EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 1
465-478
Year: 2020

COMPARISON OF MESOPOROUS SILICA XEROGEL, AMINO-FUNCTIONALIZED MESOPOROUS SILICA XEROGEL AND PARTECK SLC FOR LOADING AND RELEASE RATE OF NICARDIPINE HYDROCHLORIDE

Potdar Dipali*, Dr. Bele Mrudula, Nemane Dipak, Nikam Vishal and Lahane Ajay

Department of Pharmaceutics, M. V. P. Samaj's College of Pharmacy Nashik, 422002, Maharashtra, India.

***Corresponding Author: Potdar Dipali**
Department of Pharmaceutics, M. V. P. Samaj's College of Pharmacy Nashik, 422002, Maharashtra, India.

Article Received on 14/11/2019 **Article Revised on 05/12/2019** **Article Accepted on 26/12/2019**

ABSTRACT

Purpose: Nicardipine hydrochloride is an antihypertensive drug which blocks the calcium channel. It belongs to the BCS class II having high lipophilicity, poor water solubility and hence low bioavailability. The main aim of this study is to synthesized MSX, AMSX by using biomimetic method and also marketed parteck SLC carrier is used to check its ability to be a good drug carrier for loading and release rate of poorly water soluble drug NH. This drug loaded xerogel is compared with drug loaded parteck SLC. The dissolution media was developed for performing the *in vitro* dissolution of nicardipine hydrochloride. The porous silica were synthesized by using sol-gel method. These silica carriers then loaded with drug by using in-situ inclusion method and evaluated by performing *in vitro* dissolution study in developed dissolution media. Also the drug is loaded in marketed parteck SLC by using solvent evaporation method (1:1,1:2,1:3) and evaluated by performing in vitro dissolution study. **Methods:** The synthesized MSX,AMSX,NH-MSX,NH-AMSX was studied by using SEM. Then MSX, AMSX, NH-MSX, NH-AMSX and NH-PS (1:1,1:2,1:3) characterized by XRD, DSC, and ATR. **Results:** The in vitro drug release study revealed that the amino functionalized mesoporous silica xerogel show highest drug release (97.08%) followed by mesoporous silica xerogel (79.95%) and Parteck SLC(1:2)(68.33%). From XRD study, it can be seen that the mesoporous silica and drug loaded formulation showed no typical crystal peak, which suggest that the drug is converted into amorphous form after it is being loaded in MSX, AMSX and Parteck silica SLC. DSC study showed that nicardipine hydrochloride loaded mesoporous carriers [NH-PS (1:1,1:2,1:3)] endothermic peak due to the melting of nicardipine hydrochloride was not observed which denoted the amorphous nature of nicardipine hydrochloride in the mesoporous carriers. In case of drug loaded mesoporous silica xerogel (NH-MSX,NH-AMSX) a broad endothermic peak was observed near 259.3^{0}C and 258.6^{0}C which represents the presence of amorphous form of nicardipine hydrochloride in NH-MSX,NH-AMSX. **Conclusion:** From the results AMSX showed the higher loading capacity and enhanced dissolution release can be considered to be a good candidate as drug carrier for NH.

KEYWORDS: Mesoporous silica xerogel, Parteck SLC, NH-MSX, NH-AMSX.

1. INTRODUCTION

Absorption of an active pharmaceutical ingredient (API) from the gastrointestinal tract (GIT) is a rate limiting step for the drug to reach systemic circulation. For this, presence of drug in solution form at the absorption site is mandatory, for which solubility and dissolution are the prime requirements. Thus, the solubility and dissolution of drug are the key parameters for systemic absorption to occur.

A large fraction of new API suffers from poor aqueous solubility and dissolution. Most of them belong to class II and class IV of biopharmaceutical classification system (BCS). Improving the dissolution of these API is one of the most challenging tasks for the formulation scientists as most of the drug candidates originating from discovery are highly lipophilic in nature due to the use of advanced drug discovery tools such as combinatorial chemistry, high throughput screening and cell based assays that lead to generation of poorly soluble drug candidates.

Adsorption of drug on the silica materials to improve dissolution of poorly soluble drug is a novel approach. There is increasing interest in these potential carriers due to some of the interesting features such as large surface area, pore volume, controllable structural and textural parameters, presence of large number of silanol group on the surface which may be used for functionalization in order to control pore size and surface properties.[1,2,3]

The mesoporous silica carriers have large surface area which attributes to the high surface free energy, and thus allow adsorption of drug molecule on porous material. Adsorbed molecule is unable to retain its crystalline structure and thus exist in an amorphous state. This amorphous system is physically stable owing to decrease in Gibb's free energy. Crystallization of such amorphized drug will occur only on the change of thermodynamic state of system.[4,5]

In addition to thermodynamic consideration, porous materials also shows size constraint effect on nucleation and crystal growth which may be advantageous in enhancing the physical stability of amorphous system. In the classical theory of homogeneous nucleation, crystal growth proceeds spontaneously once a critical nucleation size is reached. If, the spatial constraints of a capillary are imposed on the clusters of molecules before they reach the critical size, nucleation and growth will be prevented and the system will remain in an intrinsically noncrystalline state.[1,2,6,7]

It has been reported that the xerogel which is synthesized by using sol-gel method considered as promising carrier due to its biodegradability, high drug loading efficiency, low processing temperature, and the ability to allow in situ incorporation of drug molecules into the silica. Therefore, it has great significance to functionalized the synthesized mesoporous silica xerogel as a drug carrier.[3,8]

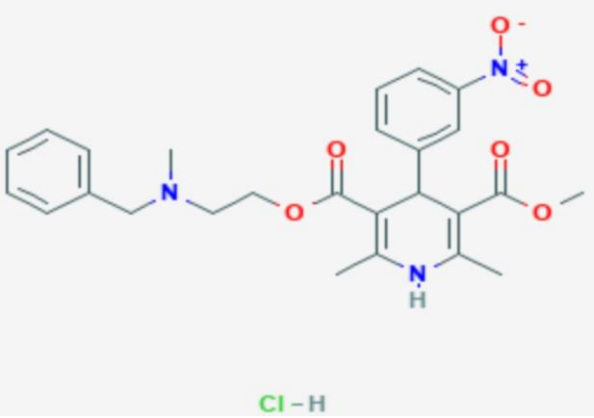


Fig. 1: Chemical Structure of Nicardipine Hydrochloride.

Recently, biomimetic synthesis of porous silica mediated by polyamines has attracted great attention.In biosilicification mechanism, amines are actively catalyze the condensation of silica precursors (tetramethoxysilane and tetraethoxysilane). Due to presence of alternating protonated and non-protonated amines group in the polyamine chains to form hydrogen bonds with the adjacent oxygen to Si and form Si-O-Si.[9,10]

Nicardipine hydrochloride (NH see Fig.1) is a poorly water-soluble and antihypertensive drug. Incorporation of NH into mesoporous silica can improve drug dissolution. In present work,amino-functionalized mesoporous silica xerogel (AMSX) was synthesized by using branched poly(ethyleneimine)s as the template and APTES as organic functional species. The mesoporous silica xerogel (MSX) without amino functionalization is also synthesized by same method. This synthesized AMSX, MSX is compared with the marketed Parteck SLC. The changes of characteristics before and after NH loading were studied by using attenuated total reflectance (ATR), differential scanning colorimetry (DSC) and X-ray diffraction.[11]

2. MATERIAL AND METHODS

2.1. Material

Tetraethoxysilane (TEOS) and 3-aminopropyltriethoxysilane (APTES) were purchased from Yarrow chem. (Mumbai), branched poly(ethyleneimine)s (PEIs) with weight-average molecular weight of < 25 kDa was purchased from Sigma Aldrich (USA), Parteck SLC Merck (Mumbai). All the other reagents were purchased from Modern lab. (Nashik).

2.2. Synthesis of AMSX and MSX

A-MSX was synthesized with biomimetic method using PEIs as the template, and its amino functionalization done by using co-condensation method with advantage of high distribution homogeneity of functional groups.

For the synthesis of A-MSX, 0.4mL PEIs was dissolved in 40.8mL aqueous solution and the mixed solution left for 48 hr. Then 1mL as-synthesized template solution was added into mixed solution consisting of 1 mL TEOS,1 mL absolute ethyl alcohol and 20µL APTES and left the sol system at ambient conditions statically until the formation of wet gel. Finally the wet gel was dried at 40°C vacuum drying oven to remove volatile solvent.

Similarly, MSX was also synthesized using the same process except no APTES was added.[1,12]

2.3. Drug loading in synthesized silica carriers

Drug loading procedure was carried out using in situ drug inclusion method. Briefly for loading procedure of NH 50 mg NH was dissolved in 1 mL of methanol, which was named as NH methanol solution was added into gelling solution that consisted of 0.5ml TEOS, 0.5 mL absolute ethyl alcohol, 0.5 mL PEIs aqueous solution (0.4mL PEIs was dissolved in 40.8mL aqueous solution) and 20µL APTES. Finally the system was stir (REMI ELECTROTECHNIK Ltd. DCS) for 10 min, left statically until the formation of wet gel and dried at 40°C vacuum drying oven to get NH-AMSX. NH-MSX was made using the drug loading procedure except no APTES was added.[13]

2.4. Determination of drug loading

Drug loading capacity for all drug loaded mesoporous silica xerogel were determined by taking weighed quantity of NH-MSX or NH-AMSX i.e. 200mg in 10 ml methanol. Then sonicated (CITIZEN LAB CD 4820) for

10 min. Concentration of nicardipine hydrochloride was determined by analyzing the supernatant by UV-visible spectrophotometer at 353nm after suitable dilutions in methanol. The percentage drug loading was calculated by using the following formula:

$$\%\ drug\ loading = \frac{\text{Weight of loaded drug}}{\text{Weight of drug loaded carrier}} * 100$$

2.5. Drug loading in Parteck SLC

Solvent evaporation method

Solvent evaporation method was used for loading of drug into mesoporous carriers. In this method, nicardipine hydrochloride was dissolved in methanol to make solution of concentration 50mg/ml and then silica carriers were soaked in this solution. The dispersion was subjected to stirring for 1hr in a well closed container, also protected from light. The product obtained was then dried in vacuum oven at 40^0 C. The dried products were properly labeled and stored in well closed amber colored container in desiccators.[14]

2.6. Determination of drug loading

Drug loading capacity of all drug loaded mesoporous silica were determined by suspending drug loaded mesoporous silica equivalent to the100 mg of nicardipine hydrochloride plain drug in 10 ml methanol (n=3). This suspension was then subjected to vortex (REMI ELECTROTECHNIK Ltd. DCS) for 15 min and then sonicated (CITZEN LAB CD 4820) for 10 min. The undissolved mesoporous silica was separated by centrifuging the suspension at 15000 rpm for 10 min. Concentration of nicardipine hydrochloride was determined by analyzing the supernatant by UV-visible spectrophotometer at 353 nm after suitable dilutions in methanol. The percentage drug loading capacity was calculated by using the following formula:[15,16]

$$\%drugloading = \frac{\text{Amt. of drug added-Amt. of drug in superntant}}{\text{Amt. of nanoparticles}} *100$$

2.7.Optimization of drug to carrier ratio

All the mesoporous carriers loaded with drug by solvent evaporation method in three different drug: carrier loading ratio i.e., 1:1,1:2,1:3. These obtained formulations with 1:1,1:2 and 1:3 ratios were evaluated for optimal loading ratio based on release performance during in vitro dissolution study.

2.8. Determination of Drug content

Nicardipine hydrochloride content in all drug loaded mesoporous silica xerogel were determined by taking weighed quantity of NH-MSX or NH-AMSX i.e. 200mg in 10 ml methanol and 250 mg NH-PS(1:1,1:2,1:3). Then sonicated (CITIZEN LAB CD 4820) for 10 min. Concentration of nicardipine hydrochloride was determined by analyzing the supernatant by UV-visible spectrophotometer at 353nm after suitable dilutions in methanol. The percentage drug content was calculated by using the following:

$$\text{Drug Content (\%)} = \frac{\text{Conc. of drug loaded mesoporous carrier}}{\text{Conc. of pure drug}} * 100$$

2.9. Characterization methods

2.9.1. Scanning electron microscopy (SEM)

SEM images of MSX, AMSX, NH-MSX, NH-AMSX were taken from the (Nova NanoSEM NPEP303)instrument to study the morphology. The powder samples were mounted over a double sided adhesive carbon tape which were mounted over aluminum pin stubs and sputter coated with gold using ion sputter. The powder samples which were not adhered on to carbon tape were blown out gently and finally the samples were visualized under SEM instrument.

2.9.2. Differential scanning calorimetry (DSC)

Thermal analysis of nicardipine hydrochloride plain drug, MSX, AMSX,D-MSX,D-AMSX,NH-PS(1:1,1:2,1:3) were carried out by using DSC 60 system operating with STAR^e software. Indium was used for calibration. The sample cell was purged with dry nitrogen at a flow rate of 100 ml/min. Accurately weighed samples of 5 mg were placed in aluminum crimped pans with a pin hole and scanned at a heating rate of 10 ^{0}C/min over a temperature range of 50 – 400^0C.

2.9.3. Powder X-ray diffraction analysis (PXRD)

PXRD pattern of plain drug and drug loaded carriers were recorded by using an Maxima X XRD-7000 (Shimadzu, Japan) X-ray diffractometer operated at a voltage of 40 kV and current of 30 mA using Cu Kα radiation source (1.54 Å) passing through K-beta filter with divergence slit ($2/3^0$), scatter slit ($2/3^0$) and receiving slit (0.3 mm) over the angular range (2θ) of 10– 90^0 at a rate of 3° min^{-1} in steps of 0.02^0 with step time of 0.3 second.

2.9.4. Attenuated total reflectance (ATR)

All FTIR spectra were obtained by using the Spectrum RX1 (Perkin-Elmer, UK) spectrometer. Accurately weighed (5 mg) samples were mixed thoroughly with 100 mg of potassium bromide IR powder and compressed under vacuum at a pressure of 12 psi for 3 min. The pellet obtained was affixed in a suitable holder and spectrum was recorded from 4000 cm^{-1} to 400 cm^{-1} in a scan time of 12 min.

2.10. In-vitro drug dissolution

A] synthesized xerogel

In-vitro dissolution was carried out using USP II apparatus (paddle apparatus) 50rpm, 37°C with Lab India DS8000 dissolution tester. Samples were exposed to intestinal buffer (pH 6.8)prepared by dissolving 28.80 gm disodium hydrogen phosphate and 11.45 gm of potassium dihydrogen phosphate in sufficient water to produce 1000mL. At predetermined time intervals, 10

mL dissolution medium was withdrawn from the release medium was added to maintain a constant dissolution volume. The withdrawn dissolution medium was filtered then analyzed using SHIMADZU 2450 at the wavelength of 239nm.

B] Parteck SLC

In-vitro dissolution was carried out using USP II apparatus (paddle apparatus) 50rpm, 37°C with Labindia DS8000 dissolution tester. Samples were exposed to intestinal buffer (pH 6.8) prepared by dissolving 28.80 gm disodium hydrogen phosphate and 11.45 gm of potassium dihydrogen phosphate in sufficient water to produce 1000mL. Add 2ml of dissolution media in dialysis bag form a suspension of NH-PS. At predetermined time intervals, 10 mL dissolution medium was withdrawn from the release medium was added to maintain a constant dissolution volume. The withdrawn dissolution medium was filtered then analyzed using SHIMADZU 2450 at the wavelength of 239nm.

3. RESULTS AND DISCUSSIONS

3.1. Drug loading and quantification of drug in mesoporous carriers

a) for synthesized mesoporous silica xerogel

In-situ inclusion method was used to load the drug into MSX and AMSX. % drug loading in MSX and AMSX formulation were depicted in table 1. Drug loading found to be high in A-MSX. Highest drug loading was observed in formulation which functionalized with amino group by using APTES. Higher drug loading in AMSX might be due to surface functionalization of mesoporous silica carrier.

Table 1: Drug load estimation (% wt), (n=3).

Silica carriers	% drug loading capacity ± SD
NH-MSX	21.73±0.59%
NH-AMSX	31.25± 0.96%

a) for Parteck SLC

Solvent evaporation method is used to load the drug into Parteck SLC. % drug loading in NH-PS(1:1,1:2,1:3) were depicted in table 2. Drug loading found to be high in NH-PS 1:1. Highest drug loading was observed in formulation which contain 1:1 ratio of drug : mesoporous carrier. As high the drug loading capacity low is the drug content or vice-versa.

Table 2: Drug load estimation (% wt), (n=3).

Silica Carriers	% drug loading capacity ±SD
NH-PS(1:1)	17.13± 1.02%
NH-PS(1:2)	6.88± 0.95%
NH-PS(1:3)	8.88± 0.65%

3.2. Drug Content

Drug content of all drug loaded mesoporous carriers were depicted in table 3.

Table 3: Drug content (%) (n=3).

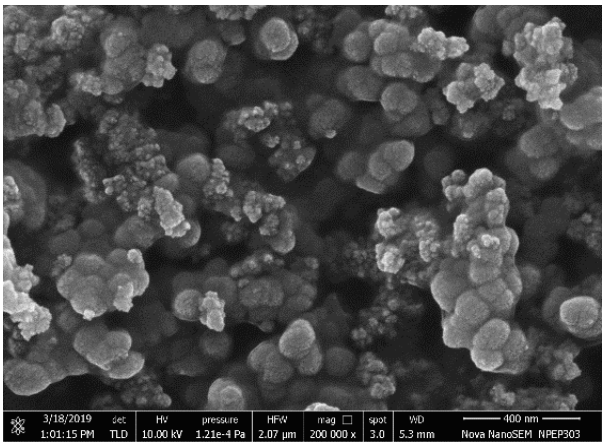
Silica Carriers	Drug content (%)
NH-MSX	89.60±0.29%
NH-AMSX	96.73±0.79%
NH-PS(1:1)	67.11±0.99%
NH-PS(1:2)	82.95±1.63%
NH-PS(1:3)	68.05±0.98%

3.3. Characterization methods

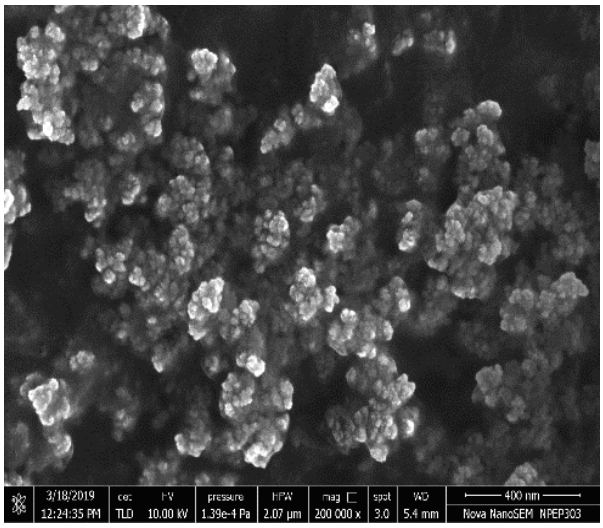
6.6.1. Scanning electron microscopy (SEM)

SEM micrograph provides important details about the morphology of MSX, AMSX, NH-MSX, NH-AMSX (figure 2). SEM micrographs showed that both MSX, AMSX,NH-MSX,NH-AMSX were quite small nanoparticles aggregated intensively due to xerogel state. Nanoparticle size of AMSX was little larger than MSX, which was related with the addition of grafted functional groups. It is worth noticing that disordered mesopores of MSX and AMSX are shaped during sol-gel process due to the following reasons:

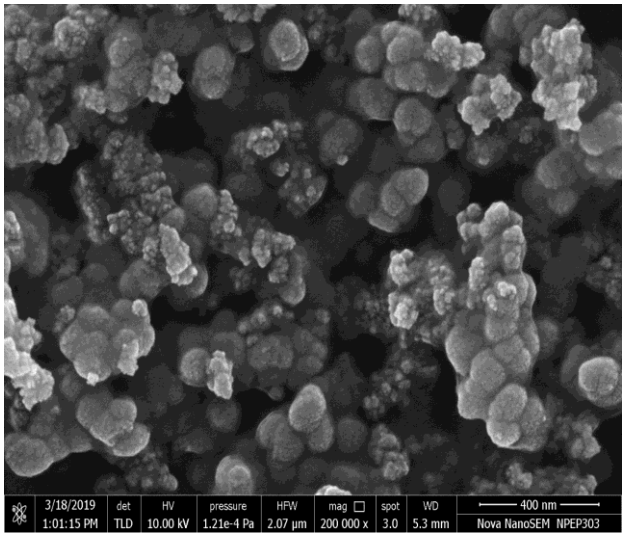
1) PEIs increase dispersion of Si-O-Si bonds through their electrostatic interaction, therefore there are mesopores in nanoparticles.
2) Mesopores can also form by inter-nanoparticles owing to the tight solid condensation of nanoparticles when ethanol is evaporated.



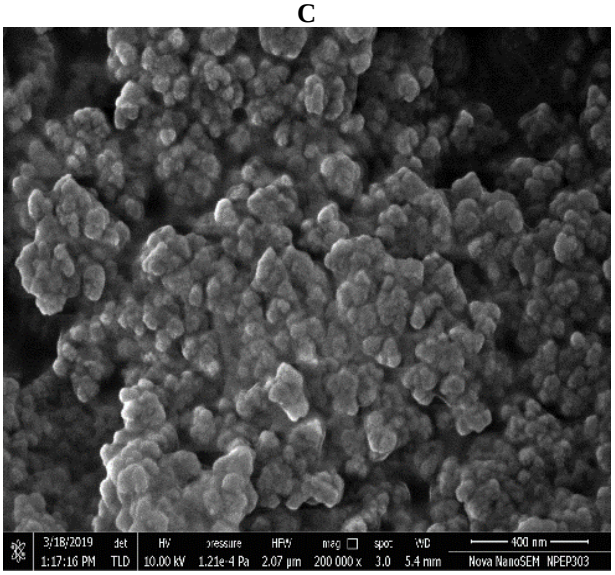
A



B



C



D

Fig 2: SEM photographs of A,MSX; B,AMSX; C,NH-MSX; D,NH-AMSX.

6.6.2. Differential scanning calorimetry (DSC)

The physical state of NH entrapped in the mesoporous carriers was determined by DSC analysis as depicted in Figure.3.A. Nicardipine hydrochloride plain drug exhibited a clear endothermic peak at 176 ^{0}C which is near to a characteristic of melting of nicardipine hydrochloride representing its crystalline nature . While, in case of nicardipine hydrochloride loaded mesoporous carriers [NH-PS(1:1,1:2,1:3)]endothermic peak due to the melting of nicardipine hydrochloride was not observed which denoted the amorphous nature nicardipine hydrochloride in the mesoporous carriers. In case of drug loaded mesoporous silica xerogel (NH-MSX,NH-AMSX) a broad endothermic peak was observed near 259.3^{0}C and 258.6^{0}C which represents the presence of amorphous form of nicardipine hydrochloride in NH-MSX, NH-AMSX.

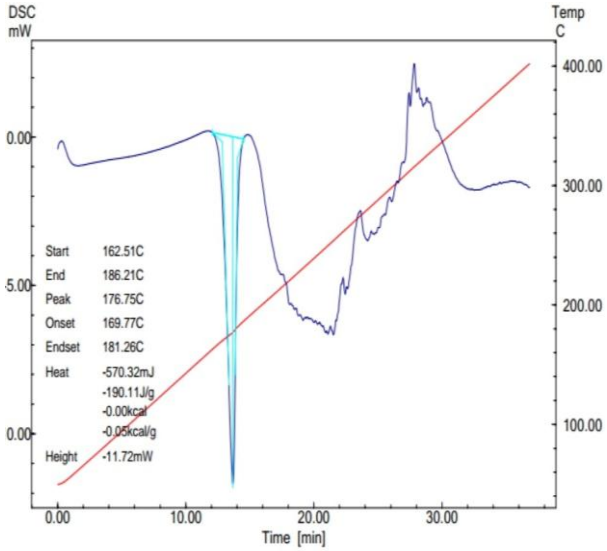


Fig. 3.A: DSC of Nicardipine Hydrochloride.

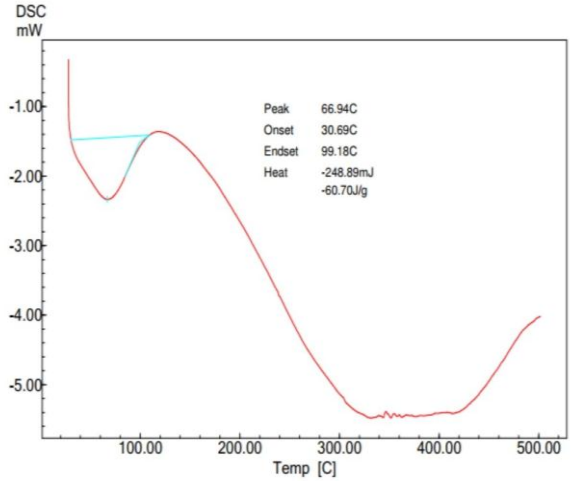


Fig. 3.B. DSC of Parteck SLC.

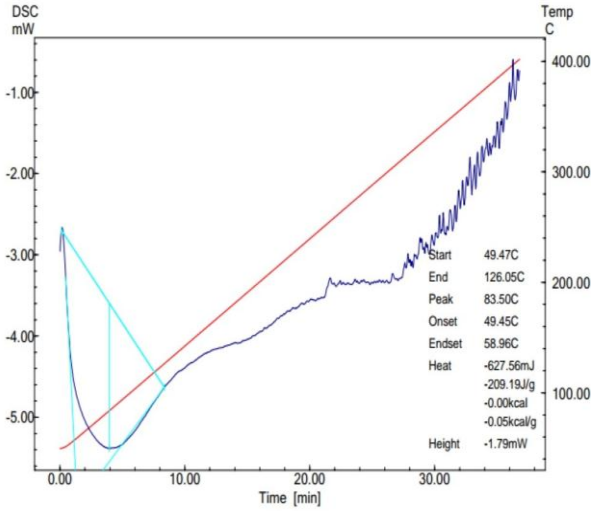


Fig.3.C. DSC of MSX.

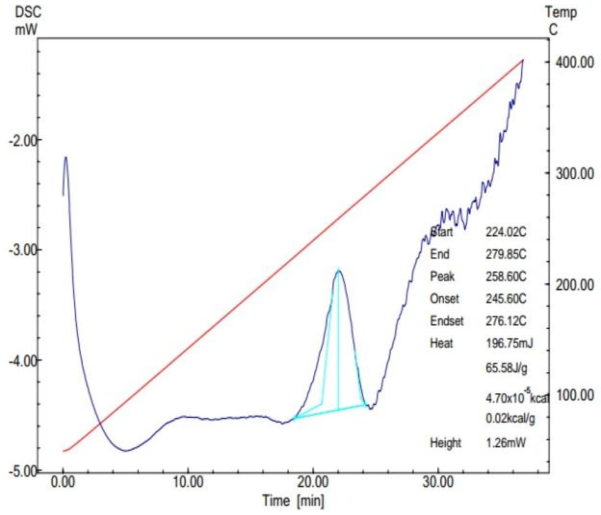


Fig.3.D. DSC of NH-MSX.

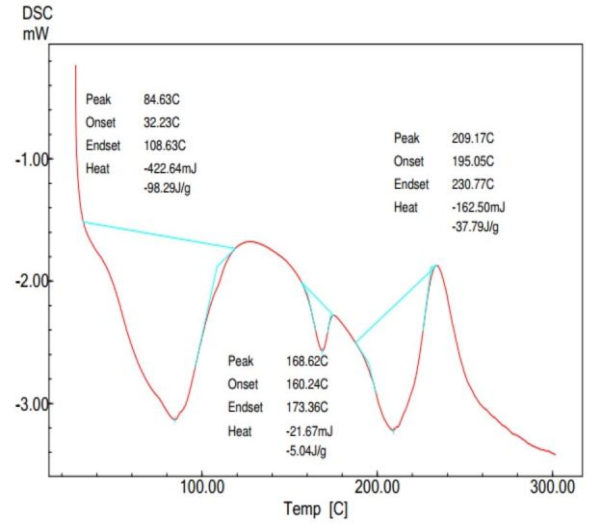


Fig.3.E. DSC of AMSX.

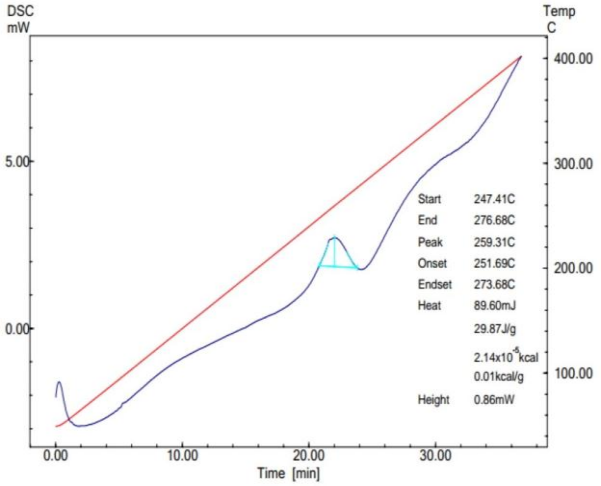


Fig.3.F. DSC of NH-AMSX.

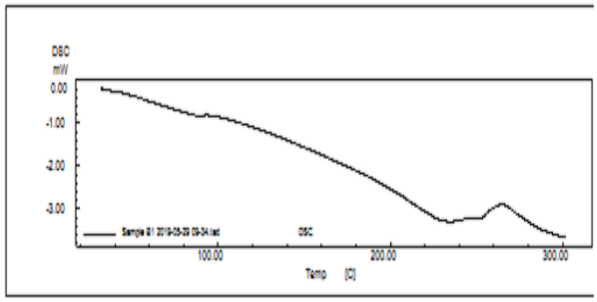


Fig.3.G. DSC of NH-PS(1:1).

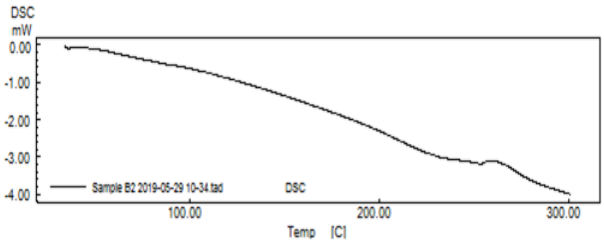


Fig.3.H. DSC of NH-PS(1:2).

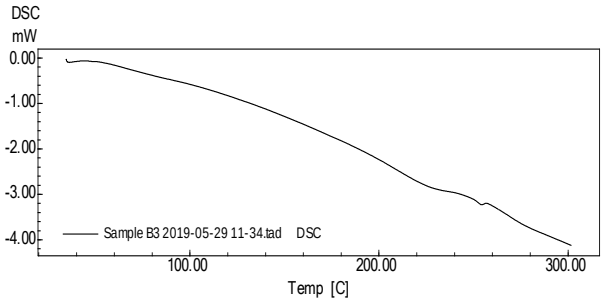


Fig. 3.I. DSC of NH-PS(1:3).

6.6.3. Powder X-ray diffraction analysis (PXRD)

Figure 8 represents the PXRD patterns of nicardipine hydrochloride plain drug, mesoporous carrires and drug loaded mesoporous carrier [NH-MSX,NH-AMSX,NH-PS(1:1,1:2,1:3)]. The PXRD pattern of the nicardipine hydrochloride plain drug confirmed crystalline nature of nicardipine hydrochloride. The drug loaded in MSX,AMSX and Parteck SLC showed the characteristic peaks of drug with reduced intensities. It indicated that drug present in crystalline form in formulation with reduced crystallinity. This reduction in crystallinity of the drug in mesoporous carriers might be due to the presence of drug in amorphous form inside the pores of carriers and those deposited on the surface in crystalline form responsible for presence peaks in PXRD pattern.

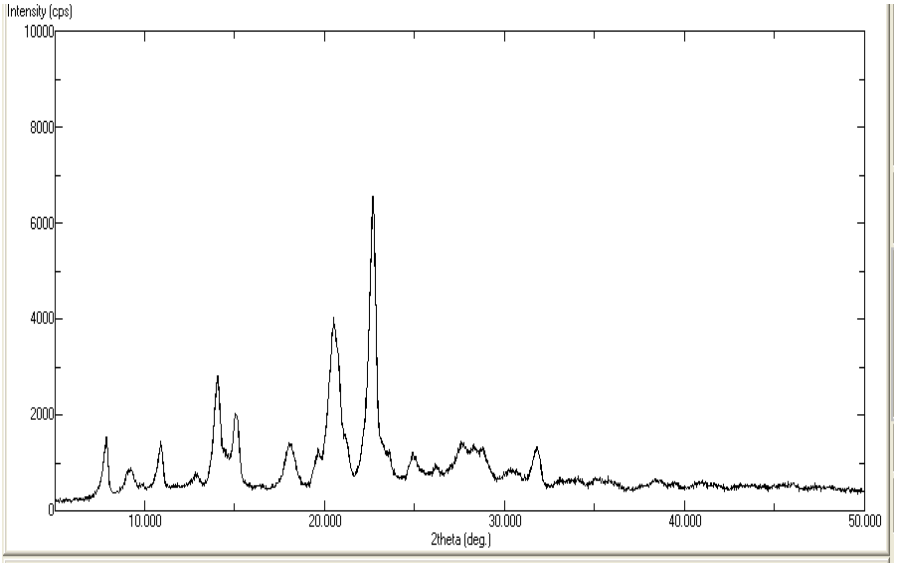


Fig. 4.1: PXRD of Nicardipine Hydrochloride.

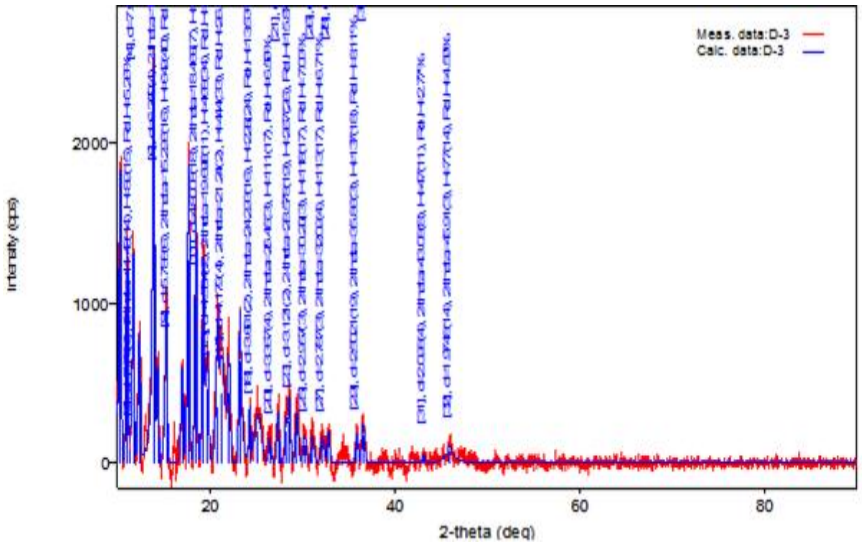


Fig.4.2: PXRD of Parteck SLC.

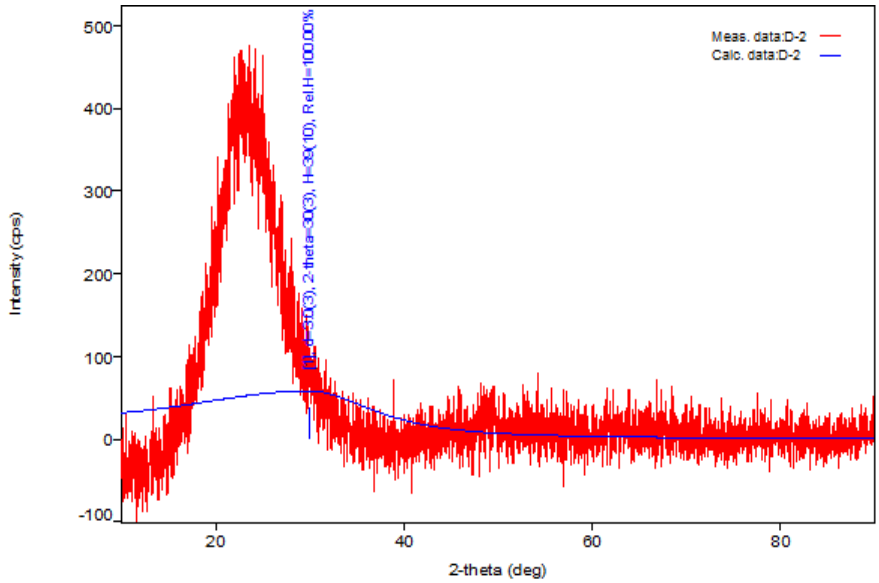


Fig.4.3: PXRD of MSX.

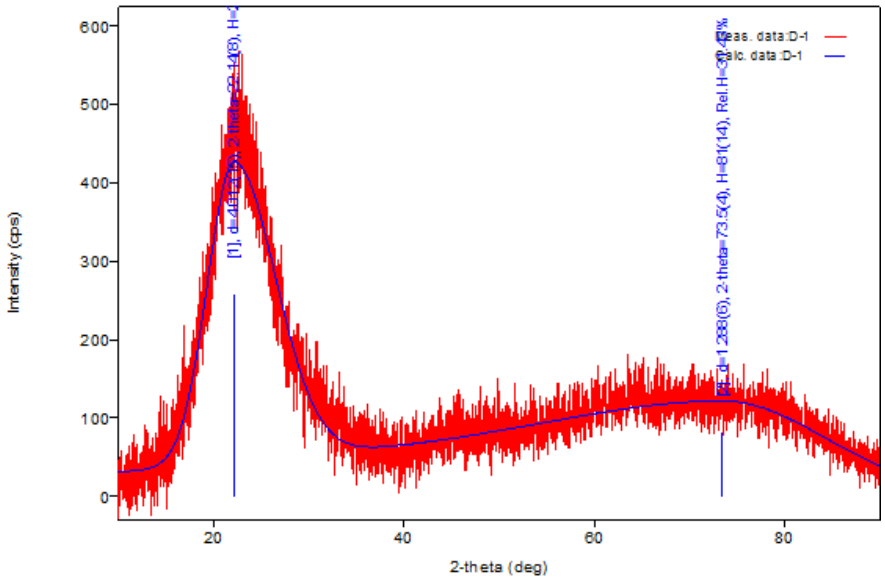


Fig.4.4.PXRD of NH-MSX.

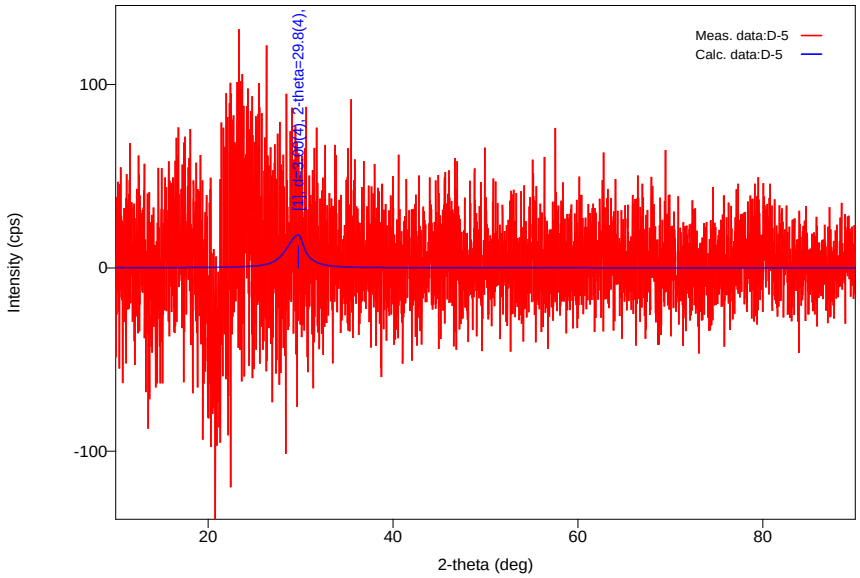


Fig.4.5. PXRD of AMSX.

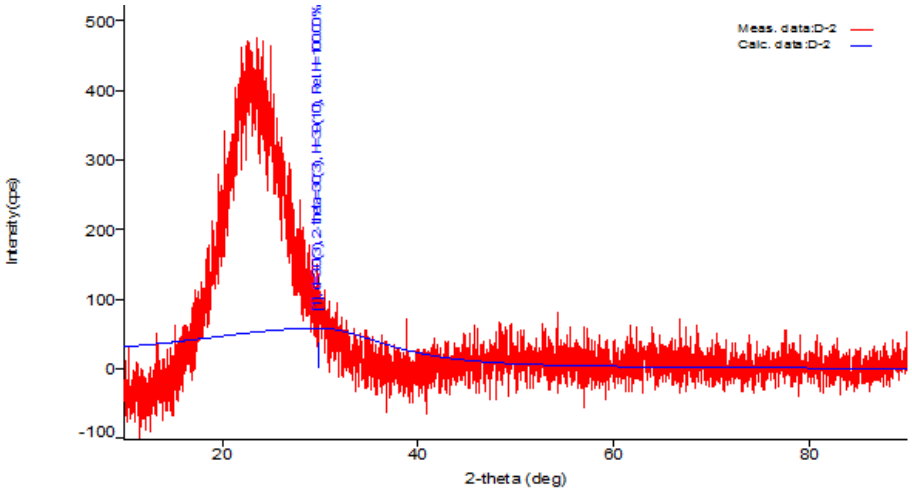


Fig.4.6: Pxrd of Nh-Amsx.

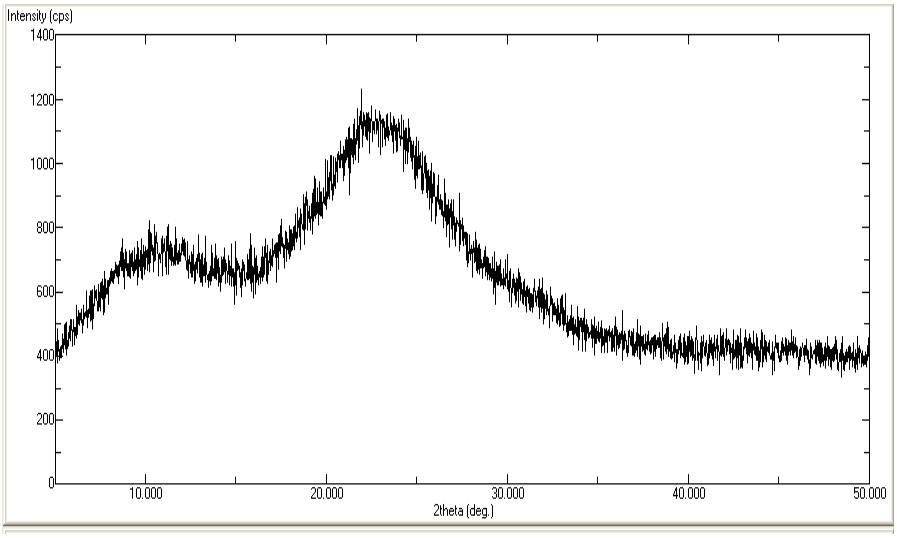


Fig.4.7. PXRD of NH-PS (1:1).

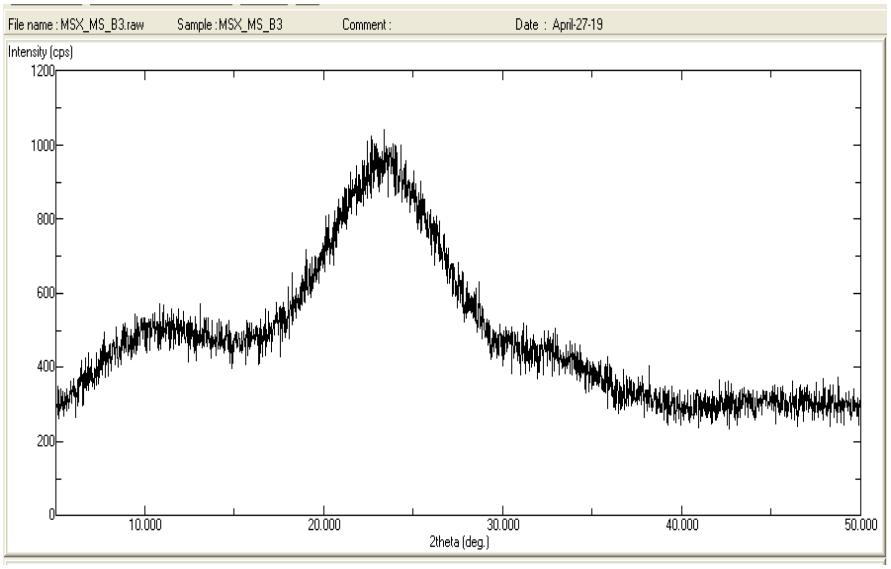


Fig.4.8: PXRD of NH-PS(1:2).

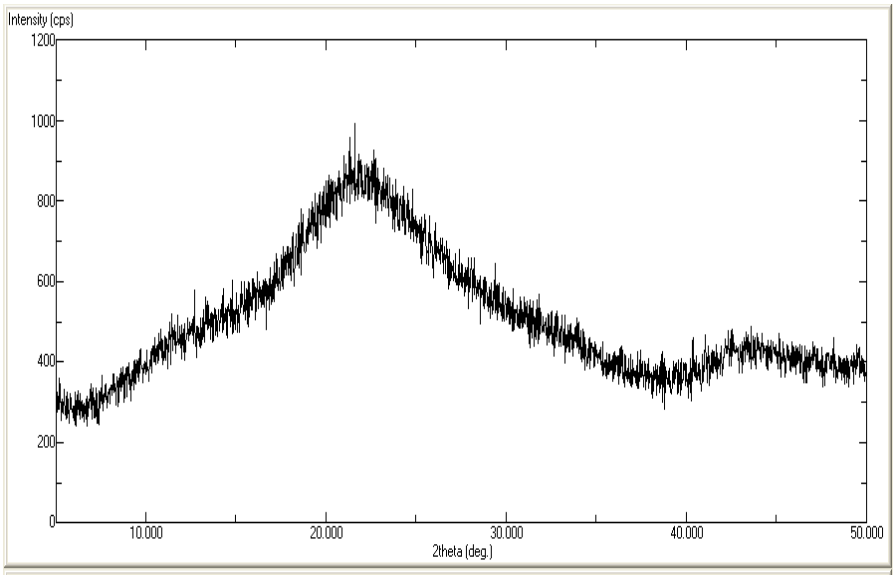


Fig.4.9. PXRD of NH-PS(1:3).

Figure 4: PXRD Pattern of Plain Drug and Drug Loaded Silica Carriers.

6.6.4. Fourier transform infrared spectroscopy (FTIR)

Interaction between nicardipine hydrochloride and mesoporous carriers was evaluated by ATR .The ATR spectra of nicardipine hydrochloride plain drug and the all the plain mesoporous carriers and drug loaded carriers are depicted in figure 5.

The nicardipine hydrochloride plain drug showed characteristic peaks of -NH, -C=O and N=O groups in IR region of 3152 cm^{-1}, 1703 cm^{-1} and 1354 cm^{-1} respectively. The characteristic peaks of plain mesoporous silica carriers and Si-O-Si stretching vibrations at 1100 – 1040 cm^{-1}. In case of ATR pattern of all drug loaded silica carriers, all the characteristic peaks of nicardipine hydrochloride could be seen in the spectrum which revealed no interaction between the drug and silica carriers.

The spectra of AMSX show the N-H bending in IR region 1541 cm-1 revealed that amino functionalization of mesoporous silica xerogel**.**

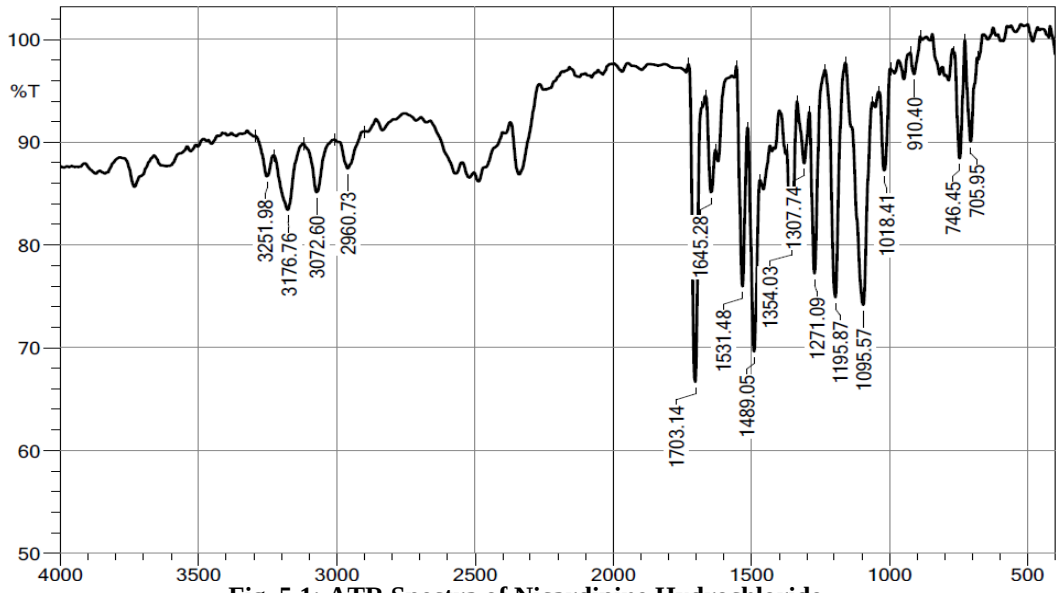


Fig. 5.1: ATR Spectra of Nicardipine Hydrochloride.

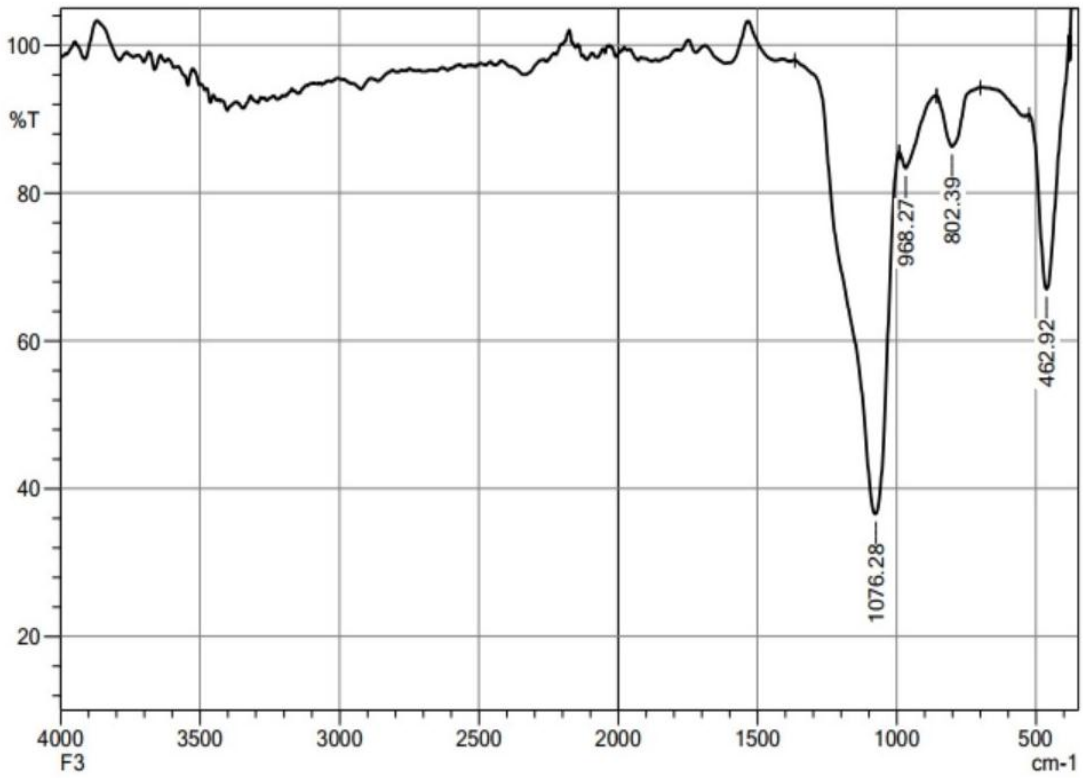


Fig.5.2: ATR spectra of Parteck SLC.

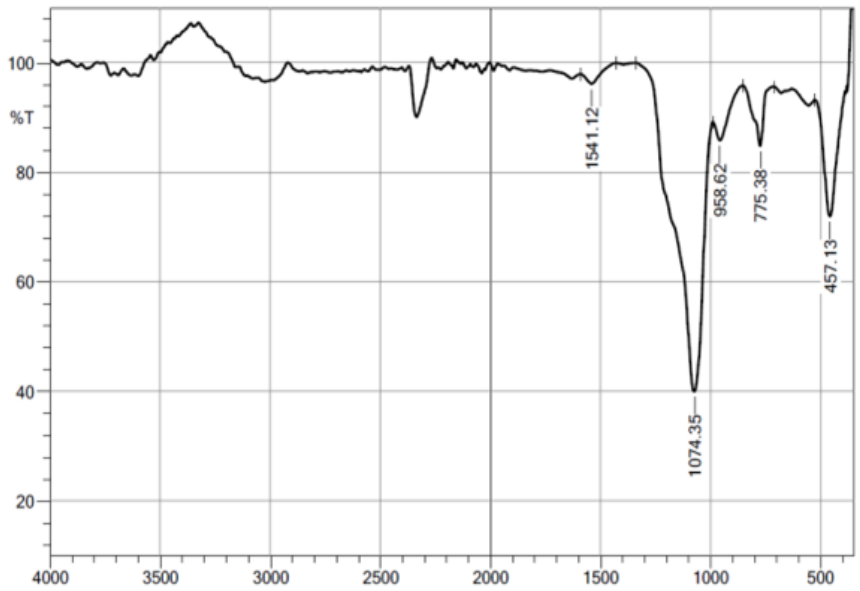


Fig. 5.3: ATR Spectra of AMSX.

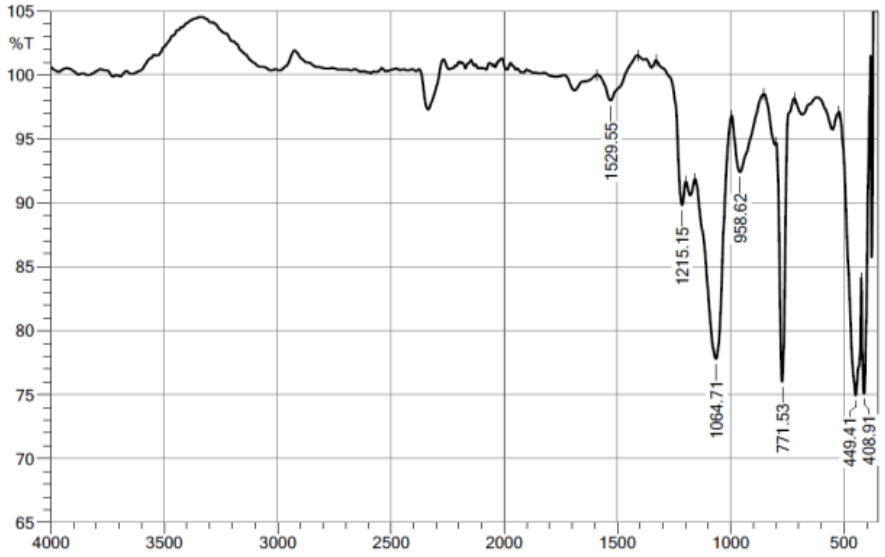


Fig. 5.4: ATR Spectra of NH-AMSX

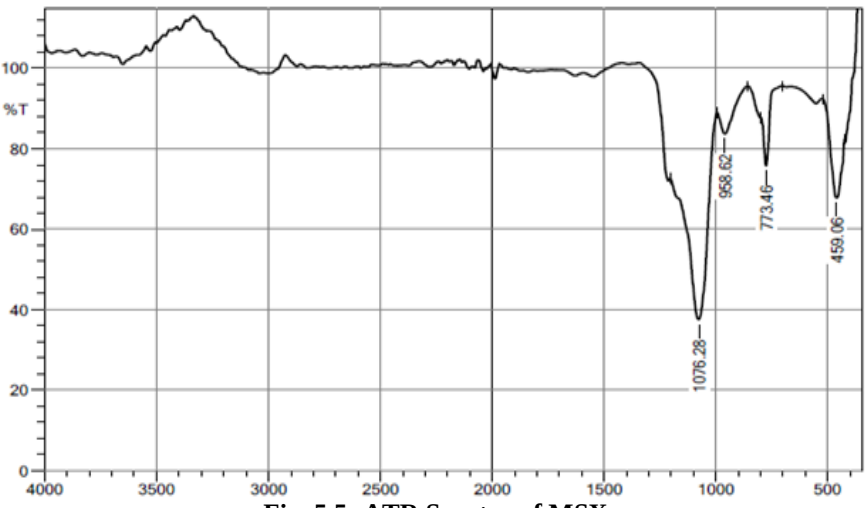


Fig. 5.5: ATR Spectra of MSX.

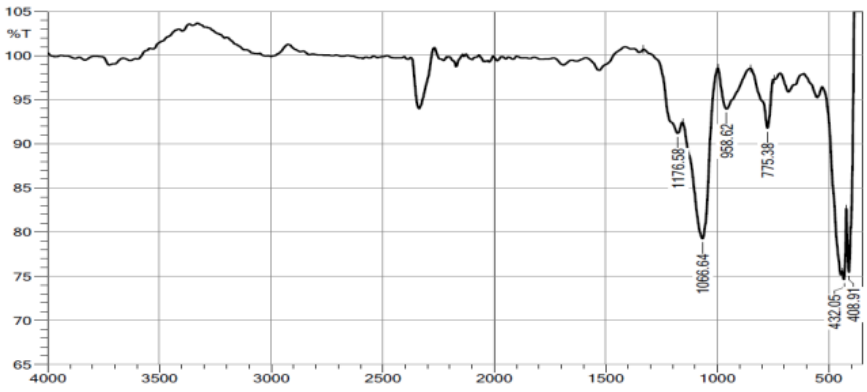


Fig. 5.6: ATR of NH-MSX.

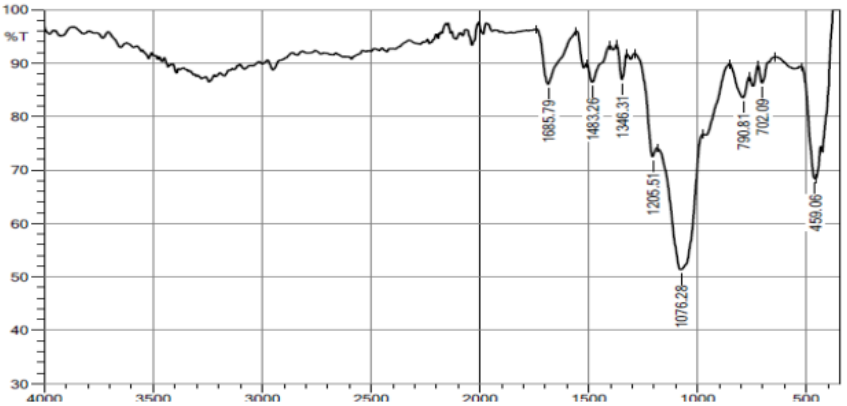


Fig. 5.7: ATR Spectra of NH-PS (1:1).

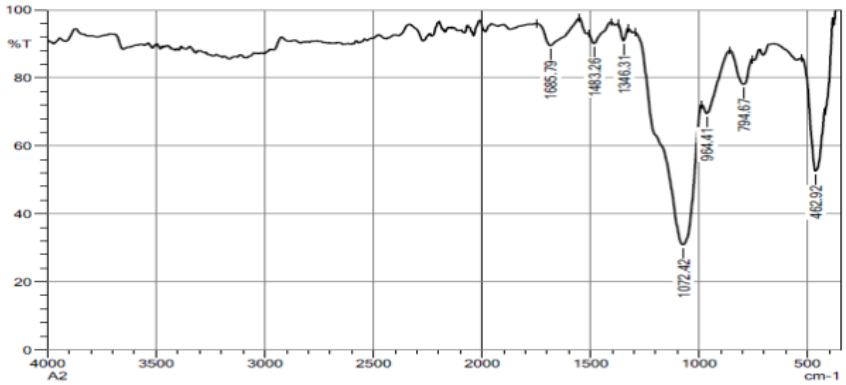


Fig. 5.8: ATR Spectra of NH-PS (1:2).

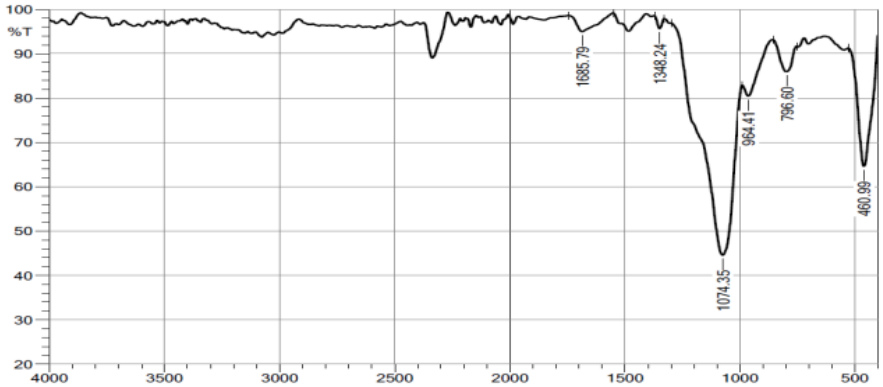


Fig.5.9. ATR Spectra of NH-PS (1:3)

Figure 5: FTIR Spectra of Plain Drug, Plain Carriers And Drug Loaded Carriers.

6.7. *In vitro* dissolution and optimization of formulation parameters

In vitro dissolution was performed and various formulation parameters were optimized based on the drug release. Fig 6. shows the dissolution profile of NH, NH-MSX and NH-AMSX. NH-AMSX shows greater dissolution rate (97.08%) in 40 min as compared to NH-MSX (79.95%).

Fig 7. Shows the dissolution of NH-PS (1:1,:2,1:3) the optimized batch is NH:PS(1:2) which shows the higher dissolution release as compared to other batches (68.33%). From the Fig.8. NH-AMSX shows the greater dissolution as compared to NH-MSX and NH-PS. The reason for improved dissolution of NH was that the mesoporous silica matrix of MSX, AMSX and PS changed solid state of NH from the crystalline state to the amorphous state(DSC and XRD).

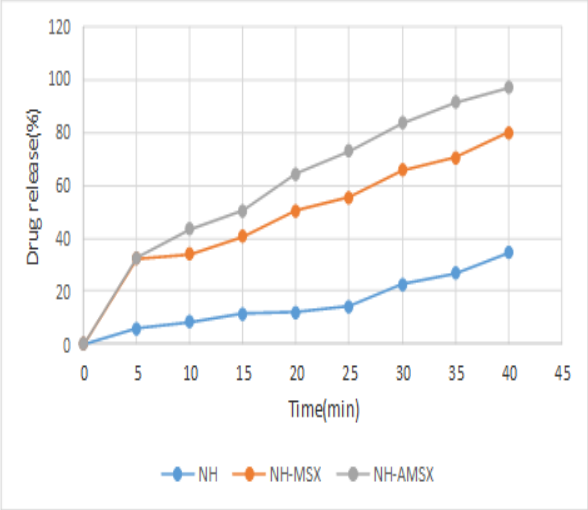


Figure 6: *In vitro* dissolution of NH, NH-MSX, NH-AMSX.

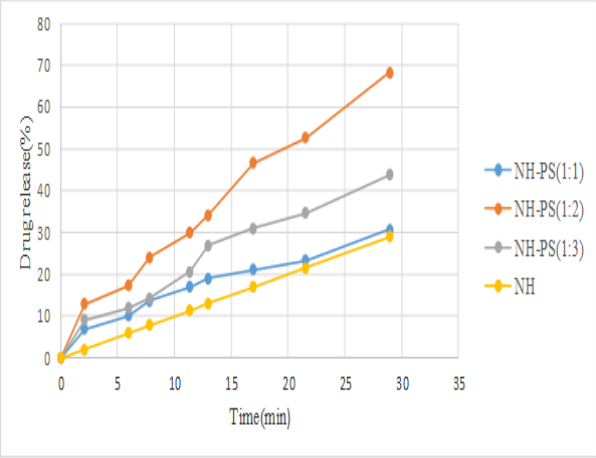


Figure 7: *In vitro* dissolution of NH, NH-PS(1:1,1:2,1:3).

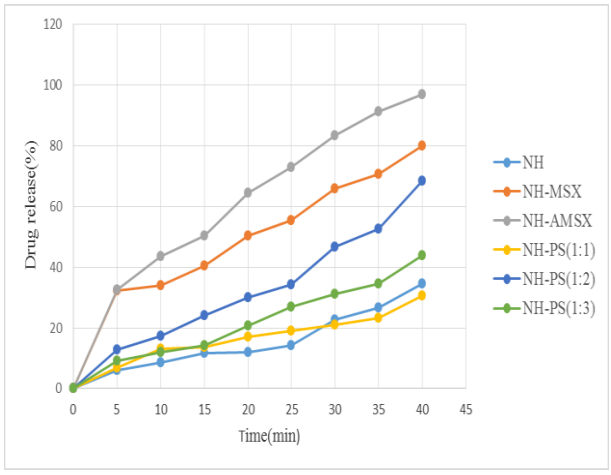


Figure 8: *In vitro* dissolution of NH,NH-MSX,NH-AMSX, NH-PS (1:1,1:2,1:3).

7. CONCLUSIONS

All mesoporous formulations of nicardipine hydrochloride showed improved dissolution than plain drug. AMSX with disordered mesoporous structure had higher NH loading capacity than MSX due to stronger hydrogen bonding force caused by amino modification. The in vitro drug release study revealed that the amino functionalized mesoporous silica xerogel show highest drug release (97.08%) followed by mesoporous silica xerogel (79.95%) and Parteck SLC(1:2) (68.33%).

From XRD study, it can be seen that the mesoporous silica and drug loaded formulation showed no typical crystal peak, which suggest that the drug is converted into amorphous form after it is being loaded in MSX, AMSX and Parteck silica SLC.

The drug loading capacity of NH-AMSX was found to be 31.25% higher than NH-MSX 21.73 % and NH:PS(1:2) 6.88 %.

Hence, AMSX is shows the higher loading capacity and enhanced dissolution release can be considered to be a good candidate as drug carrier for NH.

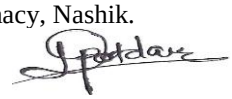
ACKNOWLEDGEMENTS

We are acknowledge to Yarrow chem. to provide chemicals, Pune university for SEM.

Declaration

This thesis is a presentation of my original work. Wherever contributions of others are involved, every effort is made to indicate this clearly, with due reference to the literature, and acknowledgement of collaborative research and discussions.

The work was done under the guidance of Assistant Professor Dr. Mrudula Bele, at the NDMVP Samaj's College of Pharmacy, Nashik.



Dipali potdar

In my capacity as Supervisor of the candidate's thesis , I certify that the above statements are true to the best of my knowledge.

Dr. Mrudula Bele

8. REFERENCES

1. McCarthy C, Ahern R, Dontireddy R, Ryan K, Crean A. Mesoporous silica formulation strategies for drug dissolution enhancement: a review. Expert Opinion on Drug Delivery, Jan 2, 2016; 13(1): 93-108.
2. Tao Z, Toms B, Goodisman J, Asefa T. Mesoporous silica microparticles enhance the cytotoxicity of anticancer platinum drugs. ACS nano, Feb 4, 2010; 4(2): 789-94.
3. Unger K, Rupprecht H, Valentin B, Kircher W. The use of porous and surface modified silicas as drug delivery and stabilizing agents. Drug Dev Ind Pharm., Jan 1, 1983; 9(1-2): 69-91.
4. Kharat R, Bathe R. A Review on: Nicardipine Hydrochloride. Int. J Pharm Biol Sci., 2016; 1(3): 33-7.
5. Aher S, Saudagar R, Shinde M. Formulation and evaluation of fast dissolving tablet of Nicardipine hydrochloride by using solid dispersion technique. The Pharma Innovation Journal, 2018; 7(8): 146-55.
6. Babu N, Umasankar K, Reddy P. Formulation and evaluation of Nicardipine hydrochloride sustained release pellets. Int. Journal of Innovative Pharmaceutical sciences and Research, Mar, 2015; 3(3): 164-75.
7. Kharad S, Tiwari R. Development and validation of HPLC method for nicardipine hydrochloride. Journal of Pharmacy Research, Jul, 2011; 4(7): 2226-7.
8. Hao N, Jayawardana K, Chen X, Yan M. One-step synthesis of amine-functionalized hollow mesoporous silica nanoparticles as efficient antibacterial and anticancer materials. ACS Appl Mater Interfaces, Jan 8, 2015; 7(2): 1040–5.
9. Li J, Xu L, Zheng N, Wang H, Lu F, Li S. Biomimetic synthesized bimodal nanoporous silica : Bimodal mesostructure formation and application for ibuprofen delivery. Materials Science nd Engineering: C., Jan 1, 2016; 58: 1105–11.
10. Kiwilsza A, Milanowski B, Drużbicki K, Coy L, Grzeszkowiak M, Jarek M, Mielcarek J, Lulek J, Pajzderska A, Wasicki J. Mesoporous drug carrier systems for enhanced delivery rate of poorly water-soluble drug: nimodipine. J Porous Mater, Jun 1, 2015; 22(3): 817–29.
11. Owens G, Singh R, Foroutan F, Alqaysi M, Han C-M, Mahapatra C, Kim H, Knoeles J. Sol–gel based materials for biomedical applications. Prog Mater Sci., Apr 1, 2016; 77: 1–79.
12. Kumar S, Malik M, Purohit R. Synthesis Methods of Mesoporous Silica Materials. Materials Today: Proceedings, Jan 1, 2017; 4(2): 350-7.
13. Li J, Xu L, Wang H, Yang B, Liu H, Pan W, Li S. Comparison of bare and amino modified mesoporous silica[@] poly(ethyleneimine)s xerogel as indomethacin carrier: Superiority of amino modification. Materials Science and Engineering: C, Feb 1, 2016; 59: 710-6.
14. Wang X, Li C, Fan N, Li J, Zhang H, Shang L, He Z, Sun J. Amino functionalized chiral mesoporous silica nanoparticles for improved loading and release of poorly water-soluble drug. Asian Journal of Pharmaceutical Sciences, Jul 1, 2019; 14(4): 405-12.
15. Xie X, Li F, Zhang H, Lu Y, Lian S, Lin H, et al. EpCAM aptamer-functionalized mesoporous silica nanoparticles for efficient colon cancer cell-targeted drug delivery. Eur J Pharm Sci., Feb 15, 2016; 83: 28–35.
16. He Y, Liang S, Long M, Xu H. Mesoporous silica nanoparticles as potential carriers for enhanced drug solubility of paclitaxel. Materials Science and Engineering: C., Sep 1, 2017; 78: 12-7.