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# Formulation and Evaluation of Sulindac Nanosponge Loaded Gel for the Treatment of Arthritis

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**ABSTRACT**
These are small, separate, and permeable matrix like structure known as NANOSPONGES. These can be used as topical, oral, inhalational delivery system. Its size is less than 1 µm. These are prepared using decomposable as well as water soluble polymeric material that allows maximum stability. Nanosponges, a promising class of nanomaterials, have garnered significant grown significantly due to their distinct and exceptional properties along with versatile applications in drug delivery. These nanostructures, characterized by their porous structure and significant surface area-to-volume ratio, exhibit exceptional capability in encapsulating a broad spectrum of therapeutic agents, encompassing small molecules, proteins, and nucleic acids. This review article examines latest advancements seen on nanosponges' research, with a focus on their synthesis methodologies, physicochemical properties, and mechanisms of drug loading and release. Furthermore, we highlight the promising therapeutic outcomes achieved through the utilization of nanosponges in various disease models, including cancer, infectious diseases, and neurological disorders. This article gives a brief about nanosponges with the introduction, merits, demerits, methodology, loading efficacy, assessment including aspects like particle size and zeta potential, SEM, entrapment effectiveness, study for release of drug along with summarizing with a mission to include it in future prospect in the field, emphasizing the need for further investigation to enlarged the perspective of full potential of nanosponge to be as innovative in delivery of drug to different platforms in clinical settings have been discussed.

**Keywords:** Nanosponges, Gel, Sulindac, Ethyl Cellulose, Eudragit RS 100, Polyvinyl Alcohol, Carbopol 934, Arthritis. NSAIDs

## I. INTRODUCTION

Nanosponges are a novel approach in drug delivery, distinguished by their nanoporous structure resembling a mesh- like network. This architecture enables them to encapsulate or suspend diverse substances, enhancing solubility for poorly soluble drugs through inclusion and non-inclusion mechanisms. Key benefits include improved drug bioavailability by shielding hydrophobic drug molecules within their cavities, facilitating targeted delivery and prolonged release for sustained therapeutic effects. Nanosponges are versatile in accommodating both hydrophilic and hydrophobic drugs, owing to their inner hydrophobic cavities and external hydrophilic branching. They act as three-dimensional networks with a polyester backbone and cross-linkers, offering potential solutions to challenges in drug solubility and delivery, thereby enhancing the efficacy of various pharmaceuticals.

**Composition of Nanosponge:**

a. Polymer
b. Cross linking agent
c. Drug substance

**Criteria for choice of drug:**

a. Molecular weight between 100-400 Daltons
b. Contain fewer than five condensed rings
c. The solubility of the substance in water is below 10 mg per millilitre
d. Melting point of substance is below 250 °C

**Method of Preparation:**

a. Hyper Cross-Linked B-Cyclodextrins
b. Quasi-Emulsion Solvent Diffusion
c. Solvent Used Method
d. Ultrasound-Assisted Synthesis
e. Polymerization:

**Advantages of Nanosponge:**

a. Targeted site-specific drug delivery
b. Flavour masking and conversion of liquids to solids
c. Reduced side effects
d. Encapsulation of hydrophobic drugs

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e. Adjustable particle size

**Disadvantages**

a. Limited inclusion of small molecules
b. Crystalline vs. paracrystalline nanosponges
c. Tunable size and drug release

## II. MATERIALS AND METHODS:

The following materials purchases from Sulindac (yarrowchem.pvt.,ltd), Ethyl Cellulose from Kemphasol.in, Poly Vinyl Alcohol purchases from SD Fine Chem Ltd, Eudragit S100 purchases from CDH Pvt Ltd, Dichloromethane

**Preparation of Nanosponges:**

Sulindac-loaded nanosponges were prepared using the quasi- emulsion solvent diffusion method with an appropriate polymer. The dispersed phase comprised a specific amount of drug and polymer dissolved in 30 ml of dichloromethane, an organic solvent. The aqueous phase consisted of a specified amount of polyvinyl alcohol dissolved in 100 ml of distilled water. The dispersed phase was gradually added to the aqueous phase while stirring on a magnetic stirrer at 1000 rpm for approximately 2 hours. The resulting nanosponges were collected through filtration and dried in an oven at 40°C for around 24 hours. Subsequently, they were placed in vacuum desiccators to eliminate any residual solvent. The polymers used for formulating the Sulindac nanosponges were ethyl cellulose and Eudragit S 100.

| S. No | Formulati on code | Wt. of drug (mg) | Wt. of polymer Ethyl cellulose (mg) | Wt. of polymer Eudragit(mg) | Wt. of PVA(mg) |
|---|---|---|---|---|---|
| 1 | NS1 | 150 | 400 | --- | 600 |
| 2 | NS2 | 150 | 600 | --- | 600 |
| 3 | NS3 | 150 | 800 | --- | 600 |
| 4 | NS4 | 150 | --- | 400 | 600 |
| 5 | NS5 | 150 | --- | 600 | 600 |
| 6 | NS6 | 150 | --- | 800 | 600 |

**Preparation of Nanosponge Gel:**

Carbopol 934 was soaked in water for 2 hours to form gel like consistency and then mixed at 600 revolutions per minute (RPM) using a magnetic stirrer to achieve a homogeneous dispersion eventually add Triethanolamine to neutralize pH further nanospong and propylene glycol was added to aqueous dispersion

| S. No | Formulation code | Wt. of Nanosponge (mg) | Wt. of Carbopol (mg) | Wt. of Triethanolamine (mg) | Wt. of PLG (ml) |
|---|---|---|---|---|---|
| 1 | G1 | 151 mg | 1000 | 500 | 5 |
| 2 | G2 | 157 mg | 1000 | 500 | 5 |

## III. RESULT AND DISCUSSION

### I. PREFORMULATION STUDIES

**Physical Characteristics:**

Assessment of Sulindac's color, odor, and texture was done. Sulindac appears as a light yellow powder, absence of odor, and possesses an amorphous texture.

Colour: Yellow

Odour: Unpleasant breath odour Taste: Metallic/ Bitter

**Melting Point**

Standard Value: 182-185 $^0$C

Actual value: 183 $^0$C

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**Solubility**

**Table: Solubility test for Sulindac in different solvents**

| S. No. | Solvent | Soluble | Sparing Soluble | Insoluble |
|---|---|---|---|---|
| **1.** | Methanol | √ | | |
| **2.** | DMSO | √ | | |
| **3.** | Distilled Water | | | √ |
| **4.** | Acetic Acid | | √ | |
| **5.** | Dichloromethane | √ | | |

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**Particle Size Determination:**

**Table: Calibration Table of Microscope**

| **Eye Piece** | **Stage Micrometre** | **Calibration factor Calculation** |
|---|---|---|
| 3 | 4 | 4×10=40 |
| 5 | 7 | 7×10=70 |
| 8 | 11 | 11×10=110 |
| 15 | 19 | 19×10=190 |

Calibration Factor was found to **13.655**

**Table: Table for Particle Size Determination**

| | | |
|---|---|---|
| **2** | **2×13.6= 27.2** | **27.2 + 40.8 + 27.2 + 68 +68 + 81.6 + 54.4 + 40.8 + 95.2 +81.6 / 10 = 584.8/ 10 = 58.48** |
| **3** | **3×13.6= 40.8** | |
| **2** | **2×13.6= 27.2** | |
| **5** | **5×13.6= 68** | |
| **5** | **5×13.6= 68** | |
| **6** | **6×13.6= 81.6** | |
| **4** | **4×13.6= 54.4** | |
| **3** | **3×13.6= 40.8** | |
| **7** | **7×13.6= 95.2** | |
| **6** | **6×13.6= 81.6** | |

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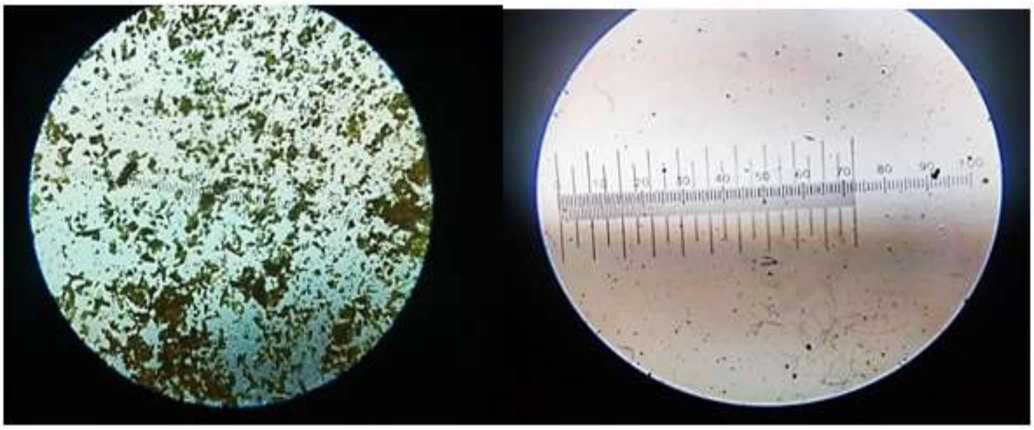


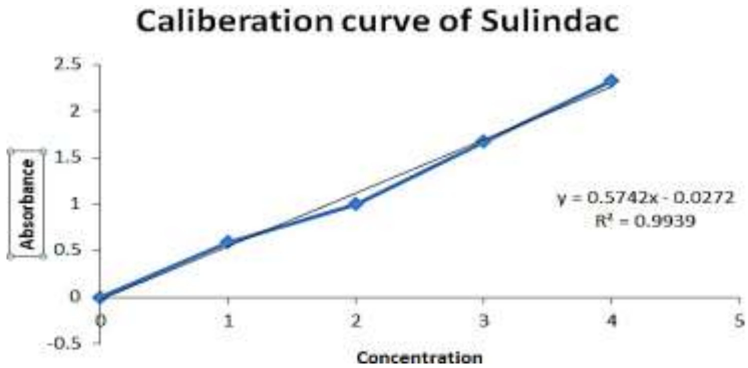
The mean particle diameter was observed to be **58.48**

**UV Spectrophotometry:**

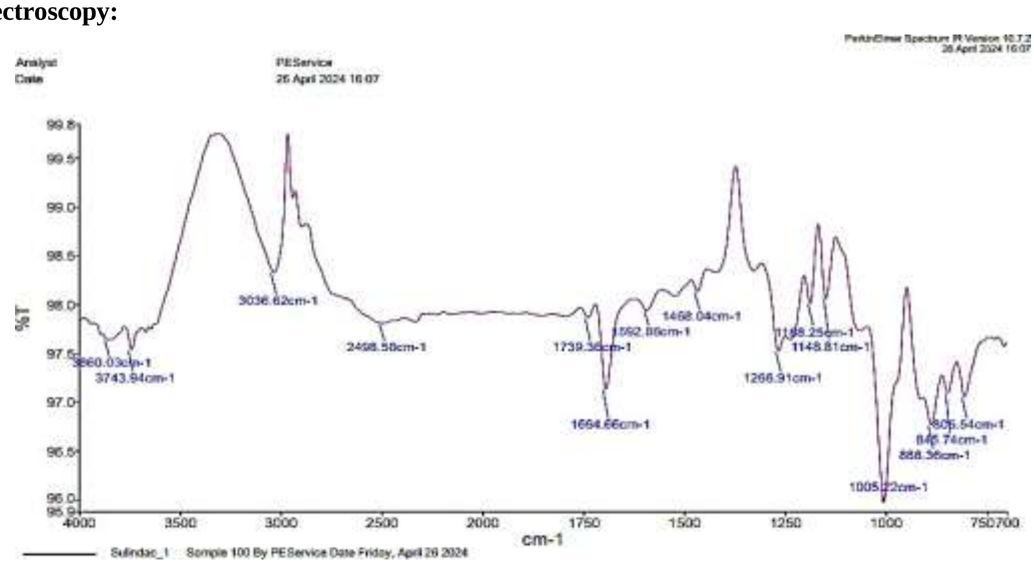
Selection of Wavelength

A solution of Sulindac at a concentration of 100 µg/mL was analyzed using a double beam UV spectrophotometer across the wavelength range of 200-400 nm to identify λ max. The absorption peak acquired is depicted here. Sulindac was determined to exhibit maximum absorption at 226 nm, leading researchers to select this wavelength for subsequent studies.

Construction of calibration curve of Sulindac




**FTIR Spectroscopy:**



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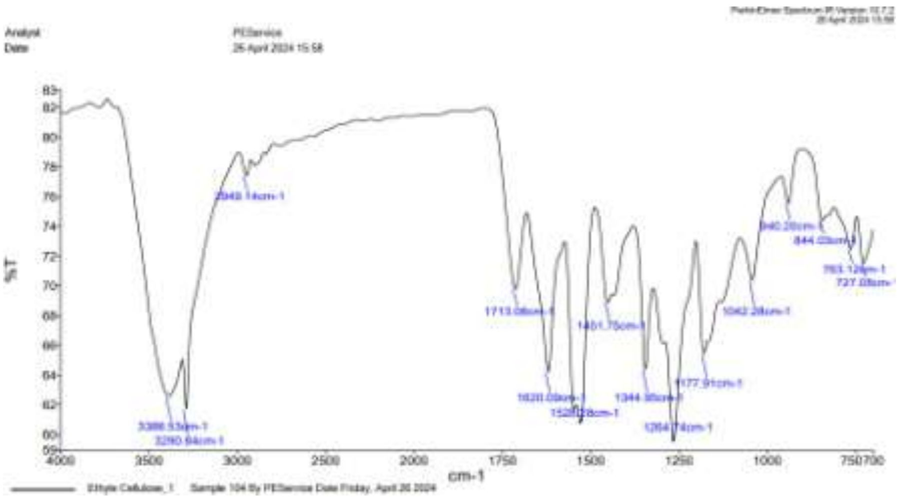
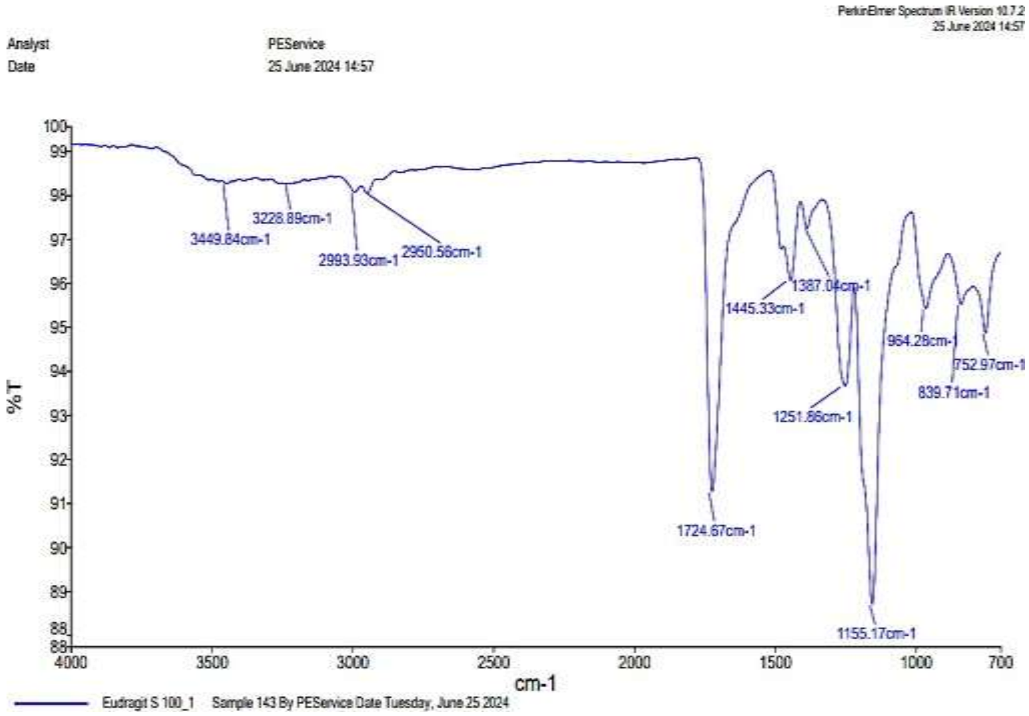
**FTIR spectrum of Sulindac**




**FTIR spectrum of Ethyl Cellulose**



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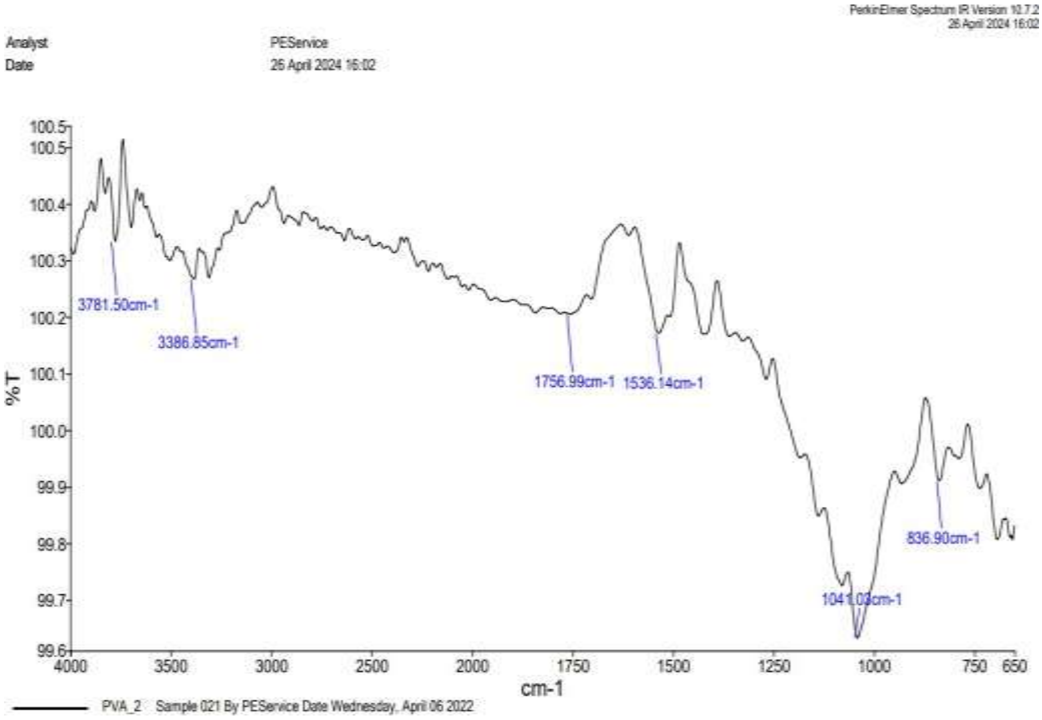
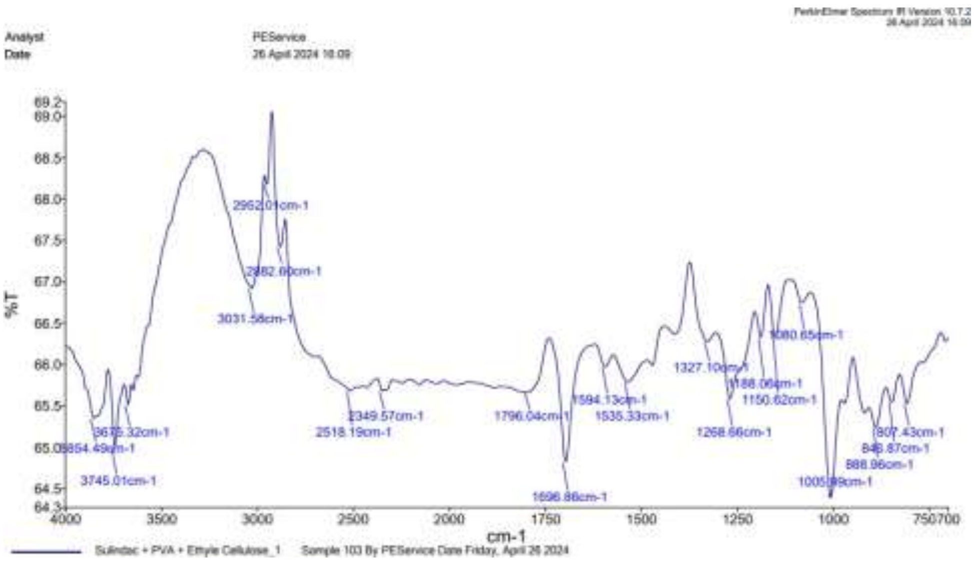
**FTIR spectrum of Eudragit**




**FTIR spectrum of Poly Vinyl Alcohol (PVA)**



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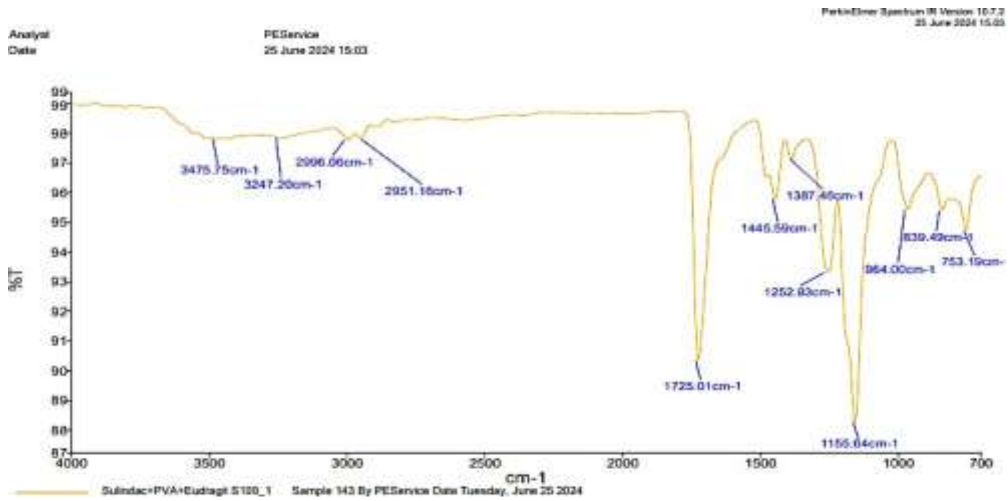
**FTIR spectrum of physical mixture containing Sulindac, EC and PVA**




**FTIR spectrum of physical mixture containing Sulindac, Eudragit and PVA Micrometric Study**

**Tapped Density**

**Tapped density= Mass of powder** =5= 1.28

**Tapped Volume** 3.9

**Bulk Density**

**Bulk density= Mass of powder Bulk Volume**

= 5 = 0.81

6.1

**Carr's Index**

**CI= Tapped-Bulk Density × 100 Tapped Density**

= 1.28-0.81× 100 = 0.47 × 100= 36.7

1.28 1.28

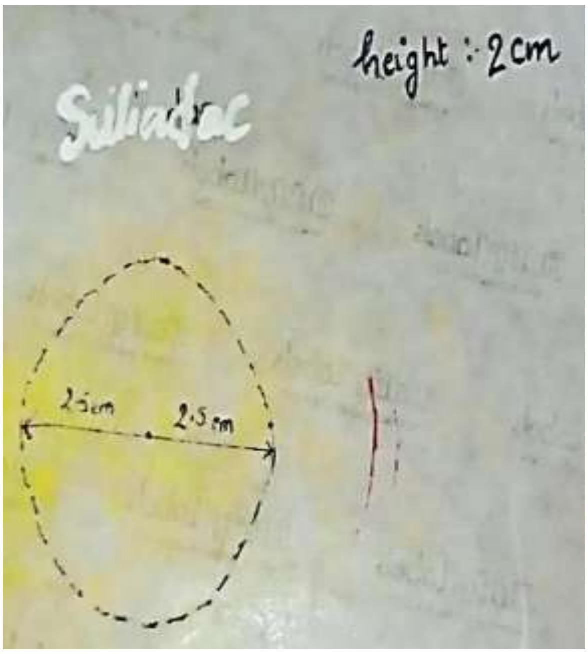
i.e. flow property of Sulindac is Very Poor

**Hausner's Ratio CI= Tapped Density Bulk Density**

= 1.28 = 1.58

0.81

i.e. flow property of Sulindac is Very Poor




**Angle of Repose Tan θ= h/r** θ=Angle of Repose h= Height of Pile

r= Radius of Pile2/2.5= 0.8

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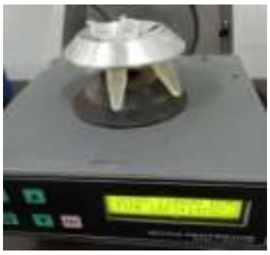
Value of Tan (0.8) is **38.7** i.e. flow property of Sulindac is Satisfactory

**Thin Layer Chromatography:**
It was done using **Ethyl Acetate (9.7): Acetic acid glacial (0.3) Solvent front =** 6.5
**Drug=** 5.8
**Rf= Distance travelled by spot Distance travelled by solvent front**
5.8/ 6.5 = 0.8

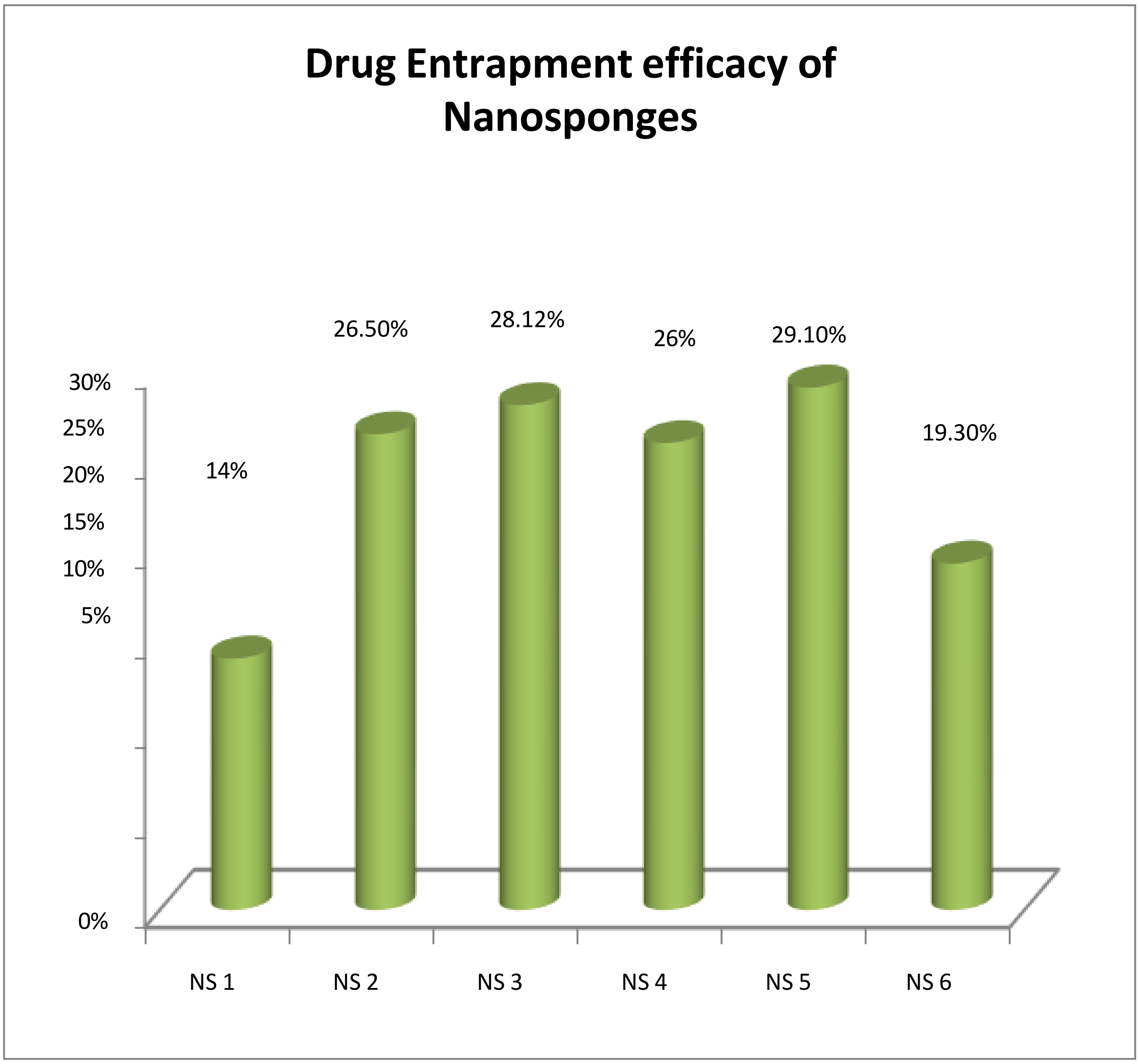
**EVALUATION OF NANOSPONGES:**
**Physical Appearance: Colour:** Light yellow Powder



**Drug Entrapment efficacy:**

| Formulation code | Drug entrapment efficacy |
|---|---|
| NS 1 | 82.8% |
| NS 2 | 99.2% |
| NS 3 | 93.27% |
| NS 4 | 95% |
| NS 5 | 87.5% |
| NS6 | 78.9% |

**Entrapment efficacy**




**Drug Entrapment efficacy of Nanosponges Production Yeild :**

| Formulation code | Drug entrapment efficacy |
|---|---|
| NS 1 | 14% |
| NS 2 | 26.5% |
| NS 3 | 28.12% |
| NS 4 | 26% |
| NS 5 | 29.1% |
| NS6 | 19.3% |

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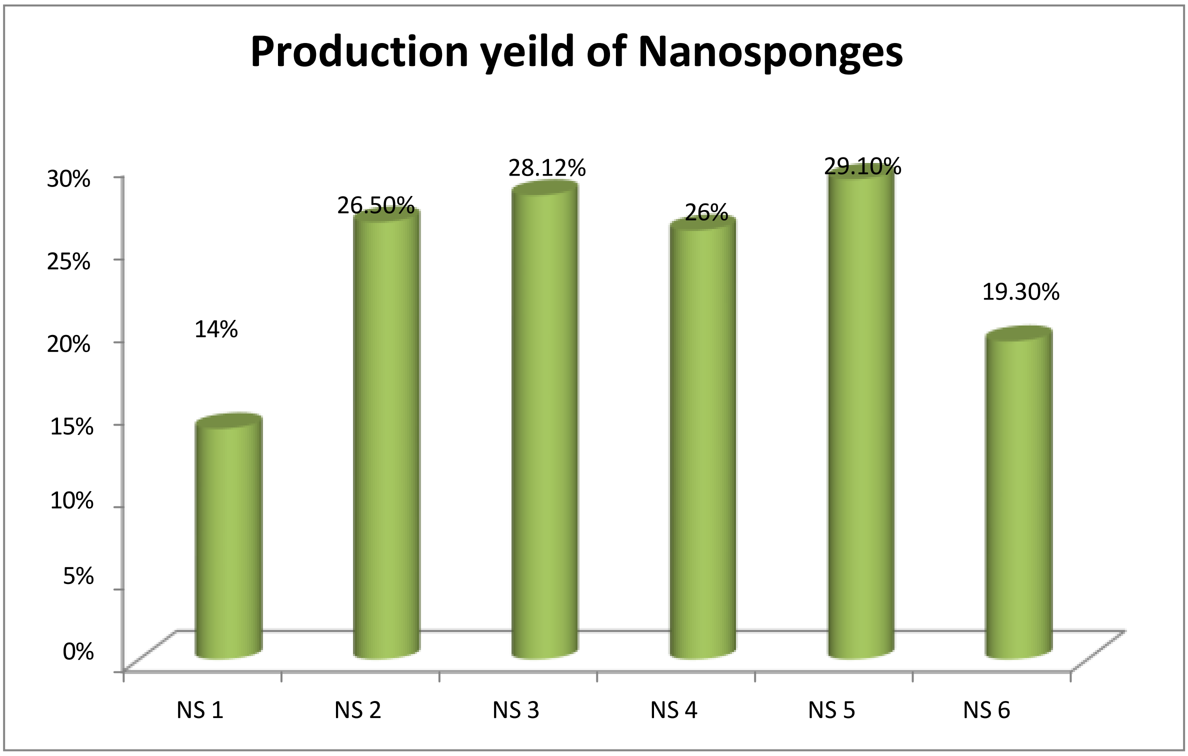
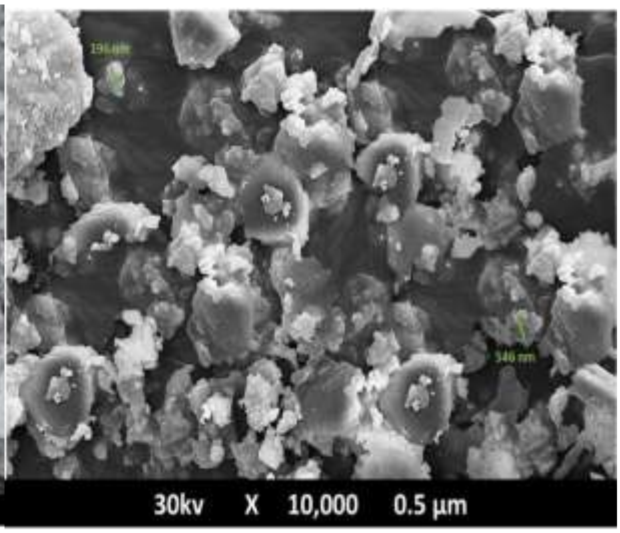
**Production Yield**




**Production yeild of Nanosponges**

**Scanning electron Microscopy (SEM):**


SEM imaging of NS2 **(Ethyl Cellulose)**




SEM imaging of NS4 **(Eudragit RS 100)**

This interprets that Eudragit loaded Nanosponge has smaller particle size i.e 95 nm and 80nm as compared to Ethyl cellulose containing Nanosponge that is largest particle 546nm and smallest is 196 nm. Hence we can say that Eudragit containing Nanosponge is more suitable for topical delivery.

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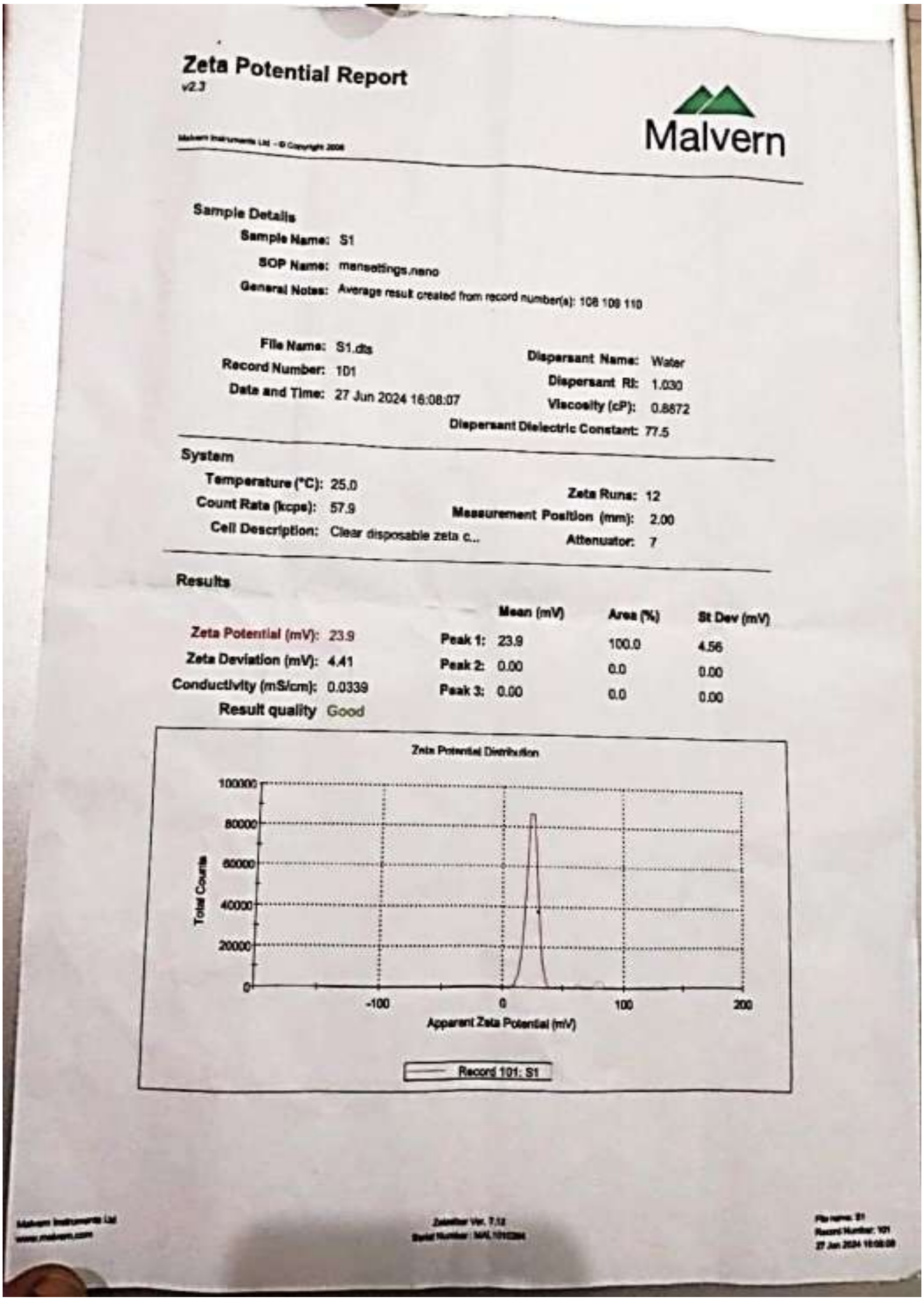
**Zeta Potential:**



## Zeta Potential Report
v2.3

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**Sample Details**

**Sample Name:** S1
**SOP Name:** mansettings.nano
**General Notes:** Average result created from record number(s): 108 109 110

**File Name:** S1.dts
**Record Number:** 101
**Date and Time:** 27 Jun 2024 16:08:07

**Dispersant Name:** Water
**Dispersant RI:** 1.030
**Viscosity (cP):** 0.8872
**Dispersant Dielectric Constant:** 77.5

**System**

**Temperature (°C):** 25.0
**Count Rate (kcps):** 57.9
**Cell Description:** Clear disposable zeta c...

**Zeta Runs:** 12
**Measurement Position (mm):** 2.00
**Attenuator:** 7

**Results**

| | | | Mean (mV) | Area (%) | St Dev (mV) |
|---|---|---|---|---|---|
| Zeta Potential (mV): | 23.9 | Peak 1: | 23.9 | 100.0 | 4.56 |
| Zeta Deviation (mV): | 4.41 | Peak 2: | 0.00 | 0.0 | 0.00 |
| Conductivity (mS/cm): | 0.0339 | Peak 3: | 0.00 | 0.0 | 0.00 |
| Result quality | Good | | | | |



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Zetasizer Ver. 7.12

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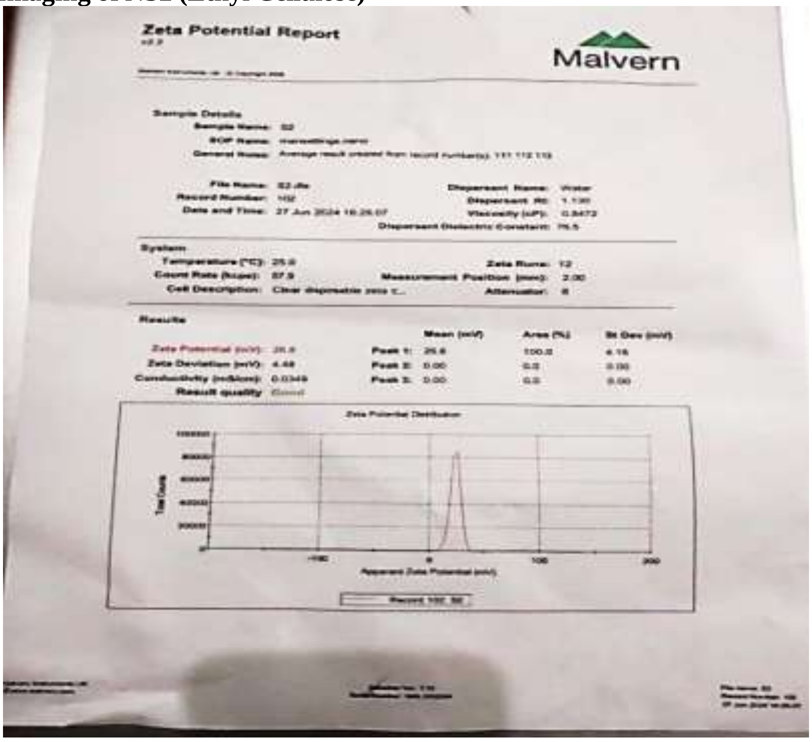
**Zeta Potential of Imaging of NS2 (Ethyl Cellulose)**




**Zeta Potential of Imaging of NS4 (Eudragit S 100) EVALUATION OF NANOSPONGE GEL:**

**Viscosity**: Testing was conducted at 25°C with spindle LV 61, specifically noting the viscosity at 100 rpm.

| S. No. | Formulation Code | pH | Viscosity (cp) |
|---|---|---|---|
| 1 | G1 | 6.22 | 7389 |
| 2 | G2 | 6.86 | 7915 |

**In-vitro Drug Release Study**: An in-vitro investigation of the gel was executed using a dialysis membrane. The receptor chamber contained phosphate buffered saline (PBS) with pH 7.4. A specifically cut dialysis membrane was utilized for the examination. The entire apparatus was positioned on a temperature-controlled magnetic stirrer, maintaining a constant temperature of 37°C throughout the entire 30 min study period. Samples were periodically extracted and subjected to spectrophotometric analysis at 226 nm.

| S. No. | Time (hours) | %Cumulative drug Release |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 5 | 12.34 |
| 3 | 10 | 19.32 |
| 4 | 15 | 26.99 |
| 5 | 20 | 36.71 |
| 6 | 25 | 49.32 |
| 7 | 30 | 58.43 |

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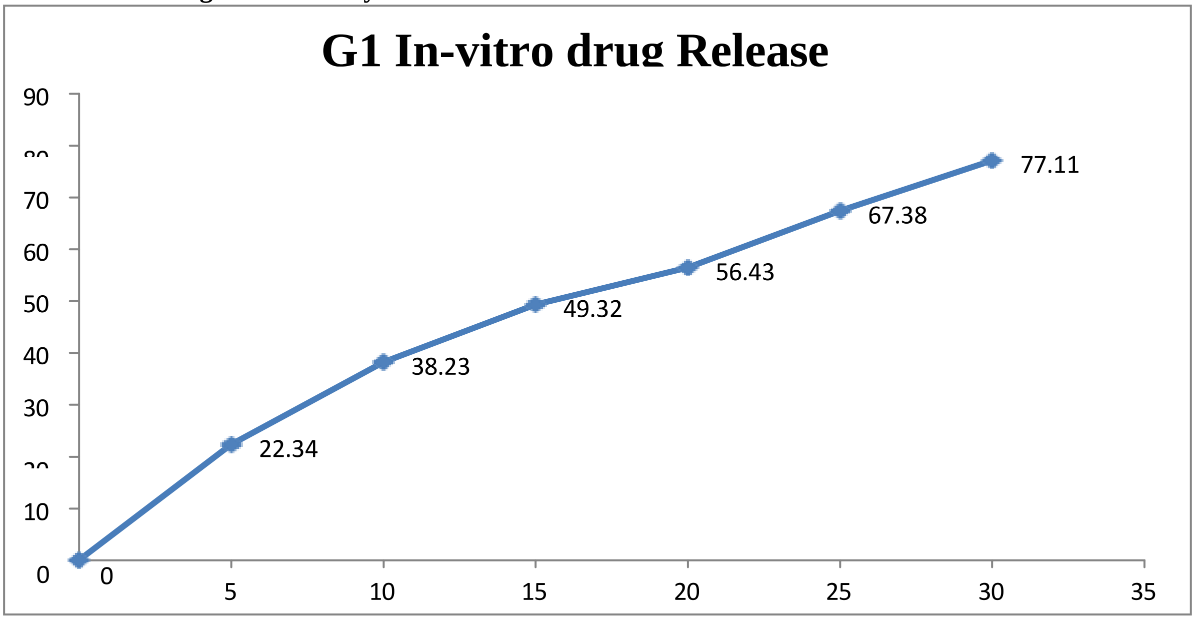
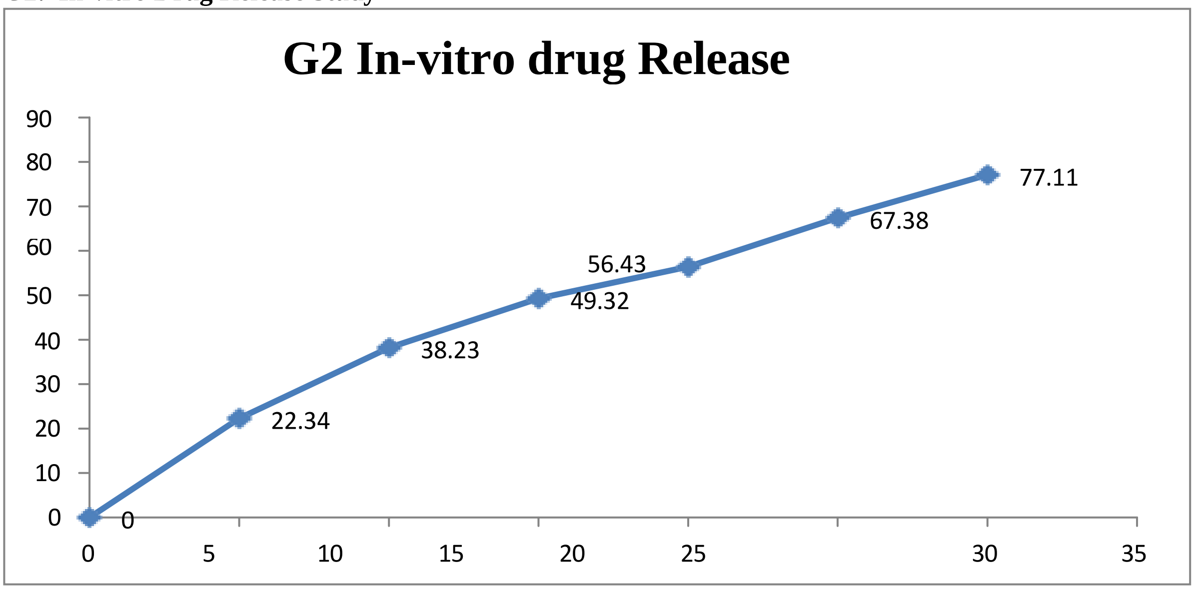
**G1: In-vitro Drug Release Study**




| S. No. | Time (hours) | %Cumulative drug Release |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 5 | 22.34 |
| 3 | 10 | 38.23 |
| 4 | 15 | 49.32 |
| 5 | 20 | 56.43 |
| 6 | 25 | 67.38 |
| 7 | 30 | 77.11 |

**G2: In-vitro Drug Release Study**



## IV. CONCLUSION:

Sulindac, a nonsteroidal anti-inflammatory drug (NSAID), is commonly used for managing arthritis but is often limited by gastrointestinal side effects and suboptimal bioavailability when administered orally. By employing nanosponges, we aimed to create a formulation that delivers Sulindac more effectively to the target site. The development process involved the synthesis of Sulindac-loaded nanosponges using a Quasi solvent diffusion method. Various formulation parameters, such as the concentration of polymer, cross-linker, and drug-to-polymer ratio, were optimized to achieve high drug loading and encapsulation efficiency. The nanosponges were then incorporated into a gel base to facilitate topical administration, aiming for a homogeneous and stable gel formulation. Characterization of the nanosponges was carried out to ensure the quality and consistency of the formulation. Particle size analysis confirmed that the nanosponges were within the nanoscale range, which is crucial for enhancing skin penetration and drug delivery efficiency. Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) revealed the porous nature and spherical shape of the nanosponges, which are essential for high drug loading and controlled release. Fourier-transform infrared spectroscopy (FTIR) analyses were performed to verify the physical state of Sulindac within the nanosponges and to check for any potential chemical interactions between the drug and the polymer matrix.

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