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# Strategic Formulation of Dasatinib Nanosponges to Enhance Oral Bioavailability

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**ABSTRACT:** Nanosponges of Dasatinib were prepared by the solvent evaporation technique by employing Ethyl Cellulose, β Cyclodextrin, and poloxamer as rate retarding polymers using PVA as a copolymer. However, at higher ratios, drug crystals were observed on the nanosponge surface. An increase in the drug/polymer ratio (1:3 to 1:1) is in increasing order due to the increase in the concentration of polymer. However, after a particular concentration, it was observed that as the ratio of Drug to polymer was increased, the particle size decreased. The particle size was found in the range of 250- 450 nm. The entrapment efficiency of different formulations was found in the range of 90.56 to 98.32%, by comparing the above dissolution studies of formulations F1-F9. Maximum drug release was found in the F6 formulation containing Drug: β-cyclodextrin in a 1:3 ratio. So F6 formulation was taken as the optimized formulation, and drug release kinetics were performed and which follows zero-order kinetics with super case II transport mechanism

**KEYWORDS:** Dasatinib, Bioavailability, Nanosponges

## INTRODUCTION

Nano-technology has revolutionized technology various fields, and one of its most promising applications is even in advanced drug delivery approaches. This interdisciplinary field of nano-technology utilizes nanoscale materials (typically less than 100 nanometers in size) to stabilize the delivery of drugs to target sites within the body tissue or receptor. Here's an exploration of how nano- technology is transforming drug delivery systems:

**Targeted Delivery Systems**

Targeted drug delivery systems which precisely perform medication to precise cells, tissues, or organs can be produced through nanotechnology. By implementing nanomaterials with substrates or antibodies that target and bind particular biomarkers on target cells, the precision can be made conceivable.

Nanotechnology minimize drug penetration into healthy tissue and delivering pharmaceuticals directly to exhausted cells, therefore minimizing undesirable effects and promoting outcomes after therapy.

## METHODOLOGY:

**PREFORMULATION STUDIES:**

The following pre-formulation parameters are evaluated.

**Physical characteristics:**

**Solubility test:**

With distilled water, 0.1N HCL, Phosphate buffer pH 6.8 by shaking flask method. The samples were centrifuged the supernatant liquid was suitably diluted and estimated for Dasatinib concentration using UV spectrometer at 321 nm.

**Formulation of Nanosponges by emulsion solvent diffusion method:**

The dispersed phase, containing the polymer (Eudragit RS 100 or Chitosan or HPMC K100) and drug (Dasatinib), was first dissolved in an appropriate concentration (in mg/ml) of the cross-linking agent dichloromethane (DCM) (in percentage). This mixture was slowly added drop wise to a defined amount of the stabilizing agent polyvinyl alcohol (PVA) which is a good stabilizer in the aqueous media of continuous phase. The final reaction mixture obtained was stirred at rate of 1000 rpm for about 2 hours of time period. The resulting nanosponges were finally collected by filtration using membrane filter (100

micron) and subjected for drying in a hot air-oven at 40°C for one day. Further, the dried nanosponges were stored in vacuum desiccators to maintain adequate humidity until further use to ensure the removal of any residual solvent.

**TABLE 1: Formulation of Dasatinib nanosponges**

| F. Code | Polymer | Drug: Polymer |
|---|---|---|
| FC1 | Eudragit RS 100 (Synthetic) | 1:2 |
| FC2 | | 1:3 |
| FC3 | | 1:4 |
| FC4 | Chitosan (Natural) | 1:2 |
| FC5 | | 1:3 |
| FC6 | | 1:4 |
| FC7 | HPMC K100 (Semisynthetic, Cellulose polymer) | 1:2 |
| FC8 | | 1:3 |
| FC9 | | 1:4 |

**CHARACTERIZATION OF NANOSPONGES:**

**Determination of Zeta Potential:**

Using zetasizer (Malvern instrument) having zeta cells, polycarbonate cell with gold plated electrodes and using water as medium for sample preparation.

**Determination of Entrapment Efficiency:**

The amount of Dasatinib in the aqueous phase (distilled water) was accurately estimated as described in the literature and the entrapment efficiency (%) was calculated by the following equation:

$$EE = Wt_{total} - Wt_{free} / Wt_{total} \times 100$$

Where, Wt total was the weight of total drug added in the preparation of nanosponges and Wt free was the weight of the free drug (API) in aqueous system like water.

**Determination of total drug content:**

About 0.1 ml of the Dasatinib loaded nanosponge formulation was dissolved in 0. 9 ml of mixture of chloroform (analytical grade) and methanol (99 % v/v) at 1:1 ratio and then further diluted with aqueous media like distilled

Water. The drug in diluted samples which was obtained was further estimated by standard UV spectroscopic method.

**Differential scanning calorimetry:**

Differential scanning calorimetry is one of the basic and best tools which were used to investigate the drug and excipient compatibility studies and crystalline behavior of molecule and other excipients.

**RESULTS AND DISCUSSION:**

**PREFORMULATIONSTUDIES:**

**Physical characteristics:**

Physical observation of drug (Dasatabin) during bench mark study is revealed that Dasatabin is odourless, color of white and crystalline powder in nature.

**Solubility:**

Regarding solubility of API, Dasatabin, soluble in ethanol (alcohol), dichloromethane (DCM), sparingly soluble in DMSO, DMF and purely insoluble in distilled water.

**Melting point:**

The melting point (MP) of the drug, Dasatabin was found to be 142○C using melting point apparatus, and it was matched with literatures obtained, which assured the identity of received sample exactly.

**Selection of Wavelength:**

The API, Dasatabin was analyzed by spectrophotometrically in between the range of 200-400nm according to Beer-Lamberts law. The absorbance maximum (ʎmax) of the API was found at 320 nm (321 nm as per compendia) which was used for quantitative analysis of drug sample. The UV spectrum of Dasatabin (API) was measured in following figure.

**Calibration Curve of Dasatinib:**

In the calibration curve, linearity of the drug was obtained between 10-100µg\ml concentration of Dasatinib and the regression value statistically was obtained to be 0.996 which is nearness to linearity. Hence, it can be finalizing that Dasatinib obeys Beer Lambert's law in aqueous media at the concentration between 10-100µg\ml.

| Concentration (mcg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 2 | 0.131 |
| 4 | 0.255 |
| 6 | 0.353 |
| 8 | 0.481 |
| 10 | 0.643 |
| 12 | 0.744 |
| 14 | 0.861 |
| 16 | 0.986 |



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**Table 2 : Standard graph of Dasatinib in 0.1N Hcl at 321 nm**

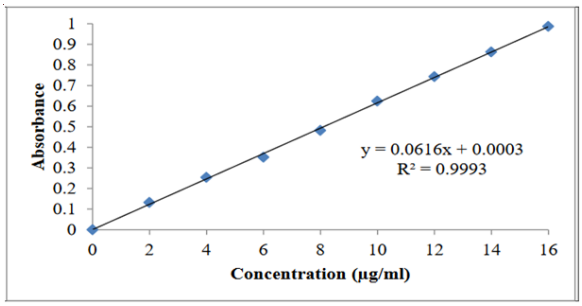


**Fig 1 : Calibration curve of Dasatinib**

**Drug-Excipients compatibility studies of nanosponges:**

**Fourier Transform Infrared Spectroscopy:**

Fourier transform infrared (FT-IR) spectra of the obtained samples were find out using a FTIR spectrophotometer by KBr disc method as per standard procedure. The spectrums results were recorded for the pure drug (API) and prepared nanosponge formulations

**Table 3 : FTIR interpretation of Drug + Polymers**

| Transition | IR Range($cm^{-1}$) | Absorption wave number ($cm^{-1}$) | | |
|---|---|---|---|---|
| | | Chitosan | Eudragit | HPMC |
| O-Hstretching | 3650-3200 | 3473.26 | 3629.69 | 3566.16 |
| C-H stretching | 2700-3300 | 2874.36 | 3002.02 | |
| CH₃stretching | 2850-2970 | - | - | 2947.05 |
| C=O stretching | 1820-1665 | 1735.11 | - | - |
| C=Cstretching | 1680-1620 | 1645.54 | - | - |
| N-Hbending | 1500-1800 | - | 1717.43 | |
| C-H bending | 1300-1500 | - | 1457.35 | - |
| COOH | 1500-1760 | - | - | 1507.41 |
| C-O stretching | 1300-1000 | 1109.84 | 1163.89 | 1218.83 |

The peaks obtained in FTIR spectrum of drig and polymers, say Dasatinib, Chitosan, Eudragit and HPMC can be observed and showed good compatibility.

**FORMULATION OF NANOSPONGES:**

Nine formulations of Dasatinib nanosponges (FC1-FC9) were prepared as per the procedure given in the previous section, with three different polymers i.e Eudragit (Hydrophobic), Chitosan and HPMC (Hydrophilic) by using emulsion solvent diffusion method.

**CHARACTERIZATION OF DASATINIB NANOSPONGES :**

**Particle Size, PDI and Zeta Potential of Prepared SLNs**

The particle size of the prepared nanosponges presented with less than 5µm. Particle size, PDI and Zeta potential of prepared nanosponges.

**Determination of Entrapment efficiency and Total drug content**

All the prepared nanosponges formulations were studied for % entrapment efficiency (EE) and total drug content (mg) by UV spectroscopic method using Beer-Lamberds law. All obtained results are tabulated and represented.

**Table 4: Drug content and %EE of prepared nanosponges.**

| Formulation code | Total drug content (mg) | Entrapment efficiency (%) |
|---|---|---|
| FC1 | 9.09±0.05 | 7 2.47±0.21 |
| FC2 | 9.13±0.09 | 75.82±0.11 |
| FC3 | 9.37±0.02 | 82.71±0.31 |
| FC4 | 9.52±0.01 | 89.23±0.10 |
| FC5 | 9.16±0.07 | 86.08±0.24 |
| FC6 | 9.02±0.04 | 84.35±0.42 |
| FC7 | 9.23±0.01 | 87.58±0.21 |
| FC8 | 9.47±0.02 | 89.47±0.31 |
| FC9 | 9.54±0.07 | 91.38±0.21 |

**SUMMARY AND CONCLUSION:**

Dasatinib nanosponges were skillfully crafted using three distinct polymers—Eudragit, Chitosan, and HPMC—through the emulsion solvent diffusion method. This straightforward manufacturing process requires no specialized equipment and holds promising potential for scalability. Preformulation studies were conducted to evaluate Dasatinib's solubility, revealing its insolubility in water but notable solubility in ethanol, methanol, and dichloromethane. FTIR and UV spectral analyses validated that the spectra of the sample drug were consistent with those of the pure standard. The UV spectrum displayed a peak of maximum absorbance at 320 nm. A comparative analysis of the FTIR spectra for Dasatinib and its nanosponge formulations confirmed the absence of any new peaks or the disappearance of existing ones, signifying no interaction between the drug and the polymers utilized in the study. Particle size and zeta potential were assessed using a Malvern zetasizer. The particle size analysis confirmed that the produced nanosponges were indeed within the nanometer range, with the optimized formulation FC6.



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exhibiting an average particle size of 200.42 ± 3.12 nm. The zeta potential measurements suggested that the nanosponges possessed stable properties. The drug entrapment efficiency in the nanosponges was calculated, revealing that all the formulations displayed a high level of drug entrapment. In-vitro release studies, conducted through the diffusion method, indicated that the FC6 formulation exhibited the highest drug release, reaching 80.45% after 24 hours. Drug release was found to increase in relation to the drug ratio, though it decreased with higher polymer concentrations, likely due to the formation of a core-shell structure with a hydrophobic core from the polymers. Data from the in-vitro release study were modeled to determine the release mechanism of Dasatinib from the nanosponges. The release model best conformed to first-order kinetics, following a diffusion-controlled mechanism. Moreover, the release process aligned with the Fickian (Case I) model, as per the Korsmeyer-Peppas model (n = 0.44). Lastly, physical stability studies confirmed that the optimized formulation remained stable for three months, adhering to ICH guidelines.

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