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Preparation and Evaluation of Cyclodextrin based Atorvastatin Nanosponges

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ABSTRACT

Cyclodextrin nanosponges are solid, porous, bio-compatible, nano-particulate three dimensional structures which form inclusion complexes with different types of lipophilic or hydrophilic drug molecules and have been used as drug carrier for different drugs. In this present work, new cyclodextrin-based nanosponges of atorvastatin were prepared by condensation polymerization and interfacial polymerization to release Atorvastatin in expected manner in the treatment of dyslipidaemia as novel carriers. Results of encapsulation efficiencies of all formulation trials revealed that condensation polymerization is the best method for nanosponges formation and that is considered as best selected method for preparation. For the selected condensation polymerization, encapsulation efficiencies of atorvastatin in nanosponge formulations were found to be 72 to 86%. SEM images revealed their porous nature and cavity was of β-cyclodextrin. The mean particle size of nanosponges was about 328 nm and Zeta potentials of the nanosponges were sufficient enough (-10 to -15 mV) due to presence of carboxylic group and inclusion complex formation which assured stability of formulations. The results of FTIR and DSC confirmed that atorvastatin was compatible with β-cyclodextrin and completely encapsulated in nanosponges structure respectively. The selected formulation produces good dissolution profile (release more than 75% atorvastatin within 60 mins in 0.1 N HCL) which indicated that the solubility of atorvastatin was improved by forming nanosponges. In accelerated stability studies, no significant changes occurred in physical appearance and drug content of atorvastatin nanopsonges formulation during 3 months stability studies. Atorvastatin nanosponges confirmed by insolubility in water and organic solvents like dimethyl formamide, dichloromethane.

Keywords: Atorvastatin, β-cyclodextrin, nanosponges, cross-linker, inclusion complex, solubility.

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INTRODUCTION

Atorvastatin is Hydroxy Methyl Glutaryl Co-enzyme A (HMG CoA) inhibitor having antihyperlipidemic activity. This anticholesteremic agent is used in the treatment of dyslipidemia. Absolute bioavailability of atorvastatin is just about 14% due to high intestinal clearance and first pass metabolism. Inclusion complex formation enhanced the solubility, dissolution rate of poorly soluble BCS class II drugs and ultimately improved bioavailability of drug molecule. In this work novel approach was used for inclusion complex formation that was nanosponge formation of poorly soluble atorvastatin. This nanosponges formation focuses on improvement in bioavailability of atorvastatin. Thus cyclodextrin based nanosponges are prepared which act as novel atorvastatin carriers.[1-5]

Cyclodextrin-based nanosponges are biocompatible, spherical, three dimensional nanoparticles used for improvement in dissolution rate, solubility and stability of drugs, masking unpleasant flavors, and prolonging the release of drug. Nanosponges are efficiently entrapping different types of drug molecules by means of inclusion complex formation. More ever, polymer mesh forms a network with nano-channel able to entrap the drug molecules. This peculiar structure organization favors molecule complexation and might be responsible for the increased solubility, dissolution, stabilization and protection capacities of nanosponges in comparison with its parent cyclodextrin.[6-8]

Mostly two methods employed for the preparation of nanosponges are cross-linking reaction by condensation polymerization and cross linking reaction by interfacial phenomenon. Nanosponges prepared by condensation polymerization reaction showed the promising results in anticancer drug delivery system, proteins delivery system, anti-inflammatory drugs and antifungal drug delivery system. Nanosponges can be obtained by cross-linking different types of cyclodextrins with different cross-linkers. Drug solubility and loading efficiency can be improved by varying ratio of cyclodextrin to cross-linker.[9-11]

MATERIALS AND METHODS

Materials

Atorvastatin was received as gift sample from Zydus Pharmaceuticals. 1,1'-Carbonyl di-imidazole was purchased from Avra Synthesis Pvt. Ltd. *β*-cyclodextrin (SD fine-chem limited) , Dimethyl formamide (Merck Pvt. Ltd.), 0.1 M KOH (Rankem Ltd.)Dichloromethane (Merck & Sigma Aldrich Ltd.), dimethyl formamide (Merck Pvt. Ltd.) potassium dihydrogen phosphate, ethanol, hydrochloric acid etc. were used present in the college store room.

Pre-formulation Studies

Physical Properties

Atorvastatin was received as gift sample from Zydus Pharmaceuticals (Ahmedabad, Gujarat). Atorvastatin was characterized by physical properties like colour, solubility, melting pointetc.

UV spectral analysis

10 mg of Atorvastatin was dissolved in methanol and dilute it with methanol, volume was made up to 100 ml with the methanol. 2 ml of the above solution was diluted upto 10 ml with methanol. The solution was scanned on Perkin Elmer U.V Spectrophotometer (Lambda 25) between 200 nm to 400 nm and showed absorption.

Analytical Methodology(Calibration curve)

Stock solution of Atorvastatin (100 µg/ml) was prepared in methanol. From the stock solution, different dilutions from 2 to 20 µg/ml were prepared by using methanol. All the dilutions were scanned on Perkin Elmer U.V Spectrophotometer (Model- Lambda 25) to prepare calibration curve at 247.5 nm.

Preparation of Cyclodextrin based Nanosponges

Condensation Polymerization[6,12]

Procedure:

In this work, cyclodextrin based atorvastatin nanosponges were prepared by self-modified procedure.100 ml anhydrous dimethyl formamide (DMF) was placed in round bottom flask. 1.5 mmol anhydrous β-cyclodextrin **[**β-cyclodextrin is preheated at 120˚C for 12 hrs.**]** was added to achieve complete dissolution. More than 130-140˚C temperature is required. Then 12 mmol 1,1 carbonyl di-imidazole(CDI) was added and reacting for 4 hours at 140 ˚C. When solution started to become viscous, 2% w/v atorvastatin was added. Once condensation reaction was completed, transparent block of cross-linked cyclodextrin was obtained, dried and finally roughly ground in mortar/mill. Obtained product was washed with water to remove excess solvent (DMF) and filter it. Residual products were completely removed by extraction with ethanol. After purification, nanosponges is dried and stored at 25 ˚C until further use. Nanosponge formulations were confirmed by insolubility in water, ethanol and DMF/DMSO. This procedure was carried out for different molar ratio of β-cyclodextrin to cross-linker like 1:4, 1:8 for which various formulations like F1, F2, F3, F4, F5, F5(R) were formulated.

Interfacial Polymerization[12]

Procedure:

1 mmol β-cyclodextrin was dissolved in 20 ml of 0.1 M KOH by means of sonication or magnetic agitation to obtain aqueous solution of cyclodextrin. 8 mmol carbonyl di-imidazole (CDI) was dissolved in 20 ml of dichloromethane to obtain organic solution of CDI. Aqueous dextrin solution was added to organic CDI solution under continuous magnetic agitation for 30 mins. Precipitate was observed, then it was washed with water and ethanol to remove unreacted materials and filter it. Filtrate was taken, water: methanol (30:70) composition was added to prepare dispersion and 2% w/v atorvastatin was added. Magnetic Agitation was carried out for 24 hours.Then centrifuge it at 3000 rpm for 15 min. Supernatant (dissolved drug) was collected and freeze-dried, nanosponges were obtained.

This procedure was carried out in the molar ratio of β-cyclodextrin to cross-linker that was 1:8 for which various formulations from F11 to F20, F20 (R) were formulated by varying water: methanol composition, drug concentration and cross-linker.

Formulation Trials

Prepared by Condensation Polymerization

Table 1 shows Formulations prepared by condensation polymerization.

Table 1: Formulations prepared by condensation polymerization

F	β-CD (% w/v)	CDI (% w/v)	DMF (ml)	Molar Ratio (β CD: CDI)	Atorvastatin	Cross-linking reaction carried out at ˚C for 4 hrs
F1	3.48	1.99	100	1: 4	-	100 ˚C
F2	3.48	1.99	100	1: 4	-	140 ˚C
F3	3.40	3.84	100	1: 8	-	140 ˚C
F4	3.40	3.84	100	1: 8	2 % w/w	140˚C
F5	3.40	3.84	100	1: 8	2 % w/v	140˚C
F5(R)	6.81	7.68	100	1: 8	2 % w/v	140˚C

Where- F stands for formulation and (R) stands for trial for reproducibility

Prepared by interfacial polymerization

Table 2 shows Formulations prepared by interfacial polymerization.

Table 2: Formulations prepared by interfacial polymerization

F	β-CD (%w/v)	Aqueous Phase (0.1 M KOH)	Cross-linker (%w/v)	Organic Phase CH_2CL_2/DMC	Molar Ratio (β CD: cross-linker)	AT (%w/v)	NS: AT	Dispersion medium (water/ water: methanol)
F11	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	-	1: 5	100 ml
F12	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	-	1: 10	100 ml
F13	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	1	-	100 ml
F14	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	2	-	100 ml

F15	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	2	-	100 ml
F16	12.2	20 ml	20 ml (DMC)		1: 80	2	-	100 ml
F17	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	2	-	70:30
F18	8.14	150 ml	20 ml (DMC)		1:16	2	-	70:30
F19	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	1	-	30:70
F20	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	2	-	30:70
F20 (R)	5.675	20 ml	6.48 (CDI)	20 ml	1: 8	2	-	30:70

AT stands for Atorvastatin, NS stands for Nanosponges

CHARACTERIZATION OF NANOSPONGES[6,7,8,12]

Scanning Electron Microscopy (SEM)

The surface morphology of nanosponge was examined by using Scanning Electron microscope (Oxford materials instrument).

Particle size analysis and Zeta Potential

Particle size and zeta potential of nanosponge were measured by using Zetasizer (Malvern instrument). Nanosponge formulation was diluted with deionized water prior to measurement at 25˚C. Each measurement was carried out in triplicate.

Differential Scanning Calorimetry (DSC)

The thermal behaviour of drug-cyclodextrin complex was studied in order to confirm the formation of complex. Thermal analysis was carried out by using Perkin Elmer instrument (Pyris 1 DSC) for which nanosponge formulation was heated from 45 -280 ˚C at 10 ˚C heating rate.

X-ray Diffraction (XRD)

X-ray diffraction pattern of nanosponges was recorded on X'pert Pro Powder X-ray diffraction system, Model PANALYTICAL with Cu anode and No as incident beam monochromator. The samples were run over range from 0 ˚C to 80 ˚C of 2θ by means of Cu-Kα radiation. The step scan mode was performed at 25 ˚C.

Solubility studies

Nanosponges were confirmed by insolubility in water and organic solvents like DMF (Dimethyl Formamide) and DMSO (Dimethyl Sulfoxide).[12]

Loading Efficiency

100 mg nanosponges dissolved in 20 ml methanol. Stirring was carried out for 10 min to break the complex. 2 ml solution was taken from above solution and diluted up to 10 ml with methanol. UV spectrophotometer was used for determination of loading efficiency of nanosponges.[13]

FT-IR

Potassium bromide (KBr) was mixed with the nanosponges and pellets made by using high-pressure hydraulic machine. FTIR of the pellet was recorded on FTIR spectrometer (Perkin Elmer Spectrum RX 1) and compared with that of the standard pure atorvastatin to check whether interaction occurs between pure atorvastatin drug and added ingredients(e.g β-cyclodextrin) or not.

***In vitro* release studies**

In vitro release of atorvastatin from nanosponge formulations were performed on dissolution USP Type II apparatus (Electrolab, TDT-08L) II at 50 rpm at 37 ˚C.100 mg of nanosponges were packed in a small tea bag of muslin cloth and tied to paddle of dissolution test apparatus. Medium used was 500 ml of 0.1 N HCl (pH 1.2) for 2 hours. At regular time intervals, aliquot samples were withdrawn and atorvastatin content was determined by using Perkin Elmer U.V spectrophotometer (Lambda 25).[12]

Accelerated Stability studies

The accelerated stability studies were carried out according to ICH guidelines. Prepared formulation (F5) was charged in stability chamber and stored at 40 ± 0.2 °C/ 75 ± 5% RH (relative humidity)for three months. The formulation subjected to stability tests was withdrawn and evaluated periodically for 3 months period for its physical appearance and drug content.

To test suitability of nanosponges for oral solid dosage forms and to check the effect of compression force on formulated nanosponges, one batch of tablets of nanosponges was formulated and evaluated.

Tablet formation of atorvastatin nanosponges

Table 3 shows Formula for Tablet formation of atorvastatin nanosponges.

Table 3: Formula for Tablet formation of atorvastatin nanosponges

Ingredients	Quantity
Atorvastatin nanosponges	Quantity equivalent to 10 mg atorvastatin
Starch (Binder)	5% w/w
Lactose(Diluent)	q. s
Cross-Povidone (Superdisintegrant)	3% w/w
Magnesium Stearate (Lubricant)	0.035% w/w
Total	150 mg

Evaluation studies of Tablets

Performed various evaluation IPQC (In Process Quality Control) tests like Hardness, Weight variation, Friability, disintegration time according to I.P.

Drug content

Take 10 tablets. Determine average weight of 10 tablets. Triturate tablets in mortar. Take quantity of powder equivalent to 10 mg atorvastatin. Dissolve powder in solvent in which atorvastatin gets dissolved. Determine drug content by using U.V spectrophotometer.

In vitro Dissolution studies[5]

In vitro dissolution studies of tablets were performed in 900 ml of 0.1 N HCL for 1 hour at 75 rpm by using USP type II apparatus.

RESULTS AND DISCUSSION:

Pre-formulation Studies

These studies were carried out to characterize and to authenticate the atorvastatin received and to check the compatibility of the ingredients with the atorvastatin.

Physical Properties

Physical properties of atorvastatin are shown in below **Table 4.**

Table 4: Physical Properties of atorvastatin

Sr. No.	Physical Properties	Inference/ found Value
1.	Appearance	White amorphous powder
2.	Solubility	Freely soluble in methanol, slightly soluble in ethanol, very slightly soluble in water
3.	Melting Point*	159-161 ˚C

*Melting point was determined by using melting point apparatus (Chemi Line CL725)

UV spectral analysis

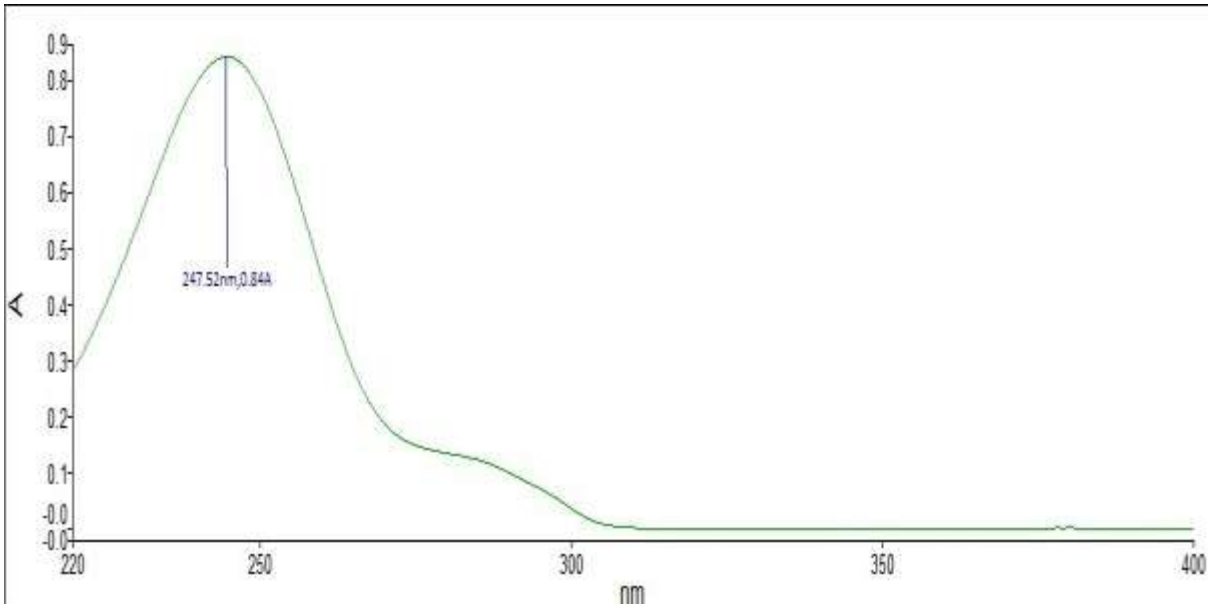

Figure 1: Wavelength maxima (λ_{max})

Figure 1 showed the λ_{max} for the atorvastatin. By using U.V spectrophotometer, λ_{max} was found to be 247.5 nm which was found to be similar to the standard value given in literature.

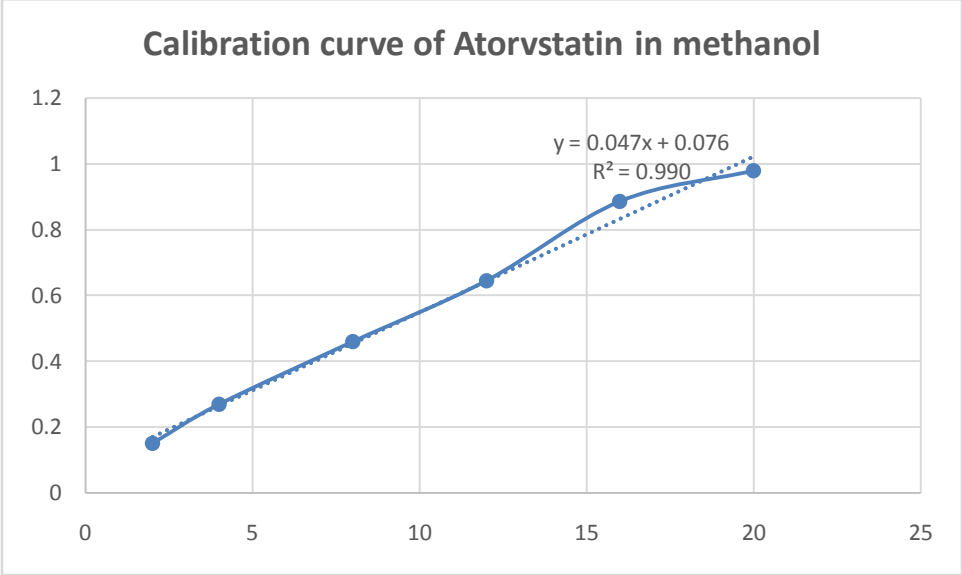

Figure 2: Calibration curve of atorvastatin in methanol

Analytical methodology

Figure 2 showed Calibration Curve of atorvastatin in methanol at 247.5 nm.

Characterization of Nanosponges

Solubility Studies

As per the literature nanosponges are insoluble in water. We also obtained the same result. All nanosponges formulations were found insoluble in water and organic solvents like DMF/DMSO.

Loading Efficiency

For Condensation Polymerization

Loading efficiency of nanosponge formulations prepared by condensation polymerization were in the order of F5 > F4 as shown in Figure 3 Loading efficiency of nanosponges prepared by condensation polymerization were found to be 72 to 86%. *Shende et al* prepared calcium carbonate nanosponges with encapsulation efficiencies of about 81 to 95%. [6]*Swaminathan et al* prepared camptothecin nanosponges with encapsulation efficiencies of about 13 to 37%. [8]*Lembo et al* prepared carboxylated nanosponges of acyclovir with encapsulation efficiency of about 69%.[7] In our study, we were able to achieve up to 86 %, which we thought good one as compared to literature, but still there is a scope for further improvement.

F5 trial was considered as the selected formula for nanosponges formulation after undergoing number of trials. Before reaching to selected formula, numbers of modifications were undertaken in experimental conditions and molar ratio of **F1** formulation trial (prepared as per patented procedure *shende et al.*) which are enlisted below: Crosslinking reaction temperature was increased from 100˚C to 140˚C. Molar ratio of β CD: CDI was increased from 1: 4 to 1: 8.

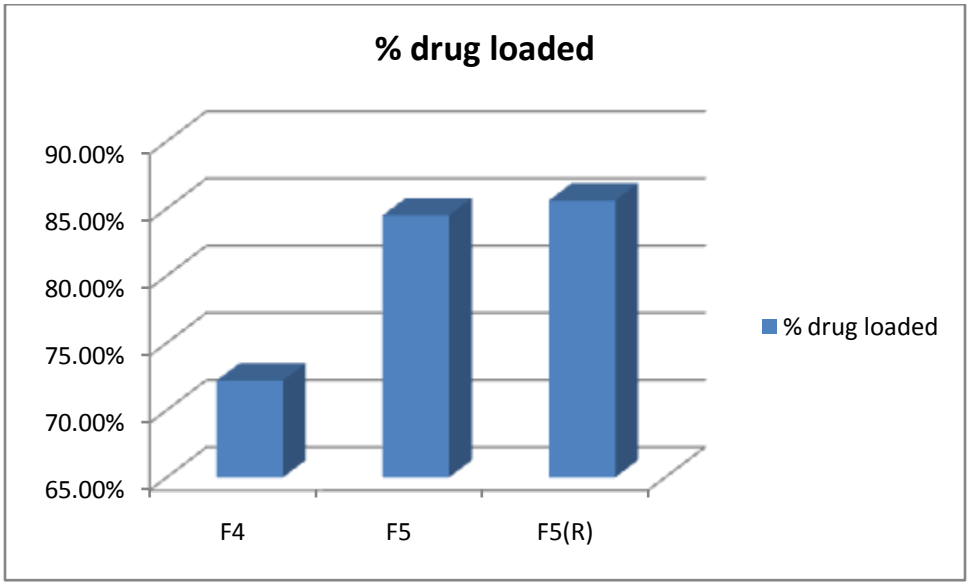

Figure 3: Loading efficiency of nanosponges prepared by condensation polymerization

For interfacial polymerization

Loading efficiency of nanosponge formulations prepared by interfacial phenomenon were in order of F20 > F19 > F18 > F15 > F17 > F14 > F11 > F13 > F16 > F12 as shown in Figure 4. Loading efficiency of nanosponges prepared by interfacial polymerization were found to be 26 to 74 %.

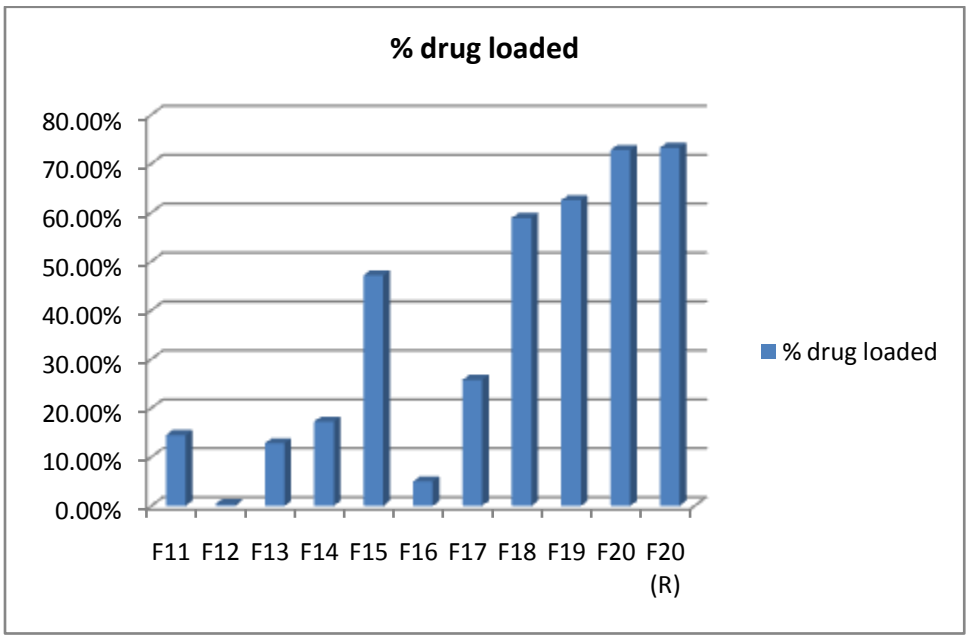

Figure 4: Loading Efficiency of formulations prepared by interfacial polymerization

F20 trial was considered as the selected formula for nanosponges formulation after undergoing number of trials. Before reaching selected formula, number of modifications were undertaken which are enlisted below :

- In first two trials F11 and F12, placebo of nanosponges was prepared firstly and then drug was to be loaded. In further trials, drug was loaded during cross-linking reaction.
- Started using water: methanol proportion instead of water only and later on Change in dispersion medium proportion water: methanol composition (30: 70 and 70: 30). (*Trotta et al.* used water only)
- Started using Sigma Aldrich made high purity dichloromethane instead of Merck made dichloromethane.

Two methods were followed for preparation of nanosponges namely, condensation polymerization and interfacial polymerization. Condensation polymerization was selected as best method for nanosponges preparation due to higher loading efficiency observed in F5. So Further characterization studies were carried on formulation F5 prepared by condensation polymerization.

Scanning Electron Microscopy

SEM images of atorvastatin loaded nanosponge formulation F5 and nanosponges formulation are shown in Figure. 5 & 6. SEM images showed shape and size of inclusion complex. By comparing with SEM images of β cyclodextrin, claimed that the cavity was of β cyclodextrin and inclusion of some material was observed that was drug

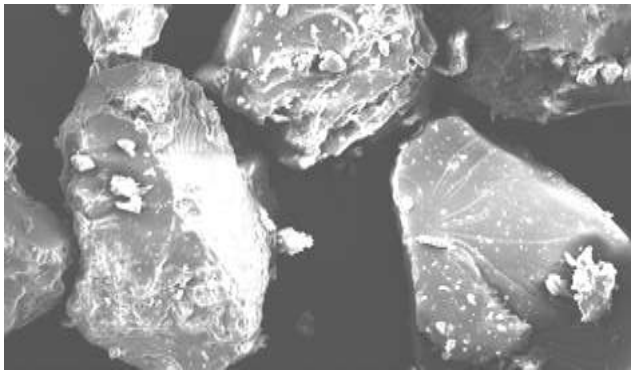

Figure 5: SEM image of Atorvastatin loaded nanosponges

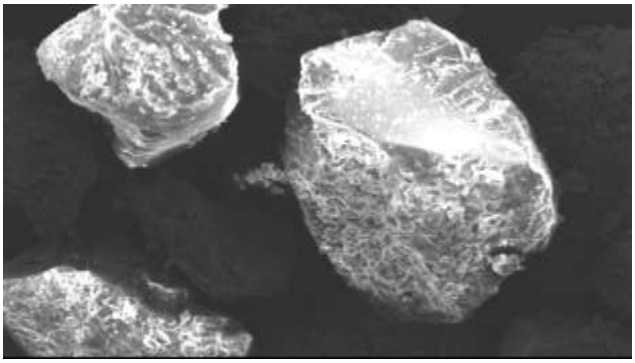

Figure 6: SEM image of β-cyclodextrin

Particle size analysis

Figure. 7 showed particle size distribution of atorvastatin nanosponges. By using Malvern Zetasizer, mean particle size was found to be about 327 nm. *Shende et al* prepared calcium carbonate nanosponges having mean particle size of about 400 nm.[6] *Swaminathan et al* prepared camptothecin nanosponges having mean particle size in range of 450 to 600 nm.[8] *Lembo et al* prepared carboxylated nanosponges of acyclovir having mean particle size of about 400 nm.[7] The size range indicates that the formed complexes were of nano size with improves surface area entrapping the still smaller size drug in the cavity, which will improve the solubility of the drug.

			Size (d.nm):	% Intensity	Width (d.nm):
Z-Average (d.nm):	327.4	Peak 1:	315.8	97.5	96.07
PdI:	0.281	Peak 2:	5371	2.5	328.0
Intercept:	0.990	Peak 3:	0.000	0.0	0.000
Result quality :	Good				

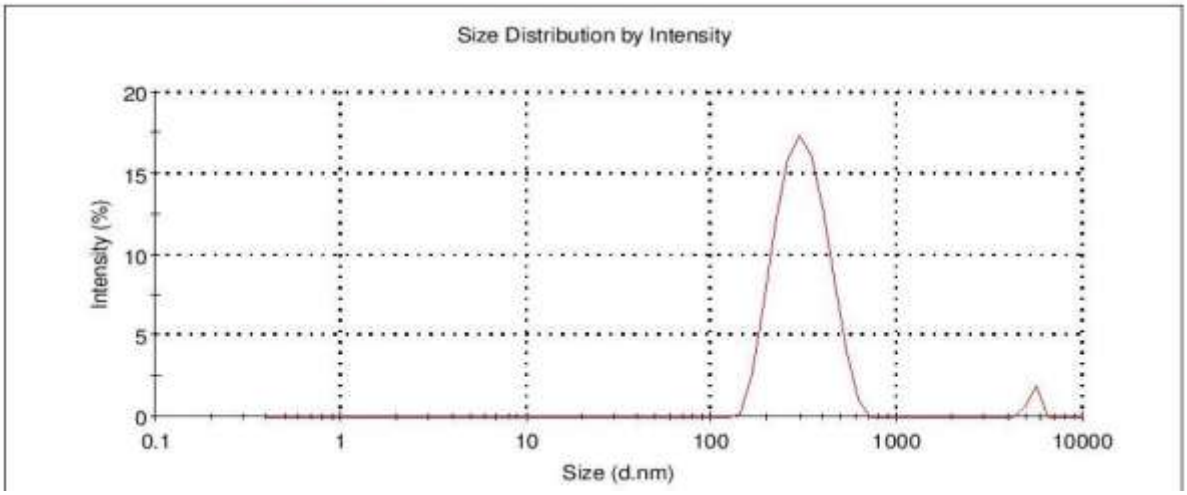

Figure 7: Particle size analysis results

Zeta potential

Figure. 8 showed zeta potential results for nanosponge formulation. By using Malvern zetasizer, Nanosponges of atorvastatin were found negatively charged with a zeta potential of -11.9 mV. *Shende et al* prepared calcium carbonate nanosponges having zeta potential of -6 mV.[6] *Swaminathan et al* prepared camptothecin nanosponges having zeta potential in range of -20 to -25 mV.[8] *Lembo et al* prepared carboxylated nanosponges of acyclovir having zeta potential of -38.3 mV.[7] The zeta potentials of atorvastatin nanosponges formulations were sufficient enough (-10 to -15 mV) to stabilize the formulation, probably due to presence of the carboxyl groups and cross-linked inclusion complex in its structure which ensured physical stability between nanosponge particles.

		Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV): -11.9	Peak 1:	100	52.5	6.73
Zeta Deviation (mV): 114	Peak 2:	-141	18.6	6.26
Conductivity (mS/cm): 0.120	Peak 3:	-121	14.4	6.45

Result quality : See result quality report

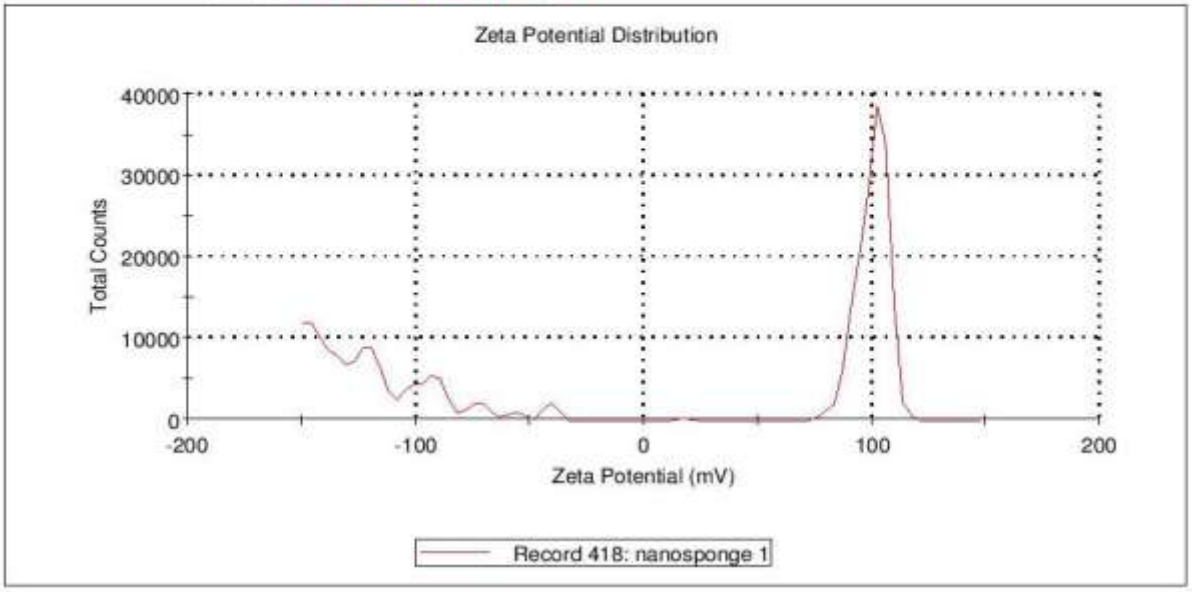

Figure 8: Zeta potential Distribution

Differential Scanning Calorimetry (DSC)

DSC thermogram of atorvastatin drug (Figure 9) was showed an endothermic peak at its melting point. DSC thermogram of nanosponge (Figure 10) was showed absence of endothermic peak which gave clear evidence that there was formation of inclusion complex. Peak observed in DSC thermogram indicates glass transition temperature of β-cyclodextrin.

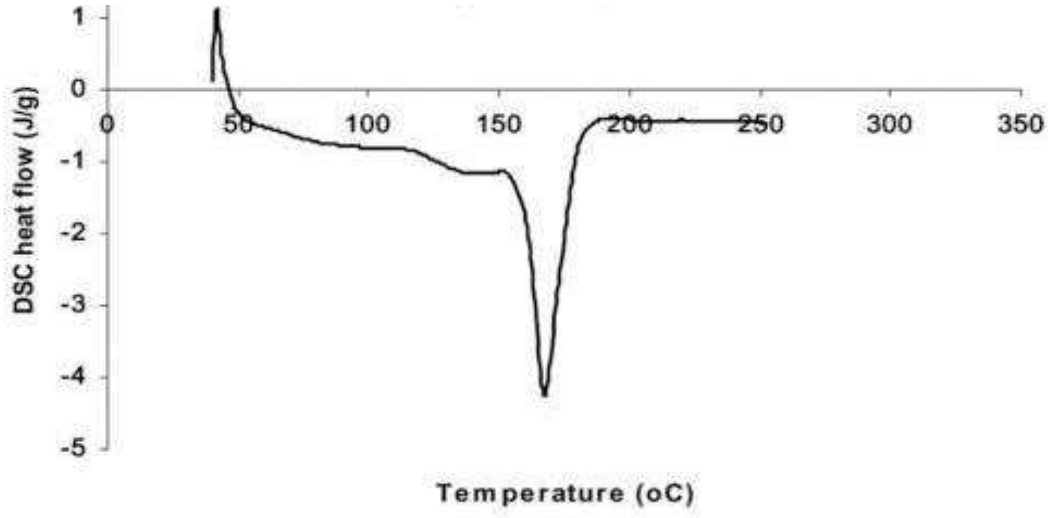

Figure 9: DSC thermogram of Atorvastatin

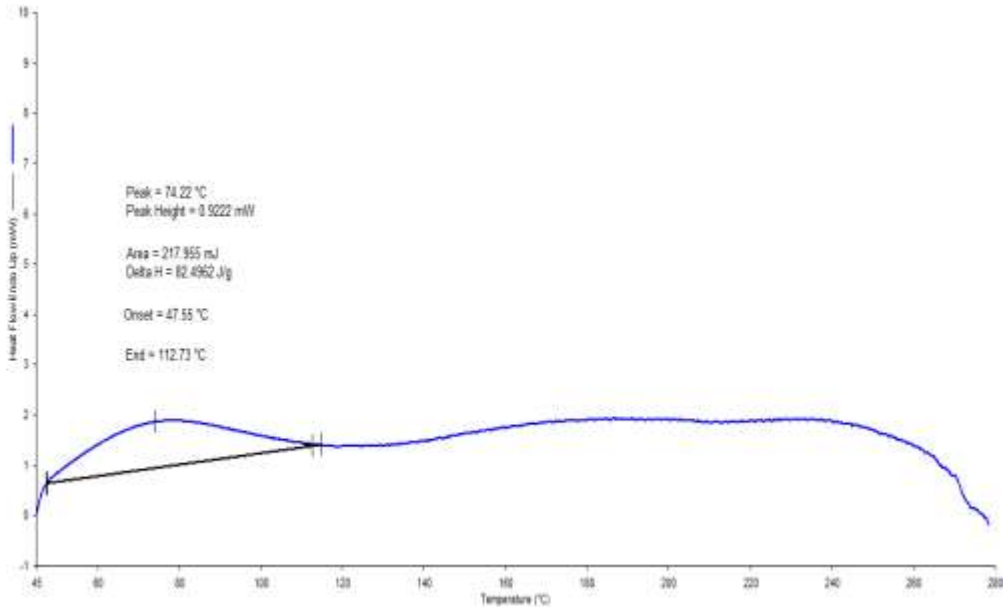

Figure 10: DSC thermogram of atorvastatin nanosponges

X-Ray Diffraction

As per literature(Kim et al.) diffraction pattern of pure atorvastatin drug showed characteristic high-intensity diffraction peaks at 9.12, 9.44, 10.23, 10.54, 11.82, 12.16, 16.97, 19.45, 21.59, 22.62, 23.22 and 23.68° of 2θ.[13] Figure 11 showed that no characteristic diffraction peaks corresponding to pure atorvastatin were observed in nanopsonges. Therefore, atorvastatin nanosponges existed as an amorphous form. Amorphous form improves surface area and higher surface area ultimately improves its solubility.

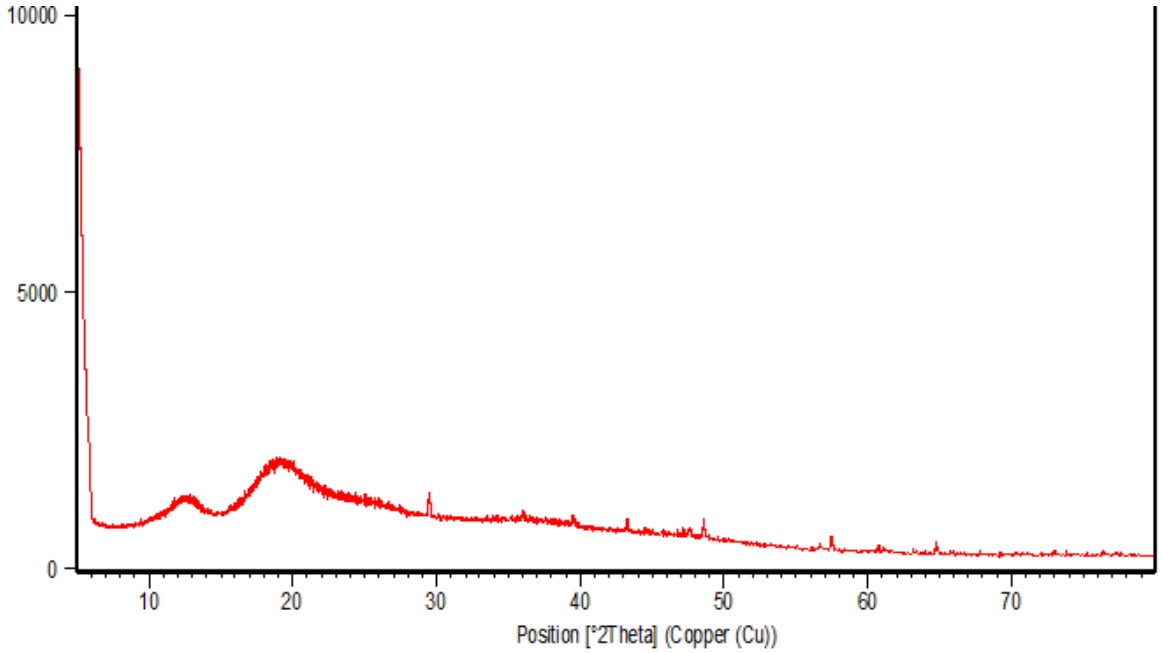

Figure 11: X-Ray Diffraction Pattern of Atorvastatin

FT-IR

Figure 12 showed FT-IR spectra of pure atorvastatin and Figure 13 showed FT-IR spectra of atorvastatin nanosponges. The FT-IR spectrum of pure atorvastatin was equivalent to the FT-IR spectra obtained by the atorvastatin nanosponges. This indicated that no interaction occurred between atorvastatin and inclusion complex of β-cyclodextrin. The results revealed no considerable changes in the IR peaks of Atorvastatin, when mixed with β-cyclodextrin.

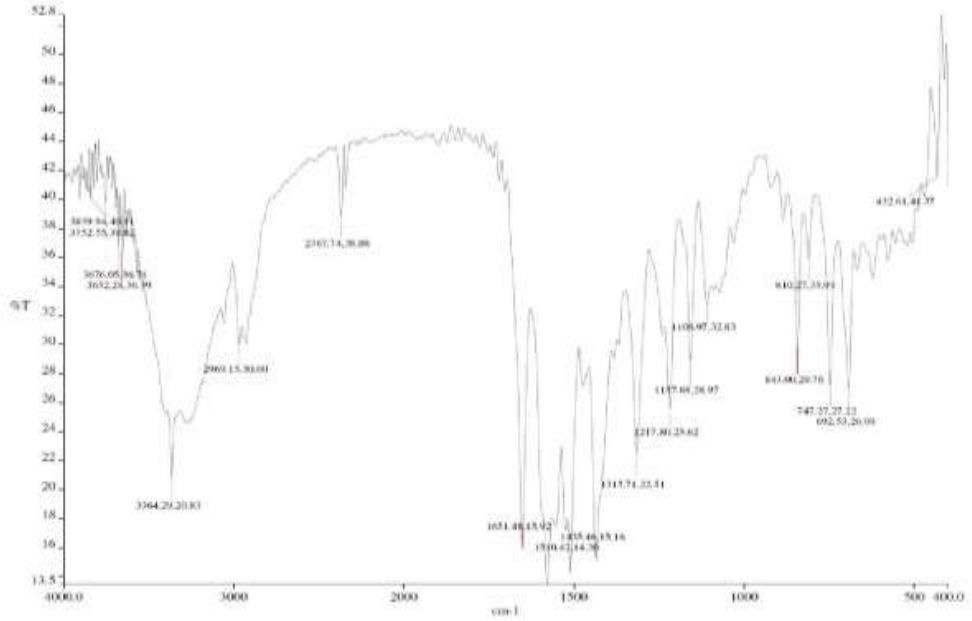

Figure 12: FT-IR spectra of pure Atorvastatin sample

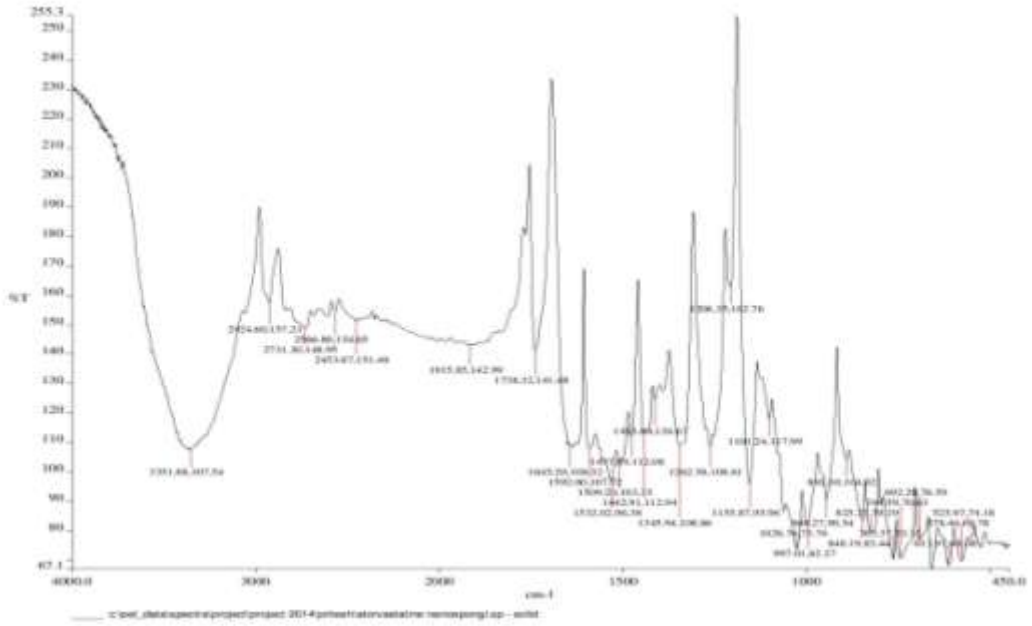

Figure 13: FT-IR spectra of Atorvastatin nanosponges

In vitro release studies

Figure 14 showed drug release profile of Atorvastatin nanosponges. Atorvastatin nanosponges showed good dissolution profile and more than 75% atorvastatin was released within 30 mins in 0.1 N HCL which gave clear indication that solubility and dissolution rate of atorvastatin was enhanced (as compared with marketed atorvastatin tablets that showed lower dissolution profile).

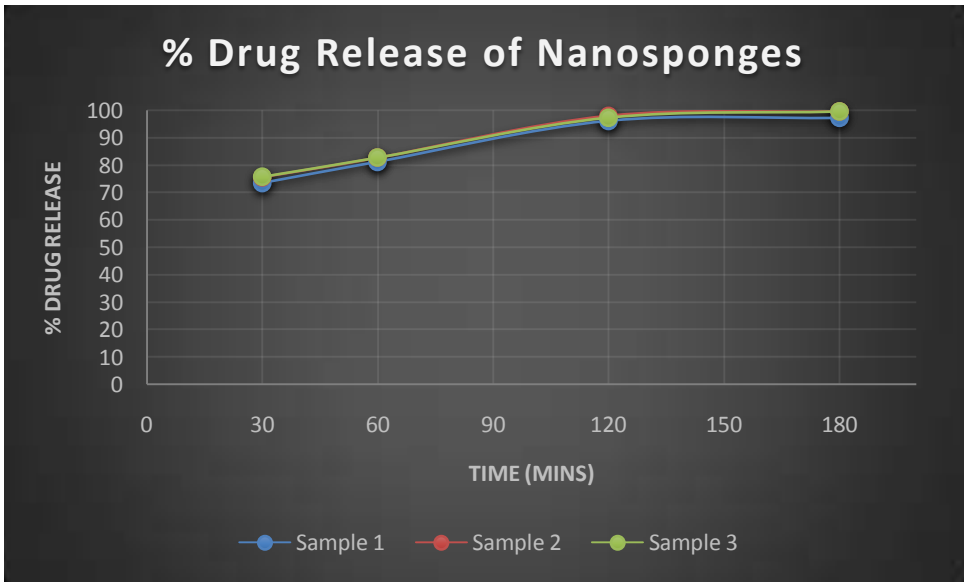

Figure14: In vitro drug release of nanosponges in 0.1 N HCL

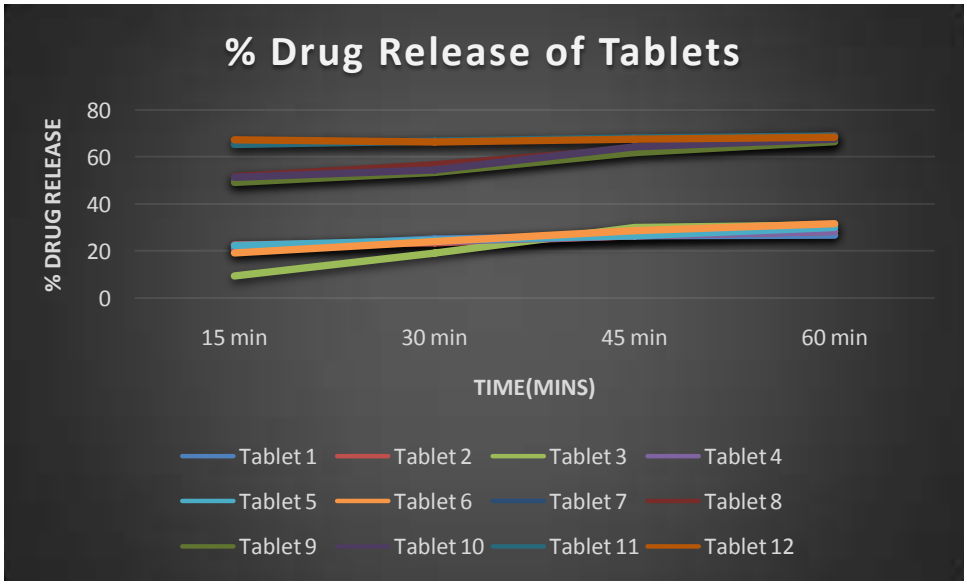

Figure 15: In vitro dissolution studies

Accelerated stability studies

Table 5 showed accelerated stability studies results and confirmed that no change was observed in physical appearance and drug content of atorvastatin nanosponges after 15th day and 1 month during 3 months accelerated stability studies when nanosponges were kept at 40 ± 0.2°C/ 75 ±

5% RH conditions in stability chamber. Hence we can say that we have successfully incorporated the atorvastatin in beta cyclodextrin with enhancing its solubility.

Table 5: Accelerated Stability studies results

Sr. No.	Time	Temperature/RH conditions	Physical Appearance	% Drug Content
1.	1st day	40 ± 0.2°C/ 75 ± 5% RH	No change	84.5%
2.	15th day	40 ± 0.2°C/ 75 ± 5% RH	No change	84.44%
3.	4th week	40 ± 0.2°C/ 75 ± 5% RH	No change	84.38%

Various dosage forms can be formulated for atorvastatin nanosponges. To check the effect of compression force on formulated nanosponges, tablets were formulated for atorvastatin nanosponges.

Tablet formation of atorvastatin nanosponges

Evaluation studies of tablets

Table 6 shows results for various IPQC (In Process Quality Control) parameters like Hardness, Weight variation, friability, disintegration time.

Table 6: IPQC Parameters

Parameters	Inference/Found value
Hardness	3 kg/cm^2
Weight variation test	Passes
Friability	Passes
Disintegration time	70 seconds

Drug Content

Drug content was found to be 100% using Perkin Elmer U.V spectrophotometer (Lambda 25).

In vitro dissolution studies

Figure. 15 showed % drug release from nanosponges in 0.1 N HCL and 0.1 N HCL with Tween 80(as surfactant to improve its dissolution and solubility).

Results of dissolution studies showed that, just about 30% drug release within 60 minutes in 0.1 N HCL and about 70% drug release within 60 minutes in 0.1 N HCL with tween80 and these results revealed that compression force might have effect on the release of atorvastatin drug from nanosponges. So tablets might not be the suitable dosage forms for formulated nanosponges or modification in the formula for tablet is needed.

CONCLUSION

One of the most significant property of cyclodextrin based nanosponges is that they are able to encapsulate a variety of different types of drug molecules. Cyclodextrin based nanosponges of atorvastatin are solid, porous, biocompatible nano-particulate three dimensional structures whose

production cost is less because of simple synthesis, purification procedures and use of limited number of reagents. With the consideration of the biocompatibility of nanosponges, the development of cyclodextrin based atorvastatin nanosponge formulations can be used in the formation of various dosage forms and in various administration routes. This work shows that atorvastatin nanosponges prepared by condensation polymerization have entrapped more atorvastatin as compared to nanosponges prepared by interfacial polymerization. So nanosponges prepared by condensation polymerization is showing best results for antihyperlipidemic drug delivery system and already showing promising results in anticancer drug delivery system, proteins delivery system, anti-inflammatory drugs delivery system etc. Final dosage form from the nanosponges needs to be designed judicially considering all formulation parameters for the better efficiency of the dosage form.

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