

## FORMULATION DEVELOPMENT AND CHARACTERIZATION OF AZELNIDIPINE LOADED NANOSPONGES FOR ENHANCE DRUG DELIVERY

<sup>1</sup>Shakeeb Akhtar Nehal Ahmad, <sup>2</sup>Shahzad Ahmed Abdul Razzaque, <sup>3</sup>Tarique A. Deshmukh, <sup>4</sup>Hammad Mohammed Athar, <sup>5</sup>Mohd Aatif Khan Rizwan Khan, <sup>6</sup>Junaid Peer Md. Khatik

<sup>1,2</sup>Department of Pharmaceutics, JMCT Institute of Pharmacy, Nashik, Maharashtra, India.

<sup>3</sup>Department of Pharmacology, Royal College of Pharmaceutical Education and Research, Malegaon, Dist. Nashik, Maharashtra, India.

<sup>4</sup>Department of Quality control and Quality Assurance, JMCT Institute of Pharmacy, Nashik, Maharashtra, India.

<sup>5</sup>Department of Pharmacology, JMCT Institute of Pharmacy, Nashik, Maharashtra, India.

<sup>6</sup>Department of Pharmacognosy, JMCT Institute of Pharmacy, Nashik, Maharashtra, India.

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### ABSTRACT

Nanosponges are microscopic sponges comparable in size to a virus (250 nm-1  $\mu$ m) that possess cavities capable of being filled with various hydrophobic and hydrophilic medications, effectively addressing challenges related to drug toxicity and poor absorption. Azelnidipine, a selective calcium channel blocker, effectively lowers blood pressure (BP) and heart rate (HR) in hypertensive patients. In the present study nanosponges of Azelnidipine were formulated and characterized for enhance drug delivery. Different batches with varying concentration of drug and excipient (A1, A2, A3, and A4) of Azelnidipine loaded nanosponges were prepared by emulsion solvent diffusion method. All the fabricated nanosponges of Azelnidipine combined with ethyl cellulose were characterized using FT-IR, DSC, XRD. As well as particle size determination, drug content and invitro release study. It was concluded that the prepared Nanosponges exhibited favourable drug content along with optimal drug release. Considering the biocompatibility of nanosponges, the development of Azelnidipine nanosponge formulations holds potential for the creation of various dosage forms and administration routes.

**Keywords:** Nanosponges, Azelnidipine, Enhance drug delivery, FT-IR, XRD.

### INTRODUCTION

Nanosponges are mesh-like minute structures that can encapsulate a large variety of substances and medication molecules (Swaminathan *et al.*, 2012, Ahire *et al.*, 2020). They enhance the solubilization capacity of both water-soluble drugs and lipid soluble drugs and also possess a spherical colloidal nature (Cavalli *et al.*, 2010). They increase the bioavailability of drugs with prolonged drug release (Eva Harth, David Calkins, 2011). Because of their internal hydrophobic chambers and exterior hydrophilic branching, nanosponges' **amphiphile** nature enables them to carry therapeutic molecules that are both hydrophilic and hydrophobic (Trotta *et al.*, 2012). They are like a 3D

network having a backbone of long-chain polyesters present in the solution along with crosslinkers that connect different parts of the polymer (Subramanian *et al.*, 2012). It has been revealed that cyclodextrins (cyclic oligosaccharides) can be treated with appropriate crosslinking agents to obtain nanosponges, a unique nanostructured material made of hyper-cross-connected cyclodextrins (Vavia *et al.*, 2012). According to the agent utilized as a crosslinker, nanosponges can be synthesized as neutral or acidic materials and swell. The result is hollow spheres with voids that can hold medicament molecules (Patel *et al.*, 2012). During preparation, the cross-linking-to-cyclodextrin proportion

\*Corresponding Author: Dr. Shakeeb Akhtar Nehal Ahmad, Associate Professor, Department of Pharmaceutics, JMCT Institute of Pharmacy, Nashik, Maharashtra, India, Email: shakeebng@gmail.com.

can be changed to enhance drug loading and provide a customized release profile. Their extremely permeable nanomeric nature, in comparison to that of the parent cyclodextrin molecules, makes it possible for drug molecules to both arrange themselves in nanosponge inclusion and interact with one another in a mode that does not involve inclusion and offer effective drug loading. Compared to other nanoparticles, they possess some advantages as they are easily reproducible using different treatments such as washing with environmentally friendly solvents, stripping with relatively innocuous hot gases, gentle heating, or changing pH or ionic strength. They are used in different fields (Darandale *et al.*, 2012).

## MATERIALS AND METHODS

Azelnidipine was a gift sample from Glenmarkpharma, Sinnar. Hydrogen Chloride, Ethanol, Ethyl cellulose, Dichloromethane was purchased from Burgoyne, Mumbai.

### Preparation of Azelnidipine nanosponges

A physical blend of Azelnidipine and ethyl cellulose was created by simply mixing the drug with the carrier in ratios ranging from 1:1 to 1:4 (drug: Polymer) for a duration of 10 minutes. This physical blend of the drug with the carrier is referred to as AZEC. (Where AZ represents Azelnidipine; EC represents ethyl cellulose).

**Table 1.** Formulation table.

Ingredients	A1	A2	A3	A4
Drug: Polymer (mg)	100:200	100:200	100:200	100:200
PVA (%w/v)	0.1	0.2	0.3	0.4
Dichloromethane	20	20	20	20
Distilled water	100	100	100	100

### Preparation of Nanosponges

The dispersed phase, which included ethyl cellulose and the drug, was dissolved in 20 ml of dichloromethane and gradually introduced into a specific quantity of polyvinyl alcohol in 100 ml of the aqueous continuous phase. The reaction mixture was stirred at 1000 rpm for duration of 2 hours. The resulting nanosponges were collected through filtration and subsequently dried in an oven at 400°C for 24 hours. The dried nanosponges were then stored in vacuum desiccators to guarantee the elimination of any residual solvent.

### Characterization of nanosponges

Characterization was conducted to evaluate any interactions between the drug and the polymer, as well as to determine which properties of the polymer contribute to its effectiveness in enhancing solubility and bioavailability. In the current study, the nanosponges of Azelnidipine combined with ethyl cellulose were characterized using FT-IR, DSC, XRD.

### Particle size Measurement

The sizes of particles are maintained during polymerization for the formation of free-following powders having fine aesthetic attributes. Particle size analysis of nanosponges

was performed by nanoparticle size analyzer, Sympatec, Germany. Cumulative graph is maintained or plotted as particle size against time to study effect of particle size on drug release (Vavia *et al.*, 2006).

### Determination of Drug content

To determine the drug content, a precisely measured amount of nanosponges (10 mg) was combined with 5 ml of methanol in a volumetric flask and shaken for 1 minute. The volume was then adjusted to 10 ml. Subsequently, the solution was filtered and diluted, and the concentration of Azelnidipine was measured spectrometrically at 253 nm.

$$\% \text{ drug content} = \frac{\text{Actual drug content in nanosponge}}{\text{Theoretical drug content}} \times 100$$

### In vitro release studies

In vitro release studies were performed in triplicate using USP Paddle method at 50 rpm and 37±0.2°C in 900 mL of first fluid. Samples were taken at appropriate time intervals for 5, 10, 15, 30, 45, 60, 90, 120min interval. The samples were measured at 269 nm by UV-Spectrophotometer. Fresh dissolution medium was replenished each time when sample is withdrawn to compensate the volume.

**Table 2.** Dissolution test for nanosponges.

S. No.	Frequency (cm-1)	Type of Vibration
1	1681.54	N-H
2	1650.06	C-H
3	1522.58	C=O
4	1484.45	CH3
5	1345.97	C-O

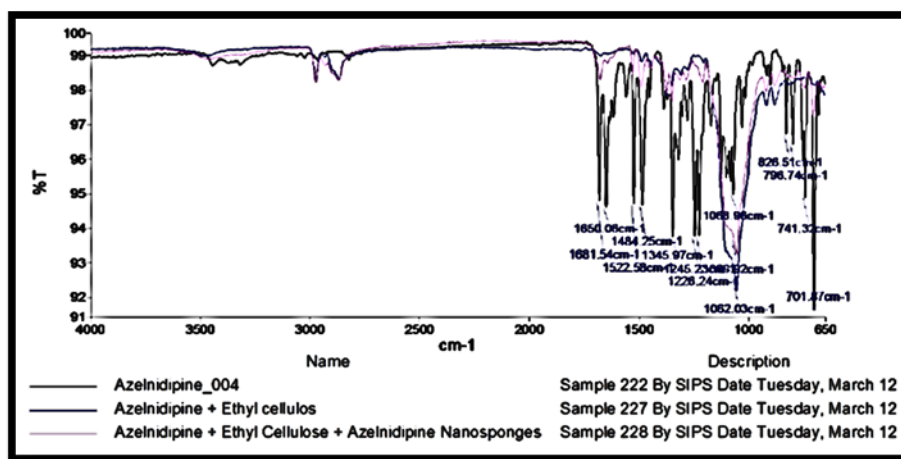
**Table 3.** FT-IR Frequencies for Nanosponges.

Drug: Polymer	Dissolution media (900ml)	Paddle speed (RPM)	Bath temperature (oC)	UV Analysis ( $\lambda_{max}$ ) (nm)	Time(hrs)
1:1 to 1:4	First fluid (JP)	50	37±0.5	210	2

**RESULT AND DISCUSSION**

The FT-IR spectra of optimized formulation of Nanosponges were taken and analyzed between 4000  $cm^{-1}$  - 650  $cm^{-1}$ . The FT-IR studies were conducted to examine the interaction between the drug and the polymer. FT-IR analyses of the drug, the polymer, and the drug-loaded

nanosponges were performed. Table 26 presents the principal peak values along with their corresponding functional groups. From this table, it can be concluded that the principal peak value of the drug remains constant in the nanosponges. Therefore, it can also be concluded that there was no chemical interaction between the drug and the polymer.



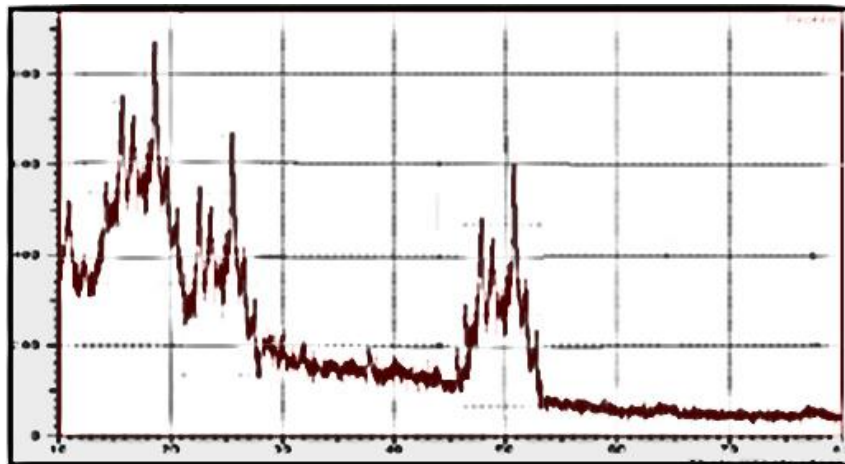
**Figure 1.** FT-IR spectra of Azelnidipine Nanosponges.

X-ray diffraction pattern of nanosponges shows 10.39°, 15.06°, 18.73° with intense peak at 18.73° distinct peaks. The DSC measurements were conducted using a Differential Scanning Calorimeter equipped with a thermal analyzer DSC-61000 (Mettler Toledo USA). The DSC measurements were carried out on the drug, polymer, a physical mixture of the drug and polymer (1:1), and the optimized formulation. All samples, accurately weighed to approximately 2 mg, were placed in a sealed aluminum pan, and the samples were heated under a nitrogen flow of 10 mL/min at a scanning rate of 10 °C per minute, ranging from 25 to 300 °C. An empty aluminum pan served as the reference.

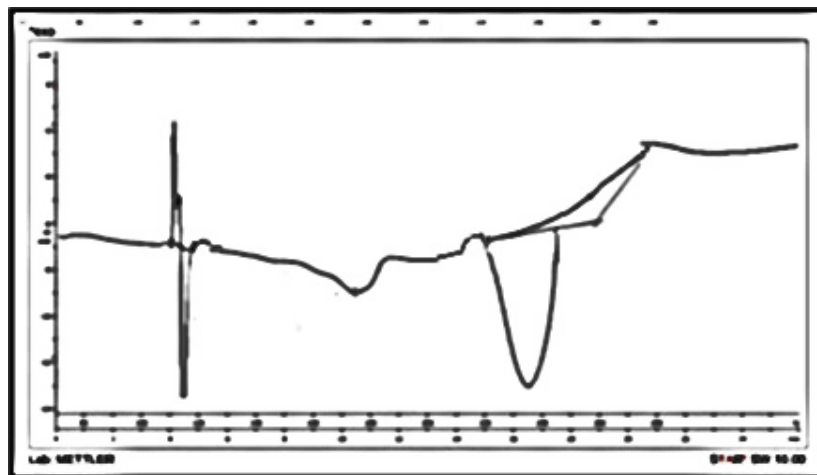
The percentage yield of various batches was assessed by weighing the Nanosponges post-drying, and it was found to range from 75% to 93.3%, as illustrated below, The different batches of Nanosponges underwent analysis for drug content. A quantity of 10mg of powdered Nanosponges was dissolved in a sufficient volume of 10ml Methanol. The UV absorbance was recorded using a UV spectrometer at a wavelength of 253nm. The drug content was determined to be within the range of 60.15 to 79.43. The highest drug content was noted in batch A1, which were 83.34.

**Table 4.** Percentage yield of different batches of Nanosponges.

S.No	Batch	Yield (%)
1	A1	32.34
2	A2	68.81
3	A3	51.20
4	A4	19.8



**Figure 2.** XRD graph of Nanosponges



**Figure 3.** SC Thermogram of Nanosponges

**Table 5.** Drug content Nanosponges.

S.No	Formulations	Drug content (%)
1	A1	83.34
2	A2	69.52
3	A3	67.73
4	A4	76.39

The *in vitro* drug release study for Azelnidipine-loaded nanosponges was conducted over a duration of 2 hours using the first fluid SLS at a temperature of  $37 \pm 5^\circ\text{C}$  with the aid of a capsule. Based on the dissolution profiles of formulations A1 through A4, it was determined that

formulation batch A1 exhibits a superior drug release profile compared to the other formulations. The cumulative percentage release is presented as an average of three preparations. The cumulative percentage drug release for all formulations is illustrated in the table below.

**Table 6.** *In-vitro* drug release.

Time	% Drug release of Nanosponges			
	A1	A2	A3	A4
0	0	0	0	0
5 min	4.820	2.321	1.325	2.852
10 min	9.235	1.258	3.258	14.369
15 min	27.369	6.321	12.358	27.963
30 min	39.852	17.025	18.365	38.258
45 min	52.147	19.325	49.325	40.325
60 min	64.321	36.325	59.852	55.964
75 min	79.852	49.325	68.345	68.258
90 min	93.587	66.741	86.321	71.854
120 min	97.999	87.236	95.369	85.369

### Statistical analysis

Based on the data derived from water quality parameters, the statistical relationship in terms of two-way Analysis of Variance for the said different parameters was analyzed. All the statistical analysis was performed using the SPSS (version 16.0). Mean and standard deviation of collected data were calculated.

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### CONFLICT OF INTERESTS

The authors declare no conflict of interest

### ETHICS APPROVAL

Not applicable

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### AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

### DATA AVAILABILITY

Data will be available on request

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