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# Design Development and Evaluation of Ibuprofen Loaded Nanosponges for Topical Application

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**Abstract :** The main perspective of study was to formulate ibuprofen loaded nanosponges for topical application. Emulsion solvent diffusion method was selected to prepare ibuprofen loaded nanosponges using different ratios of drug:polymer. The obtained nanosponges have been evaluated for physicochemical characteristics and *in vitro* release studies.The shape and morphology of drug loaded nanosponges were investigated and confirmed by SEM. FTIR results were in agreement with standard spectral studies and moreover it was identified that there was no interaction between drug and polymer. Entrapment efficiency of the NS was found to be around 70.41%. The production yield and *in vitro* release studies was also good. Overall this study resulted in porous nature of nanosponges which provides a channel for the release of the drug and the method is quick and reproducible.
**Key words :** Ibuprofen, Ethyl cellulose, Poly vinyl alcohol, nanosponges.

## I. Introduction:

Topical drug delivery is used for both local and systemic treatment.Most of drugs restricts entry through skin barrier where it becomes a challenge for formulation scientists to overcome these problems. Nanotechnologydeveloped several drug delivery systems like nanoparticles, nanoemulsions, nanosuspensions, nanosomes, nanofibres, nanosponges..,in order to deliver drug at target site in controlled and predictable manner by reducing side effects.Nanosponges were developed especially for topical delivery of drugs as they are non-irritating, non-allergic, non-toxic, non-mutagenic. They can deliver drugs that are poorly soluble in water. Nanosponges are tiny spherical particles ranging from 250 nm to 1 micrometer with large porous surface[1, 2].

Ibuprofen from isobutyl phenyl propanoicacid, is a Non Steroidal Anti-Inflammatory Drug (NSAID)used for treating arthritis, minor injuries, toothache, backpain where it works by reducing pain, fever, inflammation.Ibuprofen nanosponge incorporated gel given topically, it shows it action to target site by absorbing into skin deeper areas where there is inflammation and by giving cooling sensation. The amount of ibuprofen given toically is less when compared to oral administration. Therefore side effects caused by ibuprofen is less. Ibuprofen is poorly soluble in water (BCS II) and has less bioavailability,it's a basic problem

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faced by a formulation scientist. Therefore ibuprofen is loaded in nanosponge to improve solubility, reducing dose compared to oral administration, delivering drug at target site there by showing better bioavailability[3,4,5]. So this can be overcome by developing nanotechnology based formulation like nanosponges which may increase the bioavailability.

## 2. Materials and Methods:

### 2.1 Materials

Ibuprofen used in this experiment was purchased from a reputed raw material vendor, Chennai. PVAwas received from S.D Fine Chemical Limited, Mumbai. Ethyl cellulose was procured from Central Drug House Private Limited, New Delhi. All the reagents were of analytical grade and was utilized without any further purification. Double distilled water was used through out the experiment.

### 2.2 Preformulation Studies

#### 2.2.1. Physical Characteristics

By visual examination, the drug was identified for physical characters like colour, texture. Results were shown inTable No.1.

#### 2.2.2. Melting Point

Small amount of drug was loaded in an open ended capillary tube where one end of capillary tube was closed and kept in melting point apparatus(Sunbim Model) and temperature was noted when drug melts.

#### 2.2.3. Solubility studies

Solubility of ibuprofen was studied in distilled water, organic solvents and phosphate buffer.

### 2.3 Preparation of nanosponges[6]

Emulsion solvent diffusion method was used to formulate ibuprofen loaded nanosponges by using a suitable polymer. Dispersed phase consists of specified amount of drug and polymer which was dissolved in an organic solvent dichloromethane. Aqueous phase consists of specified amount of poly vinyl alcohol dissolved in 150 ml distilled water. Disperse phase was added drop by drop into aqueous phase by stirring on magnetic stirrer at 1000 rpm for about 2 hours. The nanosponges formed were collected by filtration and dried in oven at 40$^{o}$C for about 24 hours. They were then kept in the vacuum desiccators to remove the residual solvent [6]. Figure1 shows the image of ibuprofen loaded nanosponge prepared by emulsion solvent diffusion method.

### 2.4 Evaluation of nanosponges

The prepared nanosponges were characterized for the following parameters:

- Surface characterisitics by SEM
- Drug-Polymer interaction study using FTIR
- Percentage yield
- Entrapment efficiency and
- *In vitro* drug release profile of Ibuprofen nanosponges

#### 2.4.1. Surface characteristics by Scanning Electron Microscopy (SEM)[7]

SEM (Model FEI Quanta FEG 200) used to determine the microscopic characters (shape & morphology) of ibuprofen loaded nanosponges. Samples were placed on glass slide kept under vacuum andthen by using sputter coater unit, samples were coated with a thin gold layer, operated at 15kv acceleration voltage. Then picture of nanosponge were taken by random scanning of the stub. The representative SEM photographs of the nanosponge were shown in Figure 2 -4.

### 2.4.2. Drug-Polymer interaction study using FTIR[8]

FTIR was used to find whether any kind of interaction between drug and polymer. IR spectra for nanosponges were taken separately to know the interactions. Samples were mixed with KBr powder to make pellets by applying 5 ton pressure. By powder diffuse reflectance on FTIR, spectra were obtained at an ambient temperature using PerkinElmer Spectrum ES Version 10.5.2.The scanning range used was from 4000-400 $cm^{-1}$ at a scan period of 3 min. FTIR spectral analysis was shown in Figure 5.

### 2.4.3. Spectrophotometric characterization[9, 10 ]

#### 2.4.3.1. Determination of λ max by UV-Spectroscopy:

UV-visible spectrophotometer was used to determine the absorbance maximum (λ-max) of ibuprofen using a digital double - beam recording spectrophotometer with scanning range of 200-800 nm. Solution of ibuprofen was prepared using double distilled water. Shimadzu UV-visible spectrophotometer (Perkin Elmer, Lambda 35 Model) 1800 with spectral bandwidth of 1 nm , ± 0.3 nm wavelength accuracy and 10 mm pair of quartz cells were used to record the spectral and absorbance readings. UV spectrum was represented in Figure 6.

#### 2.4.3.2. Preparation of calibration curve of ibuprofen in methanol:

100µg/ml stock solution was prepared. From stock solution, 10µg/ml of working solution was prepared. Then serial dilutions were made by methanol to get concentrations of 1 to 5µg/ml. Using methanol as blank, samples scanned at 222 nm. Standard calibration curve was obtained by plotting graph between absorbance values and concentration.Absorbance data for calibration curve was shown in Table No.2 and Figure 7.

#### 2.4.3.3. Preparation of calibration curve of ibuprofen in phosphate buffer pH 7.2:

100µg/ml stock solution was prepared. From stock solution, 10µg/ml of working solution was prepared. Then serial dilutions were made by phosphate buffer pH 7.2 to get concentrations of 1 to 5µg/ml. Using phosphate buffer pH 7.2 as blank, samples scanned at 222 nm. Standard calibration curve was obtained by plotting graph between absorbance values and concentration. Absorbance data for calibration curve was shown in Table No.3 and Figure 8.

### 2.4.4. Percentage yield

Ibuprofen loaded nanosponges were weighed after drying. Percentage yield was calculated by

$$\% \text{ yield} = \frac{\text{Practical weight of nanosponges obtained}}{\text{Theoretical weight (drug + polymers)}} \times 100$$

### 2.4.5. Entrapment efficiency[11, 12]

50 mg from the prepared drug loaded nanosponges by emulsion solvent diffusion method using suitable polymer were suspended in 50 ml of methanol and were subjected for ultracentrifugation for 40 minutes. The percentage of incorporated ibuprofen was determined spectrophotometrically at 222nm. After centrifugation of the aqueous suspension, amount of free drug was detected in the supernatant and the amount of incorporated drug was determined as a result of the initial drug minus the free drug. The drug entrapment efficiency (EE) of ibuprofen nanosponges was determined using the formula:

$$\% \text{ of drug entrapment} = \frac{\text{Initial weight of the drug} - \text{Free drug weight}}{\text{Initial weight of the drug}} \times 100$$

### 2.4.6. In-vitro drug release study of ibuprofen nanosponges[14]

*In vitro* drug release was carried out by diffusion method using phosphate buffer pH 7.2 as dissolution media. Required quantity of sample (100 mg) was taken and then suspended in required media and then kept in the open ended apparatus. One end of the tube was kept openand the dialysis bag was tied (molecular weight cut off: 12–14kDa, surface area of 22.5cm$^2$) at the other end which was then submerged in a beaker containing 100ml of the phosphate buffer pH 7.2. Temperature of the media was kept at 37 ± 2 °C and 100 rpm speed. The samples were withdrawn at predetermined intervals and replaced by fresh medium simultaneously. Aliquots withdrawn were assayed at each time interval for the drug released at λ max of 222 nm using UV-Visible spectrophotometer by keeping phosphate buffer pH 6.8 as blank. Three trials were carried out. From this percentage drug release was calculated and mean values of cumulative % drug release were plotted versus timeand results were given inTable No.4 and Figure 9.

## 3. Results and discussion:

### 3.1Preformulation Studies

### 3.1.1. Physical Characteristics

**Table No. 1 - Physical characterization of ibuprofen**

| S. No. | Properties | Observation |
|---|---|---|
| 1. | Description | Colorless or half white, Crystalline powder |
| 2. | Odour | Characteristic odor |
| 3. | Color | Colorless or half white |

Ibuprofen was found to be colorless or half white, crystallinepowder in appearance and odourless.

### 3.1.2. Melting Point

The ibuprofen (pure drug) melting point was found to be 75- 78$^0$c, it matches with the standard expected value of ketoconazole (75- 78$^0$c).

Melting point range of the polymer experimentally was found to be 220- 240$^0$c whereas standard value is 240-255$^0$c.

### 3.1.3.Solubility studies

Ibuprofen was completely soluble in, ethanol, chloroform, methanol, dichloro methane, sparingly soluble in acetone and insoluble in distilled water.

### 3.2 Preparation of nanosponges[6]

**Figure 1 - Image of ibuprofen loaded nanosponge prepared byemulsion solvent diffusion method**

Preparation of nanosponges for topical applications was carried using emulsion solvent diffusion technique. Emulsion solvent diffusion method was found to be simple and efficient to prepare nanosponges and it was utilized successfully. Figure 1 shows the image of ibuprofen loaded nanosponge prepared byemulsion solvent diffusion method.

### 3.3 Surface characteristics byScanning Electron Microscopy (SEM)

The representative SEM photographs of the nanosponge were represented in Figure 2 -4. SEM images showed the nanosponge was porous with a smooth surface morphology and spherical in shape. Due to evaporation of solvent, the nanosponge shell found to be smooth porous where outer surface was shiny smooth and inner surface was porous.

**Figure 2** **Figure 3**

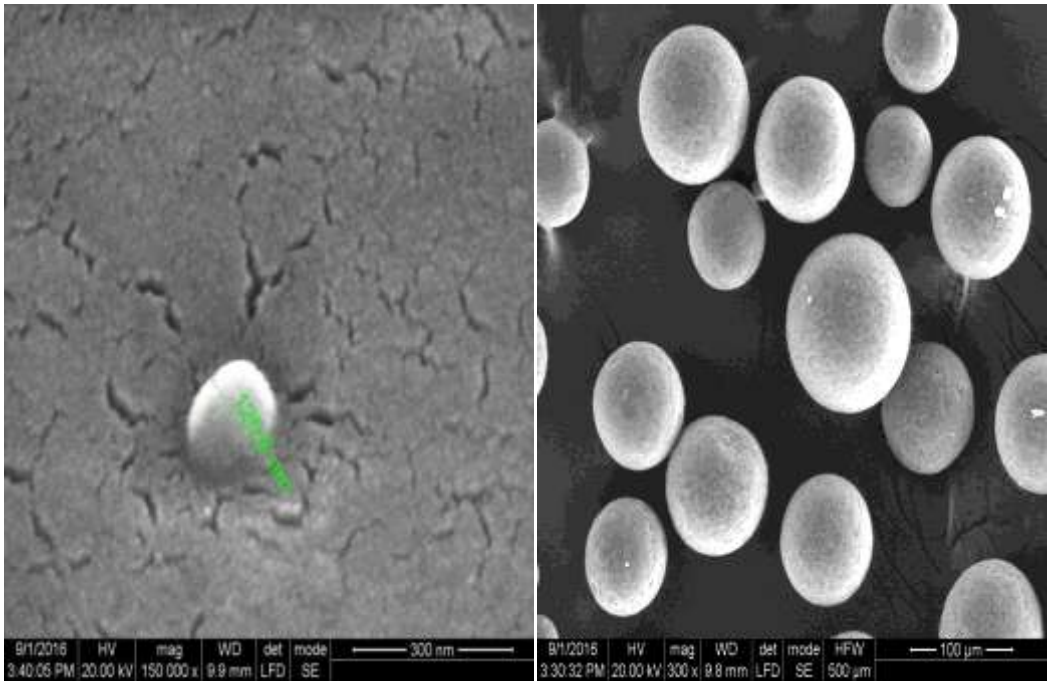



**Figure 2 - View showing smooth surface of individual nanosponge**

**Figure 3 - View showing nanosponge**

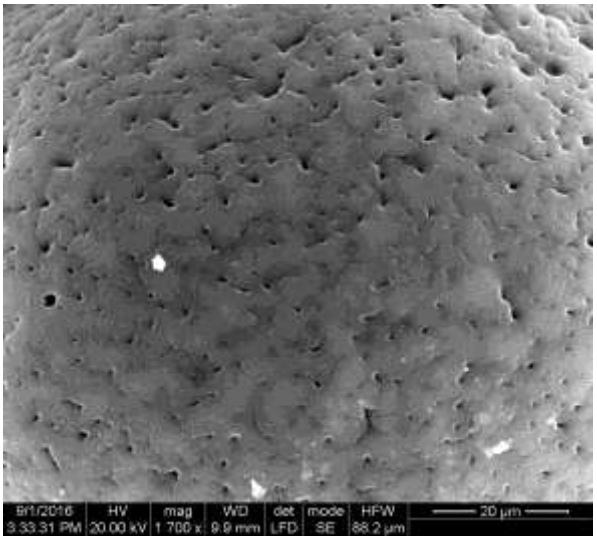
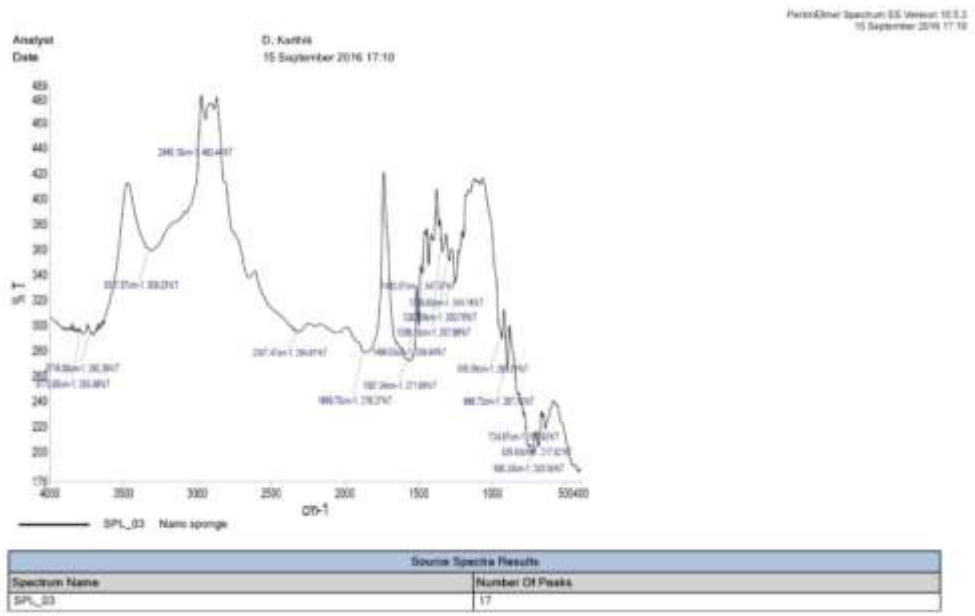



**Figure 4 – Surface view of nanosponge**

SEM results revealed that particle surface morphology has been shown to be beneficial for topical application.

### 3.4. Drug-Polymer interaction study using FTIR [8]




| Source Spectra Results | |
|---|---|
| Spectrum Name | Number Of Peaks |
| SPL_03 | 17 |

**Figure 5 – FTIR spectral analysis of nanosponge**

From the obtained results, there were no significant shifts compared to pure drug and polymers, physical mixtures of drug and polymer. Presence of functional groups does not show any major interaction when compared with standard spectrum of pure drug and polymer. Hence, ibuprofen loaded nanospongeIR spectra confirmed that drug was stable in all nanosponge batches by showing good compatibility with polymer, excipients used.

### 3.5 Spectrophotometric characterization[9, 10 ]

#### 3.5.1. Determination of λ max by UV-Spectroscopy

Ibuprofen spectrum gave the highest peak at 222 nm (Figure 6). The λ max was found to be 222nm and same was selected as λ max for further evaluation.

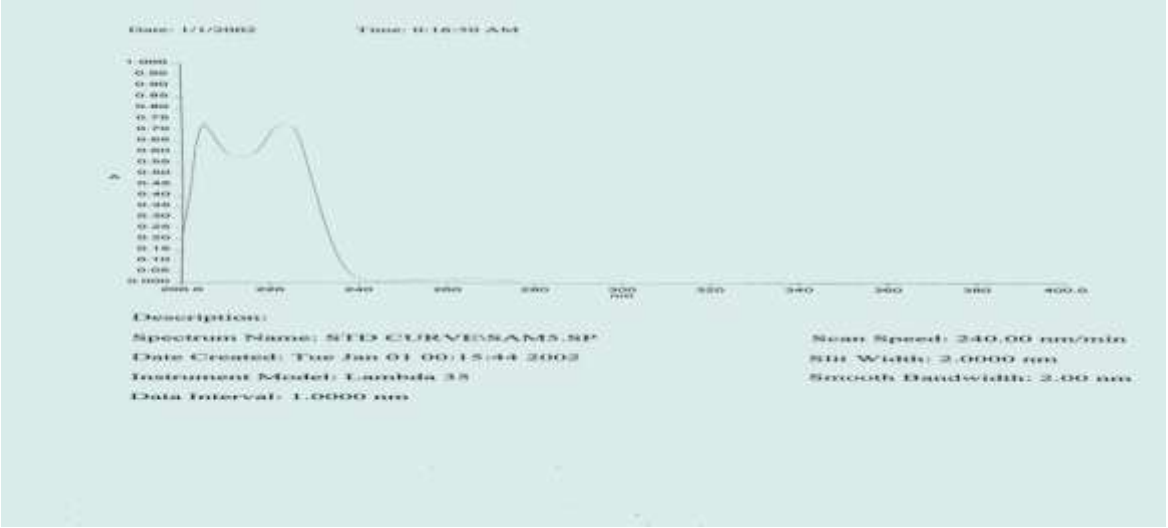



**Figure 6 - UV spectrum of ibuprofen**

### 3.5.2. Preparation of calibration curve of ibuprofen in methanol

Standard solutions of different concentrations (Table No.2) were made and their absorbance was recorded at 222 nm for ibuprofen. Drug concentrations versus absorbance curve were plotted as given in Figure 7.

**Table No. 2 - Linearity study ofibuprofen in methanol**

| S.No. | Concentration (µg/ml) | Absorbance at 222nm |
|---|---|---|
| 1. | 0 | 0 |
| 2. | 1 | 0.0972 |
| 3. | 2 | 0.1806 |
| 4. | 3 | 0.3265 |
| 5. | 4 | 0.4123 |
| 6. | 5 | 0.5421 |

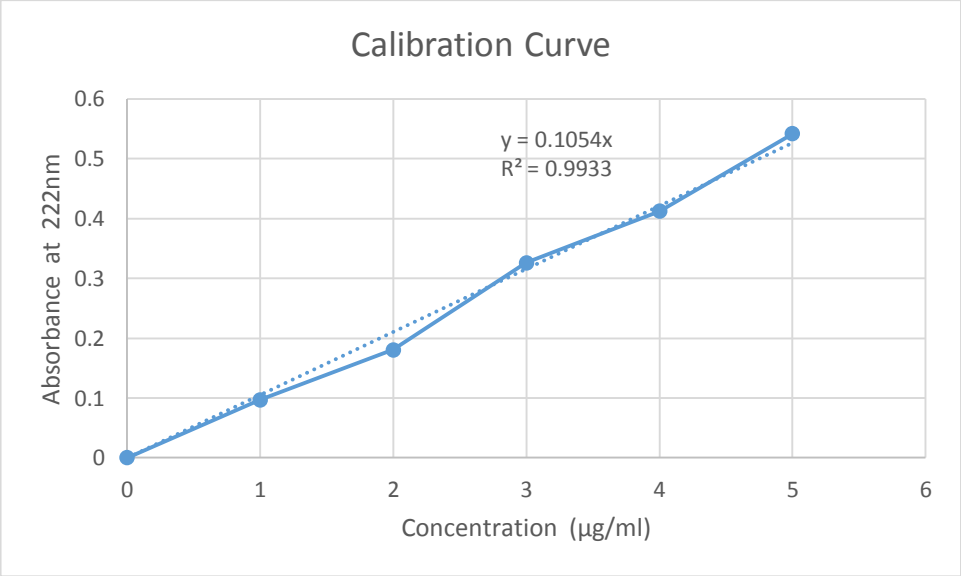



**Figure 7 - Standard plot of ibuprofen in methanol at 222 nm**

**Result:**

Linearity range was found to be in the range of 1 µg/ml to 5 µg/ml and regression coefficient ($r^2$) was found to be 0.9933 at 222 nm.

### 3.5.3. Preparation of calibration curve of ibuprofen in phosphate buffer pH 7.2

Standard solutions of different concentrations (Table No.3) were made and their absorbance was measured at 222 nm for ibuprofen. Drug concentrations versus absorbance curve were plotted as given in Figure 8.

**Table No. 3 - Linearity study ofibuprofen in phosphate buffer pH 7.2**

| S.No. | Concentration (µg/ml) | Absorbance at 222nm |
|---|---|---|
| 1. | 0 | 0 |
| 2. | 1 | 0.0704 |
| 3. | 2 | 0.1837 |
| 4. | 3 | 0.3214 |
| 5. | 4 | 0.4495 |
| 6. | 5 | 0.5270 |

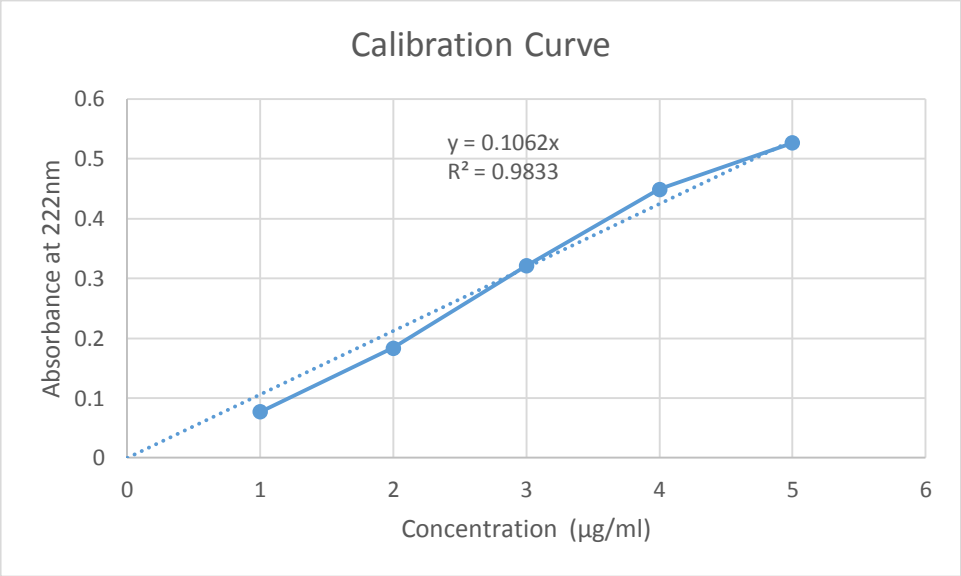



**Figure 8 - Standard plot of ibuprofen in phosphate buffer pH 7.2 at 222 nm**

**Result:**

Linearity range was found to be in the range of 1 µg/ml to 5 µg/ml and regression coefficient ($r^2$) was found to be 0.9833 at 222 nm.

### 3.6 Percentage yieldand Entrapment efficiency [11, 12]

The percentage yield was around 88- 90%and entrapment efficiency was found to be nearly 70- 72%.

### 3.7 In-vitro drug release profile of ibuprofen nanosponges[14]

**Table No.4 – Percentage drug release of ibuprofen from nanosponge**

| S.No. | Time in minutes | % amount of drug release |
|---|---|---|
| 1 | 15 | 2.25 |
| 2 | 30 | 4.64 |
| 3 | 45 | 7.38 |
| 4 | 60 | 7.38 |
| 5 | 90 | 11.27 |
| 6 | 120 | 14.17 |
| 7 | 150 | 24.56 |
| 8 | 180 | 31.97 |
| 9 | 210 | 45.10 |
| 10 | 240 | 66.55 |
| 11 | 270 | 76.69 |
| 12 | 300 | 88.35 |

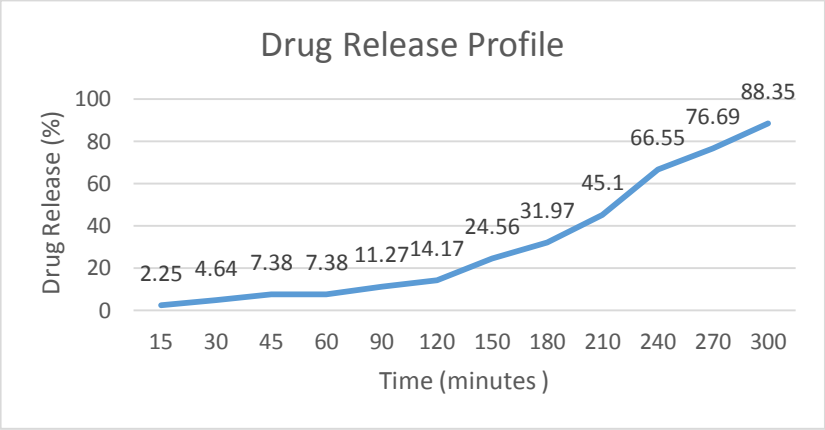



**Figure 9 – Cumulative percentage drug release profile of ibuprofen from nanosponge**

## 4. Conclusion:

In this present study, attempts have been made to prepare ibuprofen loaded nanosponges by Emulsion Solvent Diffusion technique. The reasons to choose this method as the production method was due to its simple procedure, less in cost and it is suitable method for drugs having poor water solubility.In order to obtain the best formulations, initially the effect of difference of temperature on the nanosponges formation was investigated. When there was no difference observed, the formulation was optimized.

The morphology of prepared nanosponges was verified by means of SEM and it is observed that most of the nanosponges were spherical in shape and FTIR results were in agreement with standard spectral studies and moreover confirmed that there was no interaction between drug and polymer.The production yield and entrapment efficiency of the nanosponge was found to be good. Release studies of ibuprofen nanosponges shows significant improvement compared to conventional ibuprofen formulation.Overall this study resulted in better encapsulation, solubility and permeation of ibuprofen loaded nanosponge complexes.

Nanosponges can be easily formulated into different dosage forms like parenterals, aerosols, topical, tablets and capsule due to its size and shape. For effective drug delivery,drug has to reach the target site instead of circulating throughout body. This is possible when drug is formulated in topical dosage form. Hence, this study stated that nanosponge drug delivery systems are suitable candidates for topical use and prolonged drug release which can be easily and effectively scaled up.

## 5. Acknowledgment:

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