9 | SD8 | 0.368±0.004 |
| 10 | SD9 | 0.384±0.031 |
| 11 | SD10 | 0.364±0.004 |
| 12 | SD11 | 0.388±0.011 |
| 13 | SD12 | 0.414±0.032 |
| 14 | SD13 | 0.438±0.004 |
| 15 | SD14 | 0.462±0.013 |
| 16 | SD15 | 0.492±0.041 |

**Percent Practical yield and drug content:**

The results of percent practical yield for all formulations of solid dispersions found to be 80.99±0.010% - 98.24±0.141%. Maximum yield was found to be 98.24±0.141% in formulation SD15. The drug content of the prepared solid dispersions was found to be in the range of 87.33±0.001 – 98.52±0.125%. Maximum percent drug content of 98.52±0.125 was found in the formulation SD15. The results of percent practical yield and actual drug content of all formulations are shown in table 4.

**Table 4: % Practical yield and drug content for Nimodipine solid dispersions**

| S. No | Formulation | % Practical Yield | % Drug content |
|---|---|---|---|
| 1 | SD1 | 94.21±0.101 | 92.47±0.114 |
| 2 | SD2 | 91.46±0.002 | 95.77±0.171 |
| 3 | SD3 | 93.28±0.031 | 87.33±0.001 |
| 4 | SD4 | 81.88±0.004 | 91.33±0.008 |
| 5 | SD5 | 95.55±0.005 | 93.47±0.004 |
| 6 | SD6 | 90.68±0.011 | 95.92±0.110 |
| 7 | SD7 | 90.98±0.013 | 94.50±0.116 |
| 8 | SD8 | 95.22±0.122 | 95.52±0.118 |
| 9 | SD9 | 90.87±0.121 | 92.53±0.015 |
| 10 | SD10 | 93.26±0.141 | 93.56±0.155 |
| 11 | SD11 | 80.99±0.010 | 85.57±0.004 |
| 12 | SD12 | 95.12±0.004 | 92.64±0.016 |
| 13 | SD13 | 90.87±0.051 | 93.43±0.141 |
| 14 | SD14 | 92.27±0.013 | 88.37±0.114 |
| 15 | SD15 | 98.24±0.141 | 98.52±0.125 |

***n=SD±3**

**In vitro dissolution studies**

The drug release data obtained for formulations SD1-SD15 are tabulated in tables 5and 6. It shows the cumulative percent drug released as a function of time for all formulations. In vitro studies reveal that there is marked increase in the dissolution rate of Nimodipine from all the solid dispersions when compared to pure Nimodipine itself. From the in vitro drug release profile, it can be seen that formulation SD15 containing Combination of Dug, Kolliwax RH 40 and SLS in the ratio of 1:3:2. Kolliwax RH40 and SLS combination showed higher dissolution rate 98.96±5.15% compared with other formulations. Increase in drug wettability, conversion to amorphous form and solubilisation of the drug have all helped in enhancing the solubility of the final formulation. Figures 3 and 4 are the graphical representations of the drug release data.

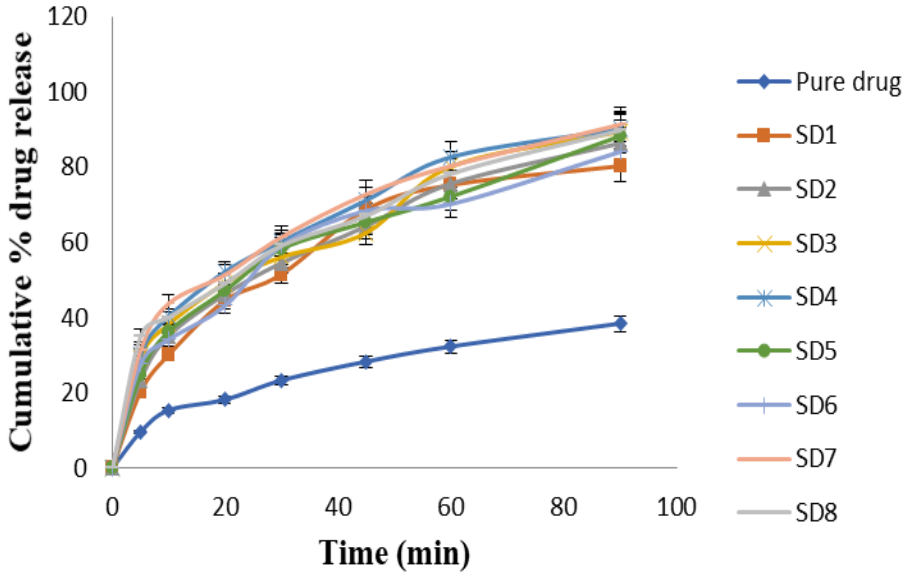


**Figure 3: In vitro dissolution profile of pure drug and different formulations of Nimodipine solid dispersions (SD1-SD8)**

**Table 5: Pharmacokinetic Parameters of Nimodipine optimized formulation and pure drug**

| Pharmacokinetic Parameters | Nimodipine pure drug | Nimodipine optimized formulation |
|---|---|---|
| $C_{max}$ (ng/ml) | 2.78±0.32 | 4.34±0.06 |
| $AUC_{0-t}$ (ng h/ml) | 5.62±1.54 | 8.52±1.24 |
| $AUC_{0-inf}$ (ng h/ml) | 8.85±1.17 | 11.05±1.54 |
| $T_{max}$ (h) | 2.00±0.01 | 1.00±0.05 |
| $t_{1/2}$ (h) | 5.02±0.02 | 3.22±0.04 |

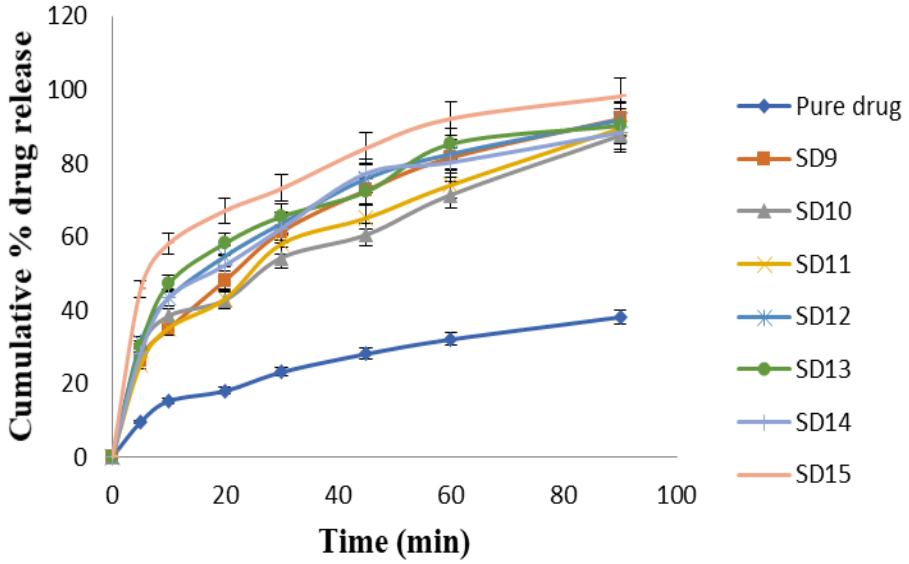


**Figure 4: In vitro dissolution profile of different formulations of Nimodipine solid dispersions (SD9-SD14)**

**FTIR studies**

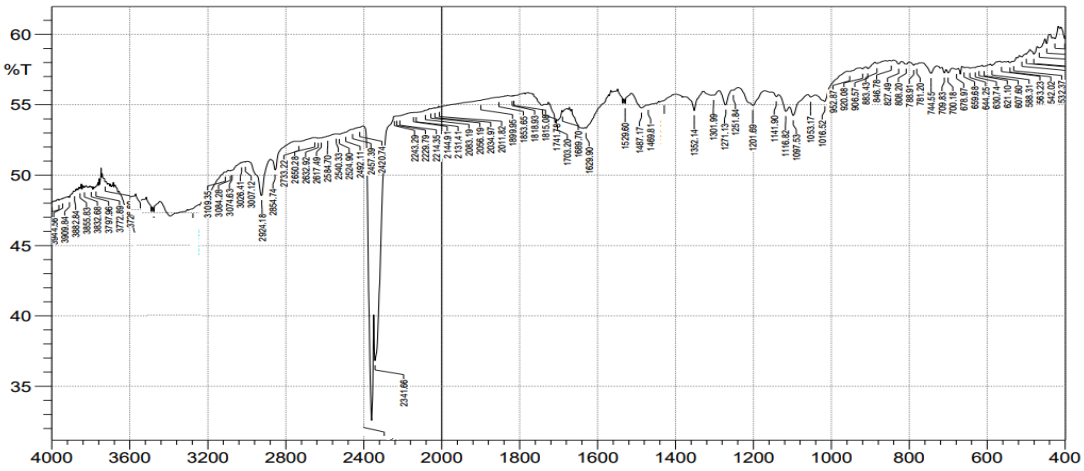


**Figure 9: FTIR Spectrum of Nimodipine pure drug**

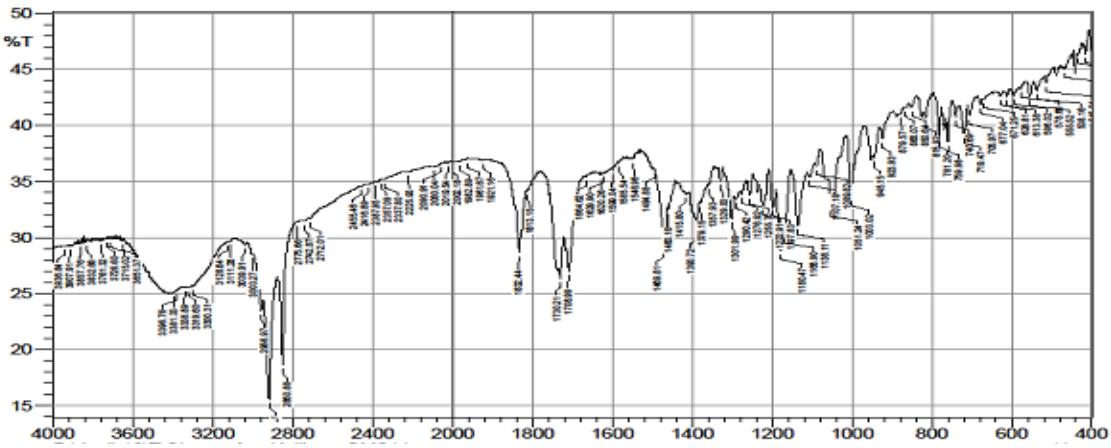


**Figure 10: FTIR Spectrum of Kolliwax RH 40**

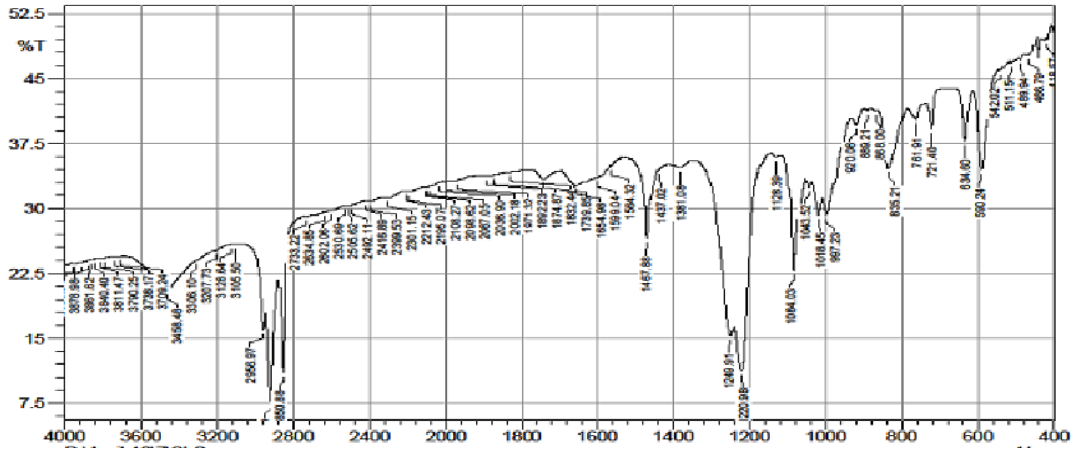


**Figure 11: FTIR Spectrum of SLS**

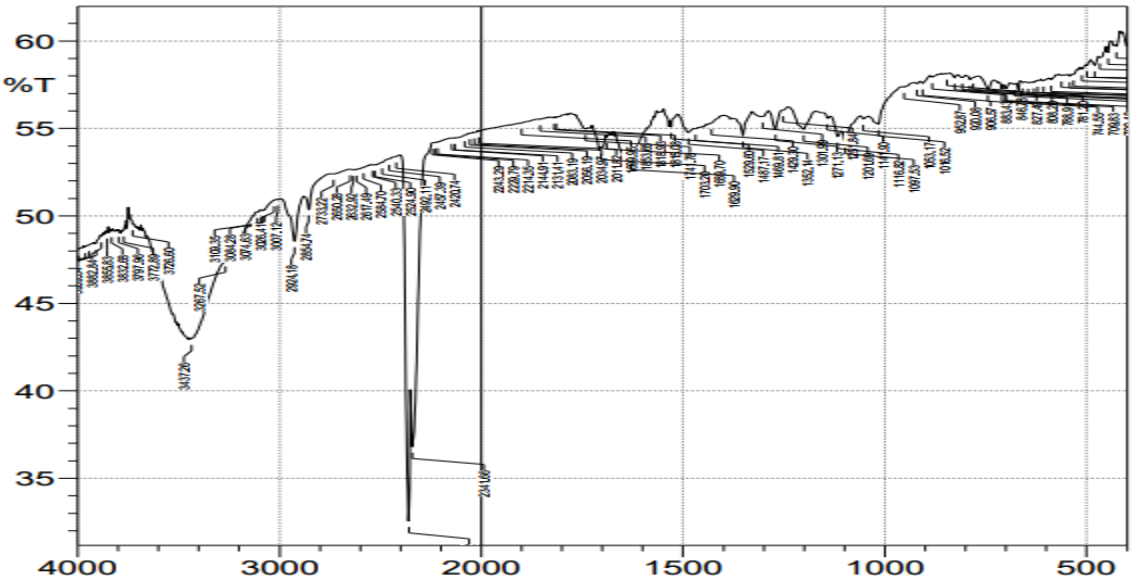


**Figure 12: FTIR Spectrum of Nimodipine Optimized formulation SD15**

The FTIR scan of Nimodipine, Kolliwax RH 40, SLS and optimized SDs are depicted in figures 9 to 12. These peaks of pure nimodipine appear in spectrum of nimodipine optimized formulation (figure 12) in which also there was broad peak from 2650cm$^{-1}$ to 3380cm$^{-1}$, this broad peak belongs to the (OH- stretching of oleic acid) that result from hydrogen bond formation between oleic acid and water. This indicates that there was drug excipient compatibility between all components of prepared formulation.

**X-Ray Diffraction Patterns**

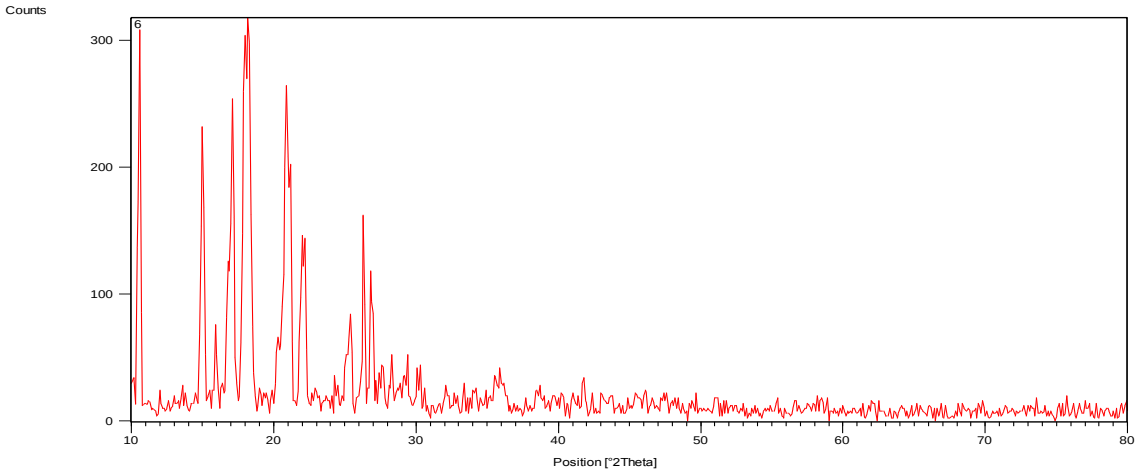


**Figure 13: X-Ray diffractograms of Nimodipine pure drug**

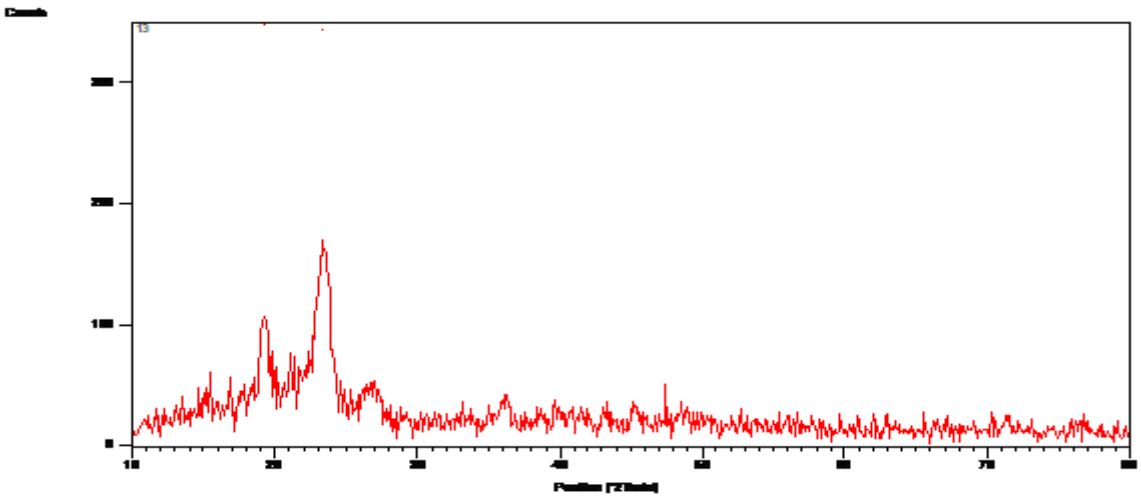

**Figure 14: X-Ray diffractograms of Nimodipine Optimized formulation SD15**

Optimized formulation SD15 of Nimodipine solid dispersions were analyzed to find out whether the solid dispersions of various drug polymer ratios are crystalline or amorphous. The presence of numerous distinct peaks in the XRD spectrum of pure Nimodipine indicates that Nimodipine was present as a crystalline material (Figure 13). On the other hand, the spectrum of optimized formulation SD15 of solid dispersion was characterized by the complete absence of any diffraction peak, which is characteristic of an amorphous compound (Figure 14). The enhancement in the dissolution rate of the drug from the drug-Kolliwax RH 40 and SLS solid dispersion is has led to a decrease in the crystallinity of the drug.

**SEM Studies**

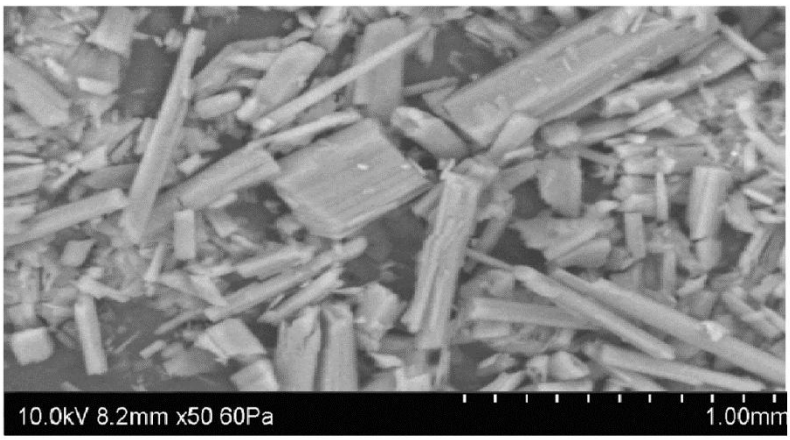


**Figure 15: Pure drug of Nimodipine**

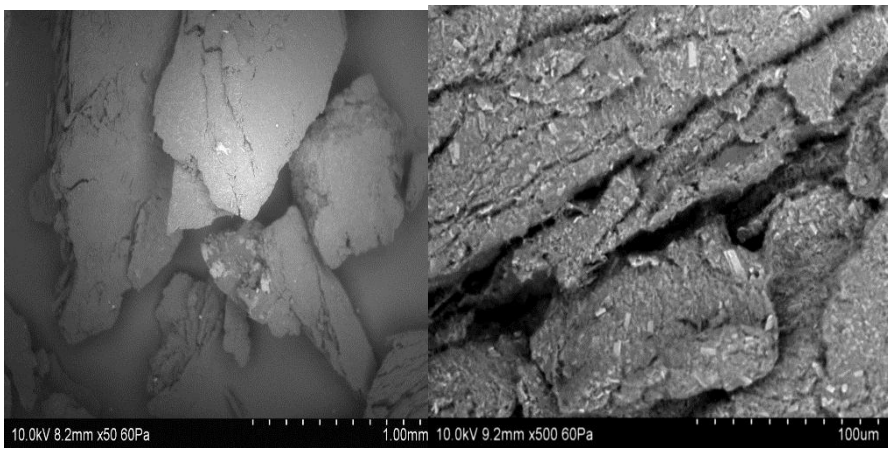


**Figure 16: Nimodipine optimized formulation SD15**

SEM photographs for pure drug and optimized formulation SD15 are shown in figures 15 and 16**.** The drug crystals appeared smooth-surfaced and irregular in shape and size. The drug surface of solid dispersion appeared to be more porous in nature. Solid dispersions appeared as uniform and homogeneously mixed mass with wrinkled surface. The solid dispersion looked like a matrix particle and incorporated into the particles of the polymers. Thus, the drug may be a dispersion of the drug in the molten polymer.

**Stability studies**

Optimized formulation (SD15) was selected for stability studies. Stability studies were conducted for drug content and *In vitro* drug release studies were carried out for 3 months at accelerated stability conditions according to ICH guidelines. The optimized formulation was stable during 3 months period. From these results it was concluded that, optimized formulation (SD15) is stable and retained their original properties with least variations (table 7).

***In vivo* bioavailability studies:**

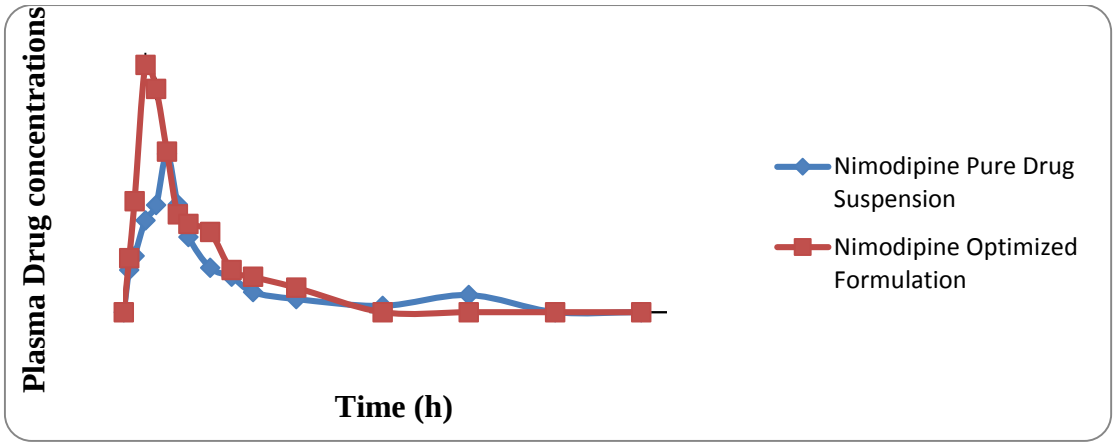


**Figure 17: Plasma concentration–time curves for the Nimodipine optimized formulation and pure drug suspension**

**Determination of Nimodipine in Pharmacokinetic parameters comparison for pure drug suspension and optimized solid dispersions formulation:**

The Nimodipine plasma concentrations in rats treated with optimized preparation of solid dispersion was significantly higher than those treated with pure drug suspension. Plasma pharmacokinetic parameters of Nimodipine after oral administration of the formulation to Wister rats are shown in Table. Based on the results, it was clearly evident that Nimodipine from a solid dispersion was significantly increased in comparison with that of the pure drug (Nimodipine suspension). $C_{max}$ of the optimized preparation of solid dispersion was 4.34±0.06ng /ml, was significantly higher as compared to $C_{max}$ of the pure drug suspension, i.e., 2.78±0.32ng/ml. $T_{max}$ of optimized preparation of solid dispersion, pure drug suspension was 1.00±0.05hr, 2.00±0.01hr respectively, AUC is an important parameter in evaluating bioavailability of drug from dosage form, as it represents the total integrated area under the blood concentration time profile and represents the total amount of drug reaching the systemic circulation after oral administration. $AUC_{0\text{-}inf}$ for optimized solid dispersion formulation was slightly higher (11.05±1.54ng h/ml) than significantly higher than $AUC_{0\text{-}inf}$ of the pure drug suspension 8.85±1.17ng h/ml. Statistically, $AUC_{0\text{-}t}$ of the optimized preparation of solid dispersion was significantly higher ($p<0.05$) as compared to pure drug suspension. Higher amount of drug concentration in blood indicated better systemic absorption of Nimodipine from optimized solid dispersion formulation as compared to the pure drug suspension.

## CONCLUSION

Solid dispersions can be an easy and effective method to formulate Nimodipine into solid dispersions by solvent evaporation method owing to the selection of polymers and preparation methods. FTIR results confirm the molecular binding of Lercanidipine with Kolliwax RH 40 and SLS. From SEM and XRD studies we can know that there is molecular binding of drug in amorphous state with the polymers. The optimized formulation SD15 containing Combination of Dug, Kolliwax RH 40 and SLS (1:3:2 ratio respectively) showed higher dissolution rate of 98.96±5.15%. Finally, it can be concluded that improved drug dissolution and bioavailability of Nimodipine can be obtained by formulating it as solid dispersions with Kolliwax RH 40 and SLS. From in vivo bioavailability studies, $C_{max}$ of the optimized formulation SD15 was 4.34±0.08ng /ml, was significantly higher as compared to pure drug suspension, i.e., 2.78±0.35ng/ml. $T_{max}$ of optimized formulation was decreased significantly when compared with pure drug (1.00±0.05hr, 2.00±0.01hr), $AUC_{0\text{-}\alpha}$ and $AUC_{0\text{-}t}$ for optimized solid dispersion formulation was significantly

higher ($p<0.05$) as compared to pure drug suspension. The present study demonstrated that formulation of Nimodipine solid dispersion by solvent evaporation technique is a highly effective strategy for enhancing the bioavailability of poorly water soluble Nimodipine.

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