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Some Studies On Exploring Potential Of Zeolites As A Drug Delivery Carrier.

Gaurav A Mahajan[1]*, and Smita S Pimple[2].

[1]Student, Department of Pharmaceutics, PES's Modern College of Pharmacy, Nigdi, Pune-411044, Maharashtra, India.
[2]Professor, Department of Pharmaceutics, PES's Modern College of Pharmacy, Nigdi, Pune-411044, Maharashtra, India.

ABSTRACT

In this work we used a combination of different techniques to investigate the adsorption properties of various prototype drugs (Atorvastatin Calcium, Metoprolol Succinate & Nabumetone) by zeolite type 4A for potential use as a drug carrier. Zeolites are inorganic crystalline aluminosilicates that have a large internal surface area and a porous structure at the nano and microscales. They can be used as pharmaceutical carrier systems to enhance the dissolution of medications that have a low water solubility by incorporating them. Here, we used SEM, PXRD, thermo gravimetric analysis (TGA), and UV-vis spectroscopy to investigate the surface properties and morphology of zeolite type 4A before and after loading of the antihyperlipidemic, antihypertensive, and NSAID (Non-Steroidal Anti-Inflammatory Drug) agent. The findings are utilized to evaluate the zeolite type 4A's loading efficiency and its post-loading structural stability. CCD (Central Composite Design) was utilised for optimization which concludes that drug to carrier ratio of 1:2 while poloxamer concentration of 0.10%w/v found to be optimum. Test formulations showed sustained drug release profile of upto 10 hours when compared with marketed ones.

Keywords: Carrier, Zeolite 4A, Central Composite Design, Drug release

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Corresponding author

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INTRODUCTION

When compared to conventional pharmacological treatments, drug delivery systems have demonstrated increased efficiency; yet, certain obstacles and restrictions still exist. Developing innovative drug delivery methods, like those based on inorganic molecular carriers, might be very helpful in resolving these issues [1,2]. Zeolite structures are among the inorganic drug carriers that have been the subject of many investigations because of their special qualities, which include high adsorption capacity and specific surface area, water solubility, strong biocompatibility, and stability in biological contexts [12,13].

Zeolites, which have a high internal surface area and a porous structure on the micro-and nanoscale, are inorganic crystalline aluminosilicates that are widely used as ion exchange materials, molecular sieves, and adsorbents in various applications. Zeolites have lately shown great promise in the medical and pharmaceutical domains because of their bioactive qualities and strong durability in biological sites [2,7,11].

In nature, aluminosilicate minerals are the form of many zeolites, and over 200 synthetic zeolites can be created in a lab. The structure of each zeolite framework is distinct and is often composed of silicon, aluminium, and oxygen atoms. Connectivity between $[SiO4]4-$ and $[AlO4]5-$ units arranges the building blocks in a periodic pattern to create cages and channels that give the material its distinctive microporous structure. Zeolites' distinct set of characteristics has led to a variety of medical uses for them, including as the transport and encapsulation of medications with antibacterial, anticancer, and antibiotic qualities [16,17]. With regard to drug delivery, a patient receiving cancer therapy, for example, could receive zeolitic structures loaded with drugs without losing the unique pharmacological effects of the medications [18].

This study examines the capacity of synthetic zeolite 4A, a Na+ exchanged variant of zeolite LTA (Figures 1 & 2), to bind the prototype medications, which are widely recognized for their medicinal properties. With an effective pore opening of approximately 4 Å and Na+ ion acting as a coordinating cation in its structure, zeolite 4A provides a more consistent and reliable drug delivery system. [19,20].

MATERIALS AND METHODS

Zeolite 4A and Pluronic F-127 (Poloxamer) were obtained from Sigma Aldrich. Atorvastatin Calcium, Metoprolol Succinate & Nabumetone were obtained as free gift sample from Accent Pharma, Cipla & Micro Labs Ltd India respectively. Every excipient and solvent used was of analytical grade.

Method of Formulating Drug Loaded Zeolite

Prior to formulation, carrier zeolite 4A is activated by placing it in muffle furnace with the help of guch crucible. Generally solvent evaporation method is employed. This activated zeolite along with Atorvastatin Calcium and poloxamer were mixed in dichloromethane which then evaporated to obtain crude powder. Finally, capsule was filled with other ingredients like magnesium stearate & microcrystalline cellulose. Same process is used for remaining two drugs i.e. Metoprolol Succinate & Nabumetone [17,18].

Preformulation Studies

The physicochemical characteristics of the drug and excipients are described by preformulation studies in order to create a stable, dependable, and safe dosage form. Preformulation studies include organoleptic properties, solubility, UV spectroscopy, melting point determination & compatibility studies (FTIR) [3-6,8,9].

Organoleptic properties

Drugs namely Atorvastatin Calcium (AC), Metoprolol Succinate (MS) & Nabumetone (NU) were observed for its colour, odour and appearance by visual observation.

UV-Visible spectroscopy

Calibration curves for all 3 drugs were performed in PBS pH 6.8 to obtain the equation and R^2 value.

Preparation of stock solution

Stock solution was prepared for concentration of 100 and 1000 µg/ml to find out fixed wavelength where the maximum peak is obtained [14].

Procedure for calibration curve of AC, MS & NU

After getting fixed wavelength different dilutions (i.e. 5, 10, 15, 20, 25 µg/ml) were prepared from the stock solution of 100 µg/ml in to a 10ml volumetric flasks. The final volume was made by the PBS pH 6.8 solvent used and absorbance was measured at 245nm, 255nm & 340nm for AC, MS & NU respectively by using Shimadzu UV-1800 UV-visible spectrophotometer with quartz cells of 10mm path length [13-15].

Experimental Work

Preliminary Study

This screening is carried out to see how different ratios of drug to carrier affected the formulation of drug loaded zeolite as shown in Table 3 & 7. These trial batches are evaluated for different parameters like particle size, zeta potential, in-vitro dissolution study and loading efficacy [17-19]. On the basis of this parameters the suitable ratio of drug to carrier is selected for further formulation. From this it was concluded that 1:2 or 1:5 could be better for optimization so taken forward [38-40].

Formulation of Drug Loaded Zeolite by Solvent Evaporation Method [10,18]

- API i.e. Atorvastatin Calcium (40mg), Activated Zeolite 4A (80mg) and Poloxamer F-127 (30mg) were dissolved in dichloromethane.
- The above mixture was stirred for few minutes & kept aside for evaporation by covering with fine sieve on beaker.
- The crude product was obtained by scrapping and allowed to dry in oven to remove volatile content (if any).

Same process has been applied for another two API namely Metoprolol Succinate & Nabumetone

Formulation and optimization of Solid dispersion

The optimization of solid dispersion was performed by central composite design [25]. A 150 mg solid dispersion was prepared by solvent evaporation method utilizing dichloromethane as solvent [10]. Ingredients used in formulation were Zeolite-4A as a carrier and Pluronic F-127 as stabiliser. Microcrystalline cellulose & magnesium stearate were other excipients for capsule filling (Shown in Table 8 & 9).

Name of design

Central Composite Design (CCD)

Independent variables

- A: API to Carrier Ratio
- B: Concentration of Poloxamer F-127 (%)

Dependent variables

- Y1: Particle Size,

- Y2: Zeta Potential &
- Y3: % CDR

Evaluation of batches

By applying Central Composite design about 13 experimental runs were obtained and particle size, zeta potential & % CDR were taken as response variable [20-23].

Particle Size

- 3 formulations from each run were evaluated for particle size and the result was noted down.
- 10mg powder of product was utilized for this test.

Zeta Potential

- About 3 formulations of each drug containing zeolite of each run were evaluated for this test
- Zeta Potential was noted for each run

% CDR

- Dissolution Medium: 900 ml of Phosphate Buffer Solution (pH 6.8)
- Temperature: 37±1^{o}C
- Speed: 50 rpm
- Dissolution apparatus: USP Type-I (Basket Apparatus)

Selection and detail evaluation of optimized batch physical mixture

From the 13 runs the optimized batch was selected and the composite mixture of the optimized batch was further evaluated [25].

Particle Size

This was determined by using Horiba Analyser Instrument. 10mg of product was dissolved in 10 ml of solvent. From this 1 ml of formulation was diluted with 10 ml distilled water and was poured into the polystyrene cuvette which was placed in thermostatic chamber maintained at 25^{0}C. Detection was carried out at scattering angle of 90^{o} [20]

Zeta Potential

Zeta potential of the formulation was determined by dynamic light scattering using particle size analyzer (Horiba). The samples were diluted with a ratio of 1:10 (v/v) with distilled water [21].

In-Vitro Dissolution Study

The dissolution study of the prepared drug loaded zeolite was performed by using USP type-I dissolution apparatus i.e. Basket. Capsule (filled with 100 mg of product) was placed in dissolution vessel and the dissolution study was carried out at 37 ± 1°C using 900 ml of phosphate buffer solution (pH 6.8) as the dissolution medium. 5 ml of sample was withdrawn periodically at 15 min, 30 min, 60 min, like that up to 10 hours and each sample is replaced with equal volume of fresh dissolution medium in order to maintain sink condition [22-23]. Samples were analyzed by UV spectrophotometer at 245 nm, 255 nm and 340 nm for AC, MS & NU release respectively (Table 11, 12 & 13)

PXRD (Powder X-ray Diffraction)

X-ray diffraction patterns for the empty and drug loaded zeolite were obtained with a Rikagu (Ultima IV X-ray diffractometer, SPPU, Pune, India). All samples were analyzed in powder form [29]. With a counting time of two seconds, diffraction data were gathered in the 2θ range, which spans 5° to 80° and corresponds to a scan speed of 10 degrees per minute.

TGA (Thermo Gravimetric Analysis)

Drug content in the Zeolite 4A formulation was additionally quantified with thermogravimetric analysis using a TA Instruments Trios V4.4.0.41128. Samples (Drug with Zeolite 4A) were analyzed in N2 atmosphere at a heating rate of 10°C/min & in the temperature range from 0°C to 800°C [30].

SEM (Scanning Electron Microscopy)

The shape and surface morphological properties of empty carrier i.e. zeolite 4A and drug (Atorvastatin Calcium, Metoprolol Succinate & Nabumetone) loaded zeolite were examined by Scanning Electron Microscopy (SPPU JEOL JSM 6360A, India). Dry zeolite 4A & product powder is sprinkled lightly on double adhesive tape which is stuck to an aluminium stub which was then placed in the SEM chamber and scanned. After that the photomicrographs taken at magnification 300x, 1000x & 10000x [26,27].

FTIR (Fourier Transform Infrared Spectroscopy)

The IR study of drug loaded zeolite was performed using potassium bromide (KBr) as blank. The samples to be analyzed and KBr were previously dried in the oven for 30 min and mixed thoroughly in 1:100 (sample : KBr) ratio in a glass mortar. These samples were then placed in a sample holder and scans were obtained at a resolution of 2cm-1 from 400 to 4000 cm-1 [35-37]

Loading Efficiency

Drug content in the Zeolite formulations was quantified using the extraction method described below. 10mg of sample was dispersed in 10 mL of PBS pH 6.8 and was magnetically stirred for 24h at 37°C. Dispersions centrifuged for 15 min, at 4500 rpm, supernatants filtered through a whatman filter of 0.45µm pore size and drug content was quantified with UV spectroscopy (UV Jasco V-630) at 245 nm, 255 nm and 340 nm respectively [29,30] (Table 10)

Drug loading efficiency was calculated according to following equation:

$$\text{Drug Loading Efficiency (\%)} = \frac{\text{Weight of drug in the particles}}{\text{Weight of particles}} \times 100$$

Drug content

The powder of drug loaded zeolite equivalent to 10 mg drug was dissolved in 100ml of water. One ml of above solution was withdrawn and volume was made up to 10 ml [28]. The absorbance was measured at 245, 255 & 340 nm against the PBS pH 6.8 as blank solution by using UV Spectrophotometer (Table 10).

Docking study

For this Atorvastatin calcium complexed with zeolite was taken as ligand while SARS CoV-2 was taken as receptor. The structures were generated initially in the 2D form utilizing Chemdraw® Ultra software. LigPrep program of the Maestro 9.1 software was employed in preparing the ligands for molecular docking study. The receptor co-crystal structures of COVID-19 main protease in complex with an inhibitor N3 (PDB ID: 6LU7) was obtained from the RCSB Protein Data Bank. The protein structures were prepared using Protein Preparation Wizard of Maestro 9.1 [31].

Stability study

On the basis of ICH-Q1A guidelines, the stability testing of optimized drug loaded zeolite batch formulation was performed [32-34]. The optimized samples were kept in air tight amber coloured glass container for 1 month to perform accelerated stability study. Factors like appearance, average weight & moisture content were evaluated after 1 month of time period (Table 15).

RESULTS AND DISCUSSION

Preformulation studies

Identification of drug

Organoleptic properties, solubility and melting point of AC, MS & NU

The organoleptic properties, solubility & melting point are summarized in (Table 1).

UV-Visible Spectrophotometry

Calibration curve for AC, MS & NU were performed in PBS pH 6.8. According to Beer-Lambert's law, the absorption maximum was observed at 245nm for AC, 255nm for MS & 340nm for NU. Absorbance data and calibration curves for AC, MS & NU in PBS pH 6.8 are given in following (Table 2 and Figure 3,4,5).

Result & Discussion For Formulation And Evaluation of Drug Loaded Zeolite

Evaluation of batches

13 runs obtained by applying central composite design were further evaluated for their particle size, zeta potential & % CDR. Run 1 (Batch Code F1) results were found to be relatively good as compare to other runs as shown in (Table 9). From this run 1 was found to be the optimized batch.

Particle size distribution

Particle size of optimized drug loaded zeolite formulations was found to be 90.9 nm (Atorvastatin Calcium), 70.8 nm (Metoprolol Succinate) & 122.8 nm (Nabumetone) respectively i.e. size is in the range specified for nanocarriers (Shown in Table 10 & Figure 7,8,9).

Zeta Potential

Zeta potential of the optimized drug loaded zeolite batch was found to be -23.7 mV (AC), - 16.1 mV (MS) & -11.3 mV (NU) respectively. The values were found in the standard range hence it can be concluded that the optimized batch is stable (Shown in Table 10 & Figure 10,11,12).

In vitro drug release kinetics for optimized batch of solid dispersion (Run 1)

The potential of solid dispersion to modulate drug release is shown by their in vitro release kinetics, which is an important metric to take into account when evaluating the products' safety, effectiveness, and quality. (Table 14) shows the drug release kinetics [41-49].

Comparative study of formulated capsule with the marketed formulation

For marketed comparison, Ecosprin 40/75 AV (USV Pvt Ltd) contains 40mg Atorvastatin Calcium & Metolar XR 50 (Cipla) contains 50mg Metoprolol Succinate were taken as reference brands for drug release comparison. It has shown drug release occurred upto 8 hours in marketed ones while test formulations showed upto 9-10 hours (Shown in Table-11,12 & Figure 16 & 17).

FTIR (Fourier Transfer Infrared Spectrophotometer)

FTIR spectra of pure drug and drug loaded zeolite were evaluated (Shown in Table 4,5,6 & Figure 6). The FTIR study for both pure drug & solid dispersion was carried out and the observed peaks were noted. The peaks of the drug were retained in the solid dispersion formulation as in pure drug, which indicates drug and excipients were found to be compatible with each other [35- 37].

PXRD Study

Figure 18 displays all of the distinctive peaks for both the drug and zeolite 4A. It is evident from XRD that the framework has not altered. Peak intensity decreases after drug adsorption indicated a slight drop in zeolite crystallinity.

TGA Study

Thermogravimetric analysis (TGA) profile of product is shown in figure 20. It can be observed a first weight loss in the temperature range 50-100^{o}C corresponding mainly to volatile content & water desorption and a second step between 100 and 400^{o}C attributed to the decomposition and combustion of the organic fraction (drug). From the weight loss calculated for both steps, about 42-77% w/w drug presence on the surface of zeolite. This may be due to the interaction between silanol groups and carbonyl/hydroxyl groups of AC, MS & NU.

Scanning Electron Microscopy (SEM)

Morphological characteristics of empty zeolite & drug loaded zeolite were observed using SEM analysis. SEM photomicrograph of optimized formulation at magnification 300x & 1000x as shown in figure 19. On the basis of SEM results it can be evident that drug has been loaded on zeolitic surface and average size was found between 10-50 microns.

Docking Study

As per the docking study & binding energy (Shown Figure 21 & Table 16), it can be evident that the ligand Atorvastatin has higher affinity towards SARS-CoV 2 receptor than zeolite than complex. So from this it is clear that atorvastatin has more than 1 target i.e. HMG-CoA reductase enzyme & SARS-CoV 2 receptor.

Stability studies

Stability testing under expedited circumstances the optimized solid dispersions were demonstrated to be stable over a one-month period at 40°C±2°C/75%RH±5%RH relative humidity by the lack of substantial alterations in their physical characteristics and in the following parameters (Figure 22)

CONCLUSION

Solid dispersions of drug loaded zeolite proved to be one of the successful approaches to overcome the problem associated with conventional drug delivery (like low bioavailability & frequent dosing); also which enhances patient compliance and sustained drug release profile. Atorvastatin Calcium, Metoprolol Succinate & Nabumetone were loaded onto the zeolitic surface for enhanced drug release. Central composite design was employed for optimization study. Particle size, zeta potential & % drug release were crucial response parameters. Results are encouraging with respect to zeolite solid dispersion. Optimized batch showed better & sustained drug release as compared to marketed formulations. The optimized batch's stability study yielded satisfactory results as well. Main building blocks adopted in this work are molecular weight, hydrophobicity, functional groups & drug:carrier ratio; these could be explored in depth in addition with others to get more insights in zeolites. Study has wide future scope with respect to methods of preparation, incorporation & physicochemical properties of drug such as solubility, polymorphism, etc. Potent drugs with complex metabolism can be tried to deliver using this carrier.

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For providing all laboratory facilities needed to conduct this research, the authors are grateful to the Department of Pharmaceutics at PES's Modern College of Pharmacy, Nigdi, Pune.

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Table 1: Preformulation Study of AC, MS & NU

Parameter	Observation		
	AC	MS	NU
Physical description	Solid	Solid	Solid
Structure	Crystalline	Crystalline	Crystalline
Colour	White	White	White
Odour	Odourless	Odourless	Odourless
Taste	Unpleasant taste	Unpleasant taste	Unpleasant taste
Solubility	Soluble in organic solvent (Dichloromethane)	Soluble in organic solvent (Dichloromethane)	Soluble in organic solvent (Dichloromethane)
Melting point	164±2°C	138±2°C	80±2°C

Table 2: Concentration vs Absorbance values for development of standard curve in PBS pH 6.8

Conc. (µg/ml)	AC i) Abs (245 nm)	MS ii) Abs (255 nm)	NU iii) Abs (340 nm)
5	0.38	0.14	0.09
10	0.65	0.28	0.18
15	0.98	0.41	0.26
20	1.22	0.51	0.35
25	1.52	0.68	0.43

Table 3: Preliminary trial batches for optimum drug to carrier ratio

Batch Code	Drug to Carrier Ratio
B1	1:1
B2	1:2
B3	1:5
B4	1:10

Table 4: FTIR Spectra Elucidation of AC loaded zeolite

Functional Group	Observed Value (cm-1)	Reference Value (cm-1)
Al-O	716	700-800
Si-O	946	900-1000
C=O	1665	1650-1800
C-H (Aliphatic)	2927	2850-2980
C-H (Aromatic)	3067	3000-3100
O-H	3630	3500-3700

Table 5: FTIR Spectra Elucidation of MS loaded zeolite

Functional Group	Observed Value (cm-1)	Reference Value (cm-1)
Al-O	808	700-800
Si-O	966	900-1000
C-H (Aliphatic)	2973	2850-2980
N-H	3273	3100-3300
O-H	3584	3500-3700

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Table 6: FTIR Spectra Elucidation of NU loaded zeolite

Functional Group	Observed Value (cm-1)	Reference Value (cm-1)
Al-O	716	700-800
Si-O	946	900-1000
C=O	1767	1650-1800
C-H (Aliphatic)	2896	2850-2960
C-H (Aromatic)	3053	3000-3100

Table 7: Preliminary trial batches for selection of drug to carrier ratio

Preliminary Study					
Batch Code	Drug to Carrier Ratio	Particle Size (nm)	Zeta Potential (mV)	% CDR	Loading Efficiency (%)
B1	01:01	350.5	-10.9	90	50
B2	01:02	90.9	-23.7	32	80
B3	01:05	283.1	-36	23	70
B4	01:10	400.8	-15.6	10	45

Table 8: Capsule filling formula

Sr No	Ingredient	Amount (mg)
1.	Crystallized Powder (Atorvastatin-Zeolite Dispersion)	80
2.	Magnesium Stearate	10
3.	Microcrystalline Cellulose	10

Table 9: Composition of different batches of Atorvastatin Calcium loaded zeolite using CCD

Sr. No.	Batch Code	A: API to Carrier Ratio	B: Conc. of Poloxamer F-127 (%)
1	F1	2	0.1
2	F2	5	0.1
3	F3	2	0.25
4	F4	5	0.25
5	F5	1.37868	0.175
6	F6	5.62132	0.175
7	F7	3.5	0.068934
8	F8	3.5	0.281066
9	F9	3.5	0.175
10	F10	3.5	0.175
11	F11	3.5	0.175
12	F12	3.5	0.175
13	F13	3.5	0.175

Table 10: Summary of evaluated parameters of optimized batch F1 with SD (Standard Deviation)

Sr. No.	Formulation	Particle Size (nm) Mean±SD	Zeta Potential (mV) Mean±SD	Drug Loading (%) Mean±SD	Drug Content (%) Mean±SD
1	AC+Zeolite 4A	92.63±2.12	-23.4±0.80	80.5±1.80	76.33 ±1.53
2	MS+Zeolite 4A	72.93±2.1	-15.56±0.61	72.5±0.5	73.9 ± 1.1
3	NU+Zeolite 4A	122.37±2.08	-12.16±0.70	71.3±1.13	72.13 ± 0.71

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Table 11: In-vitro drug release of test vs marketed formulation Ecosprin 75/40 AV

Time (Hr)	% CDR (Zeolite+AC)	% CDR Marketed (Ecosprin 75/40 AV)
0.25	0.8	8.2
0.5	2.9	15.0
1	9.3	22.9
2	19.7	31.0
3	26.2	41.7
4	37.7	51.8
5	59.8	63.0
6	78.1	77.0
7	88.4	93.0
8	94.9	101.1
9	97.4	-
10	100.3	-

Table 12: In-vitro drug release of test vs marketed formulation Metolar XR 50

Time (Hr)	% CDR (Zeo+MS)	% CDR Marketed (Metolar XR 50)
0.25	3.4	13.3
0.5	10.9	26.5
1	18.5	27.6
2	21.9	29.8
3	29.5	33.3
4	41.3	45.2
5	53.8	57.2
6	86.4	71.1
7	98.2	87.0
8	101.6	97.9
9	-	101.3

Table 13: In-vitro drug release of NU loaded zeolite in PBS pH 6.8

Time (Hr)	% CDR (NU) loaded Zeolite
0.25	6.6
0.5	18.5
1	26.5
2	39.7
3	47.6
4	62.2
5	78.1
6	88.7
7	96.6
8	101.1

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Table 14: Drug Release Kinetics profile of drugs

Batch Code	Model					Best Fit Model
	1st Order	Zero Order	Higuchi Plot	Korsmeyer-Peppas Plot		
	R^2	R^2	R^2	R^2	n	
AC (F4)	0.8949	0.9693	0.9496	0.9846	1.29	KP Plot
MS (F4)	0.9999	0.9581	0.8879	0.9571	1.16	1st Order
NU (F4)	0.8883	0.9333	0.9857	0.9757	0.727	Higuchi Plot

Table 15: Storage conditions for stability study of drug loaded zeolite

Study	Storage conditions	Time period
Accelerated	40°C ± 2°C & 75% RH ± 5% RH	1 month

Table 16: Binding energies of various ligands on SARS CoV-2 receptor

Sr. No.	Molecule	Binding Energy (Gscore)
1	Atorvastatin Calcium	-6.8482
2	Zeolite	-3.9174
3	Complex	-2.4633

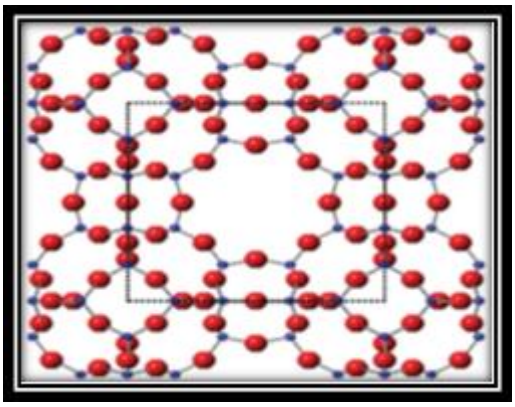

Figure 1: Zeolite Linde type A (LTA) framework Red: Oxygen atoms; Blue: Si/Al atoms

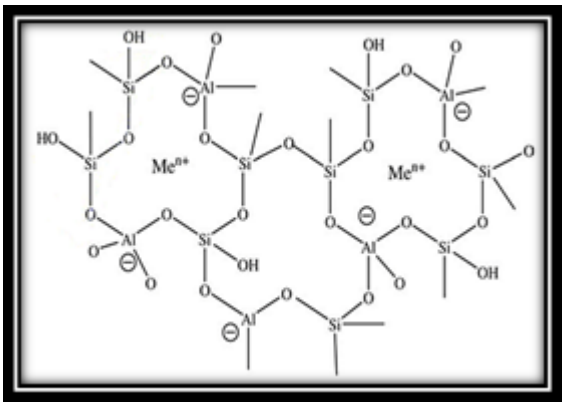

Figure 2: Chemical Structure of Zeolite

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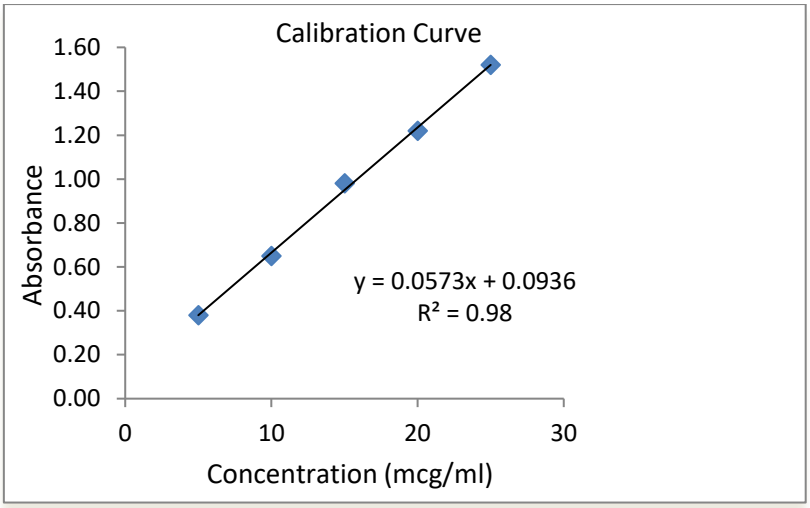

Figure 3: Calibration curve of AC in PBS pH 6.8

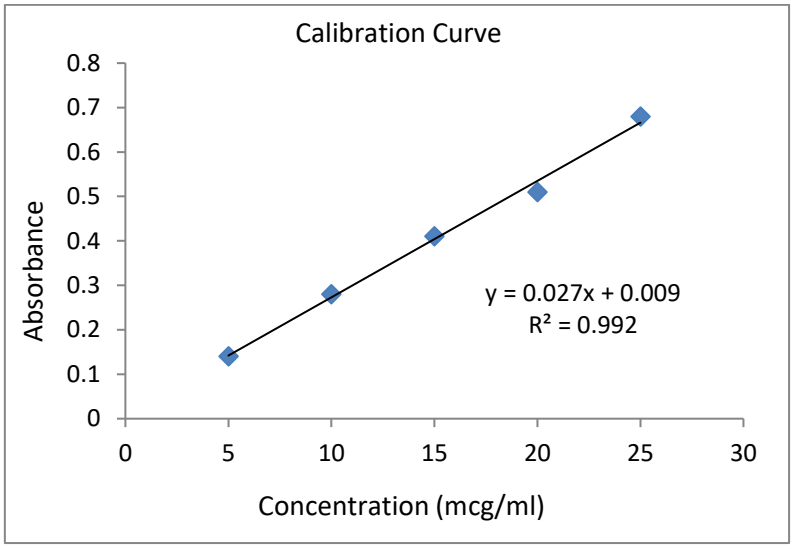

Figure 4: Calibration curve of MS in PBS pH 6.8

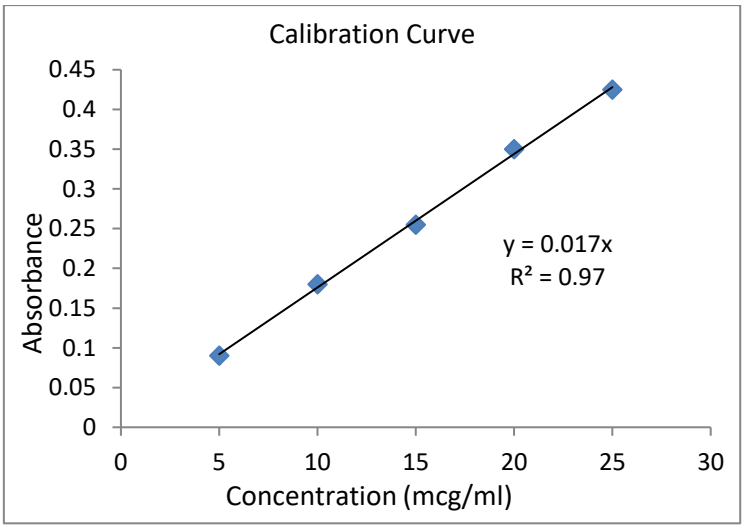

Figure 5: Calibration curve of NU in PBS pH 6.8

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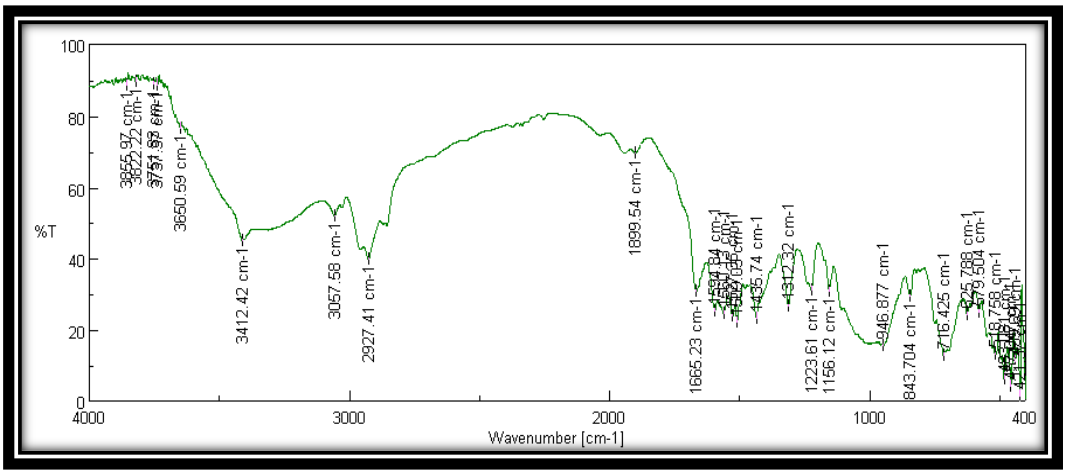

Figure 6: FTIR spectra of Atorvastatin Ca loaded Zeolite

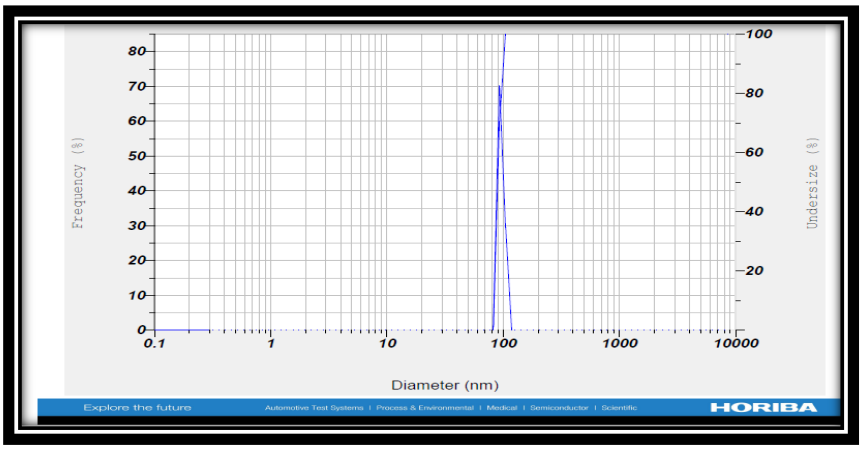

Figure 7: Particle size of optimized F1 AC loaded zeolite

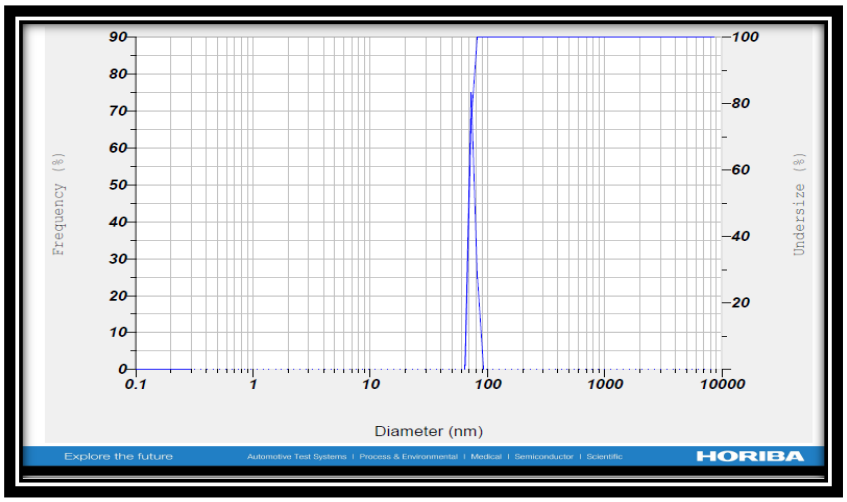

Figure 8: Particle size of optimized F1 MS loaded zeolite

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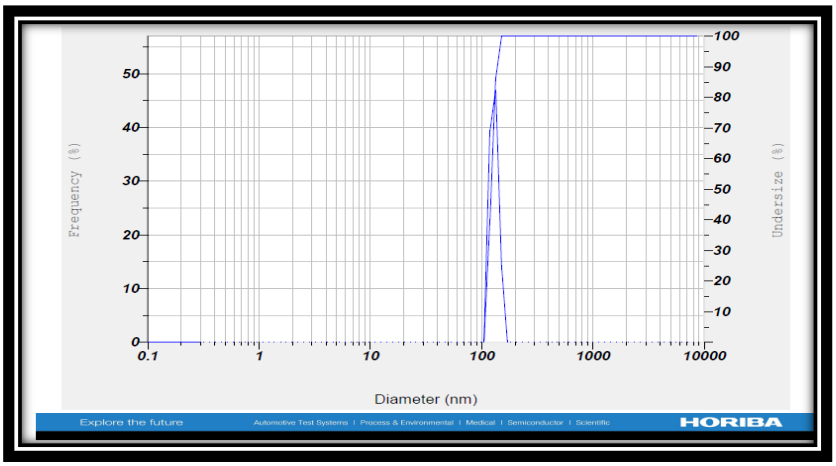
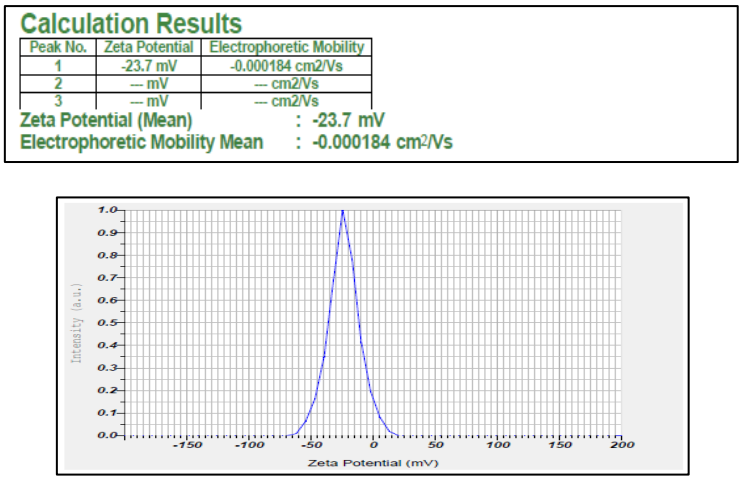


Figure 9: Particle size of optimized F1 NU loaded zeolite

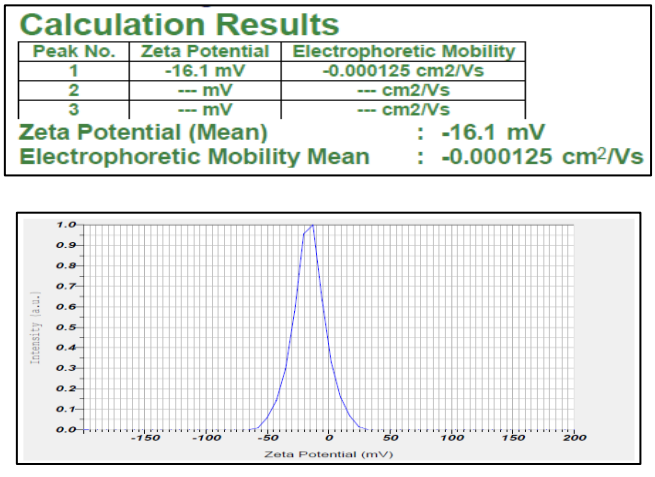


Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-23.7 mV	-0.000184 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -23.7 mV
Electrophoretic Mobility Mean : -0.000184 cm^2/Vs

Figure 10: Zeta Potential of optimized F1 AC loaded zeolite



Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-16.1 mV	-0.000125 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -16.1 mV
Electrophoretic Mobility Mean : -0.000125 cm^2/Vs

Figure 11: Zeta Potential of optimized F1 MS loaded zeolite

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Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-11.3 mV	-0.000088 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -11.3 mV

Electrophoretic Mobility Mean : -0.000088 cm^2/Vs

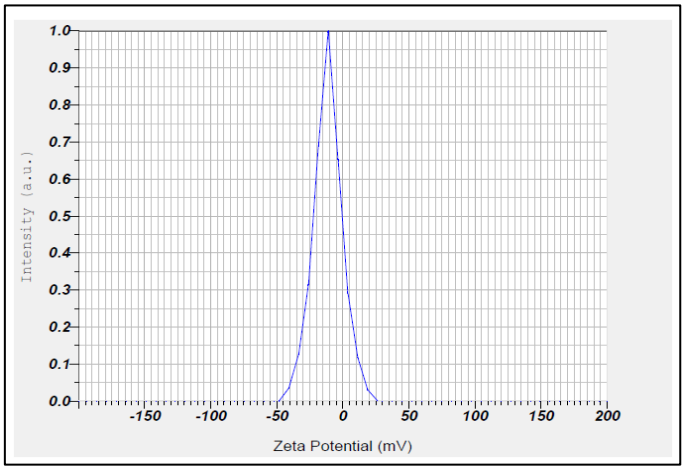

Figure 12: Zeta Potential of optimized F1 NU loaded zeolite

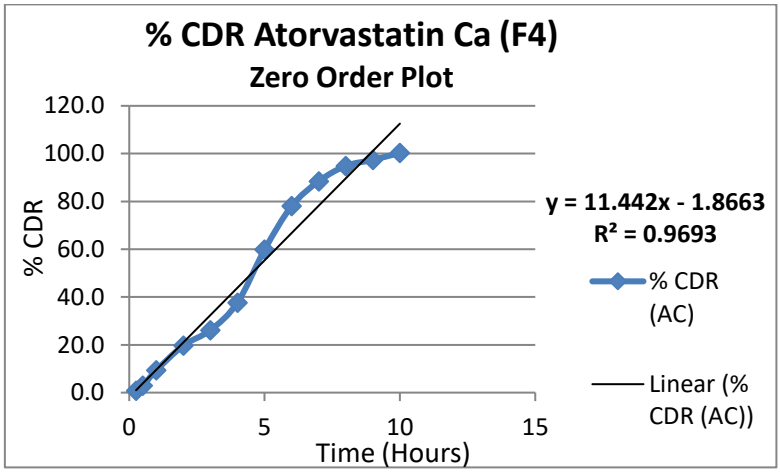

Figure 13: In-vitro drug release study of AC loaded zeolite in PBS pH 6.8

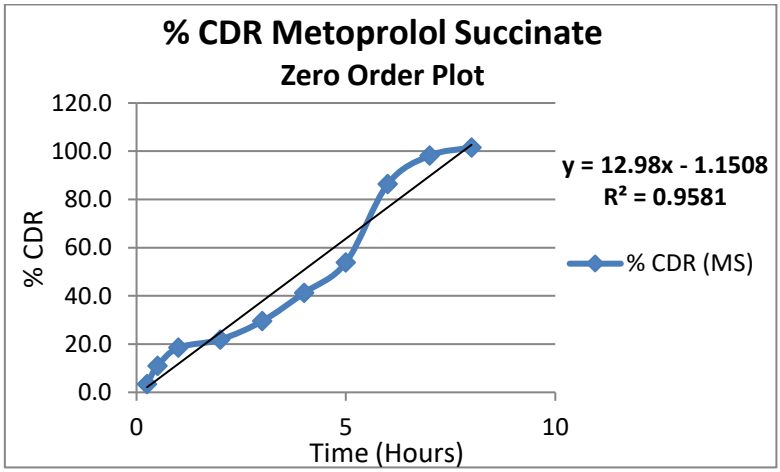

Figure 14: In-vitro drug release study of MS loaded zeolite in PBS pH 6.8

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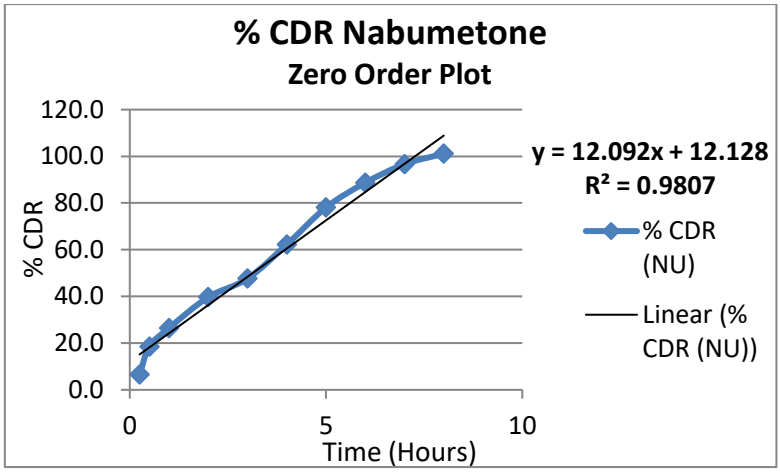

Figure 15: In-vitro drug release study of NU loaded zeolite in PBS pH 6.8

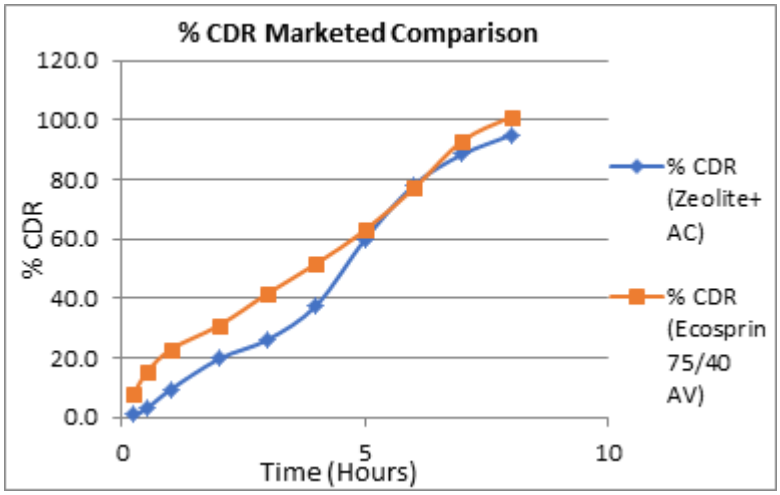

Figure 16: %CDR of Ecosprin 75/40 AV (Marketed) vs Test Formulation

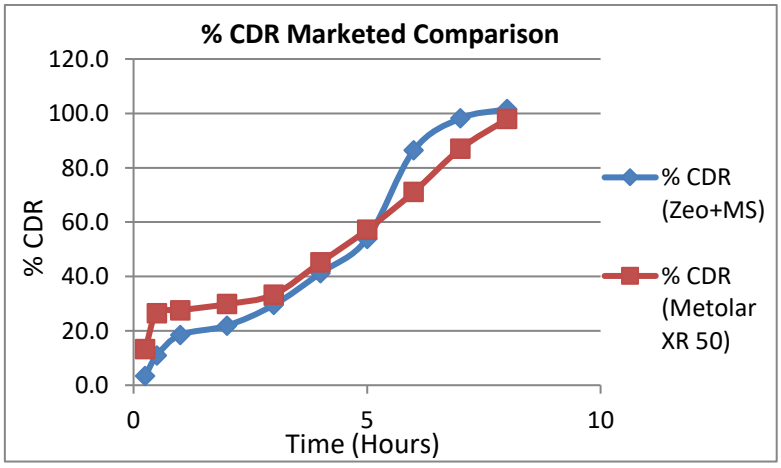

Figure 17: %CDR of Metolar XR 50 (Marketed) vs Test Formulation

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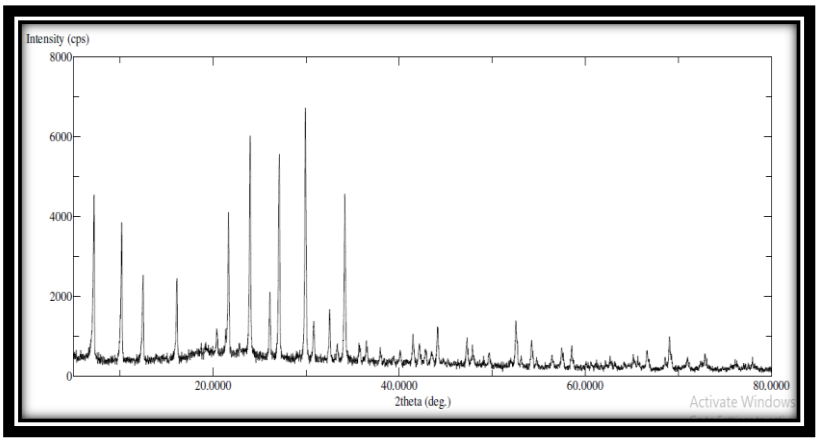

Figure 18: PXRD graph of AC loaded zeolite

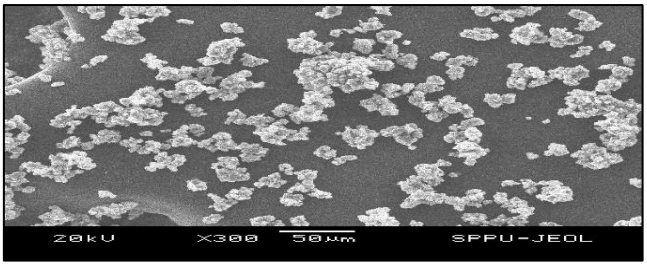

Figure 19: SEM image of AC loaded zeolite

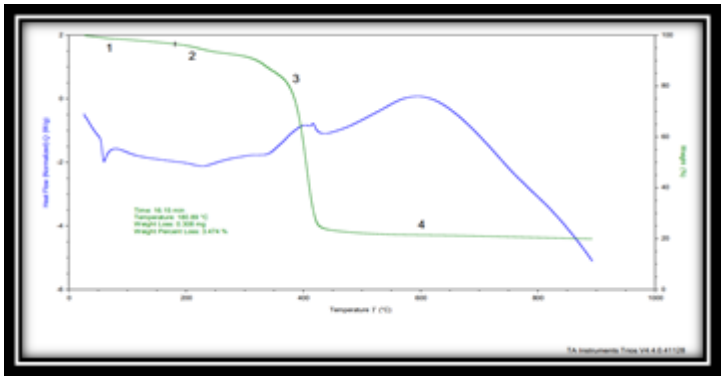

Figure 20: TGA of AC loaded zeolite

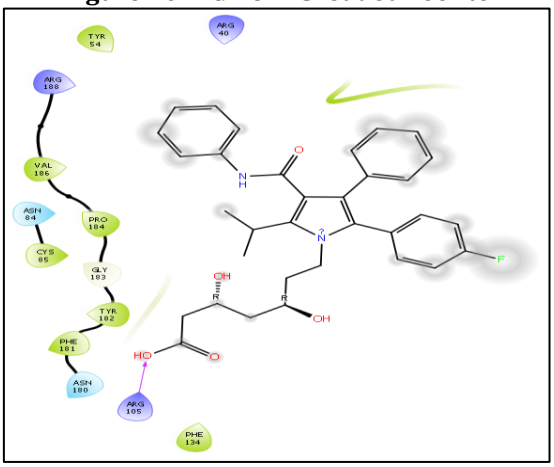

Figure 21: Docking site of Atorvastatin Calcium with receptor SARS CoV-2

Sr No	Parameters	Before Stability Study			After Stability Study		
		AC	MS	NU	AC	MS	NU
1	Appearance	Powder	Powder	Powder	Powder	Powder	Powder
2	Average Weight (mg)	100	100	100	99.5	99.2	99.1
3	Moisture Content (%)	4.50	5.00	4.74	4.45	4.90	4.40

Figure 22: Stability study of drug loaded zeolite at storage condition of 40°C±2°C/75%RH±5%RH

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