**IJPSR (2024), Volume 15, Issue 3** **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 17 July 2022; received in revised form, 08 December 2023; accepted, 20 February 2024; published 01 March 2014

# DEVELOPMENT AND CHARACTERIZATION OF ACECLOFENAC-LOADED NANOSPONGE GEL FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS

Sherin Koshy [1], Celestie George [*1] and Shajan Abraham [2]

Nazareth College of Pharmacy [1], Othera P.O Thiruvalla - 689546, Kerala, India.
Department of Pharmaceutics [2], Nazareth College of Pharmacy, Othera P.O Thiruvalla - 689546, Kerala, India.

**Keywords:**

Nanosponge, Rheumatoid arthritis, Aceclofenac, Gel

**Correspondence to Author:**
**Celestie George**

M. Pharm Delegate,
Nazareth College of Pharmacy,
Othera P.O Thiruvalla - 689546,
Kerala, India.

**E-mail:** celestiegeorge7@gmail.com

**ABSTRACT:** Rheumatoid arthritis is an autoimmune and inflammatory disease, in which immune system attacks healthy cells in your body by mistake, causing inflammation (painful swelling) in the affected parts of the body. Aceclofenac is a phenyl acetic acid derivative and NSAID with anti-inflammatory, analgesic and antipyretic effects. Nanosponges were prepared by the Emulsion solvent diffusion method with varying concentrations of Ethyl cellulose and Poly vinyl alcohol. FTIR and DSC study reports confirmed the absence of incompatibilities between the drug and the excipients. Nine Nanosponge formulations were prepared (F1- F9) and evaluated for particle size, PDI, Production yield, entrapment efficiency, Zeta potential, SEM analysis, *in-vitro* drug release and kinetic studies. The kinetic data analysis of Nanosponges fit to Higuchi model and follows Zero order kinetics. All the Nanosponge formulations were incorporated into 1% Carbopol gel base to produce drug loaded Nanosponge gel. The drug-loaded Nanosponge gel was evaluated for physical properties, pH, Viscosity, Spreadability, Extrudability, Drug content and *in-vitro* drug release, *in-vitro* anti-inflammatory activity, *ex-vivo* permeation study, kinetic study and stability study. These findings suggest that the Nanosponges will be potentially useful for the treatment of Rheumatoid arthritis providing prolonged drug release and good stability.

**INTRODUCTION:** Rheumatoid arthritis is an autoimmune and inflammatory disease in which the immune system attacks healthy cells in your body by mistake, causing inflammation (painful swelling) in the affected parts of the body. Rheumatoid arthritis attacks mainly the joints, usually many joints at once. Rheumatoid arthritis affects joints in the hands, wrists, and knees. In a joint with Rheumatoid arthritis, the lining of the joint becomes inflamed, causing damage to the joint tissue.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(3).763-70

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(3).763-70

This tissue damage can cause long-lasting or chronic pain, deformity, and unsteadiness. Rheumatoid arthritis can affect other tissues throughout the body and cause problems in organs such as the lungs, heart, and eyes [1]. Nanosponges are a new class of materials that are tiny mesh-like nanoporous structures made of microscopic particles with a few nanometers wide cavities in which a large variety of substances can be encapsulated or suspended. Then it can be incorporated into a dosage form.

These particles can carry both lipophilic and hydrophilic substances and improve the solubility of poorly water-soluble molecules. They have a proven spherical colloidal shape and are reported to have a very high solubilization capacity for poorly soluble drugs by their inclusion and non-inclusion behavior [2].

Nanosponges are able to encapsulate both hydrophilic and hydrophobic drug molecules because of their properties like inner hydrophobic cavities and external hydrophilic branching, thereby, they can offer unparalleled flexibility [3]. Nanosponges are more like a three-dimensional network or a scaffold structure. The backbone is a long length of polyester mixed in a solution with small molecules called crosslinkers, and they can act like tiny grappling hooks to fasten different parts of the polymer together [4, 5]. The preparation of nanosponges depends upon the type of delivery system, polymers, and nature of drug and solvents. Various approaches used to form nanosponges are the Emulsion solvent diffusion method, Ultrasound-Assisted synthesis and quasi–emulsion solvent diffusion [6, 7].

## EXPERIMENTATION:

**MATERIALS AND METHODS:** Materials used in this study were Aceclofenac, Ethyl Cellulose, Polyvinyl Alcohol, Dichloromethane, Carbopol 934, Propylene Glycol, Methyl Paraben, Propyl Paraben, Triethanolamine.

**Preformulation Study:** Preformulation studies such as identification of drugs, Organoleptic Evaluation, Determination of Melting Point, and solubility were carried out. Analytical methods such as determining λmax, compatibility studies, FTIR, DSC were carried out.

**Identification of Drug:** The monograph of Aceclofenac signified that the substance under examination was intimately mixed with potassium bromide. FTIR spectrum of the sample was taken using the Potassium bromide pellet method. The spectrum of the test specimen was recorded over the range from 4000cm$^{-1}$ to 500cm$^{-1}$ and compared with the corresponding IP reference standard [8].

**FTIR (Fourier Transform Infrared) Study:** The IR spectra were recorded using an FTIR spectrophotometer. The samples were prepared by mixing the drug and the excipients in 1:1 ratio and the mixtures were stored in closed containers for 1 month. FTIR spectrum of the samples was taken using the Potassium bromide pellet method. The physical mixtures of Aceclofenac and excipients were scanned in the wavelength region between 4000 and 500 cm$^{-1}$ and compared to check the compatibility of the drug with excipient [9].

**Formulation of Nanosponges:** Nanosponges of Aceclofenac were prepared using the emulsion solvent diffusion method. The organic phase comprises the accurately weighed amount of Aceclofenac and ethyl cellulose dissolved in dichloromethane [13]. The aqueous phase, which consists of polyvinyl alcohol dissolved in warm water, was used as the emulsifying or stabilizing agent. The organic phase was gradually added into an aqueous phase and stirred mechanically at 1200 rpm for 2 hrs at room temperature to remove the solvent dichloromethane from the mixture. Nanosponges formed were filtered and dried at room temperature and stored in a tightly closed container [10].

**TABLE 1: FORMULATION DESIGN OF NANOSPONGES**

| Formulation | Drug (gm) | Ethyl Cellulose (gm) | Polyvinyl Alcohol (gm) | Dichloro Methane (ml) | Water (ml) |
|---|---|---|---|---|---|
| F1 | 1 | 0.4 | 1.4 | 20 | 50 |
| F2 | 1 | 0.8 | 1.8 | 20 | 50 |
| F3 | 1 | 1.2 | 2.2 | 20 | 50 |
| F4 | 1 | 1.6 | 2.6 | 20 | 50 |
| F5 | 1 | 2.0 | 3.0 | 20 | 50 |
| F6 | 1 | 2.4 | 3.4 | 20 | 50 |
| F7 | 1 | 2.8 | 3.8 | 20 | 50 |
| F8 | 1 | 3.2 | 4.2 | 20 | 50 |
| F9 | 1 | 3.6 | 4.6 | 20 | 50 |

**Evaluation of Nanosponges:** Formulated Nanosponge formulations were subjected to preliminary evaluation tests. They include Physicochemical properties such as Particle size determination, Polydispersiblity index, Zeta potential, Microscopy studies, Loading efficiency, production yield, *in-vitro* release, Drug release kinetics, and Stability Studies [11].

**Scanning Electron Microscopy (SEM):** The sample was prepared by lightly sprinkling on a double adhesive tape stuck to an aluminum stub.

The stubs were then coated with platinum. The stub containing the coated sample was placed in a scanning electron microscope. The samples were randomly scanned and photomicrographs were taken at the acceleration voltage of 20 kV.

**Preparation of Nanosponge Gel:** Accurately weighed amount of carbopol 934 was taken and soaked in water for 24 hours for complete polymer swelling. To the weighed amount of carbopol gel base, drug-loaded nanosponges equivalent to 1 %w/w were uniformly dispersed. Propylene glycol is added as a penetration enhancer. Methylparaben and propylparaben are added as a preservative. Triethanolamine is added dropwise with gentle stirring using a homogenizer to adjust the pH. The final dispersion is agitated until a smooth gel is formed without lumps.

**Evaluation of Nanosponge Gel:** Various evaluations of drug-loaded nanosponge gel were carried out such as determination of pH, viscosity, drug content, spreadability, *in-vitro* drug release studies, *ex-vivo* skin permeation study, *in-vitro* anti inflammatory activity [12].

***In-vitro* Drug Release Studies:** *In-vitro* release study of Aceclofenac loaded Nanosponge gel was carried out by using Franz diffusion cell. The formulation was taken in the donor compartment and phosphate buffer saline was taken in the receptor compartment. The cellophane membrane previously soaked overnight in the diffusion medium was placed between the donor and receptor compartment. 1 g of the formulation was spread uniformly on the cellophane membrane, which is in contact with the receptor medium. The whole assembly was placed on the thermostatically controlled magnetic stirrer with continuous stirring and the temperature of the medium was maintained at 37± 0.5°C. At specific intervals, 1 ml of sample was withdrawn from the receptor compartment and replaced with an equal volume of PBS 7.4. After suitable dilutions, the absorbance of the sample was determined at nm by UV-visible spectrophotometer.

***Ex-vivo* Skin Permeation Study:** *Using goat ear skin, ex-vivo skin permeation studies were performed*. The superficial skin was collected from the back of the goat's ear. The dermal part of the skin was wiped 3 to 4 times with a wet cotton swab soaked in isopropanol. The skin specimens were then cut into appropriate sizes after carefully removing subcutaneous fat and washing them with normal saline. The skin was then mounted in a modified Franz diffusion cell at 37 ºC. A weighed quantity of Nanosponge gel was then spread on the skin's stratum corneum side, and the dermis side faced the receptor compartment. The receptor compartment contains 25 ml of pH 7.4 phosphate buffer and after every one hour 1 ml of sample was taken and replaced with the same volume of phosphate buffer. After 6 hours of sampling, absorbance was measured at 276 nm against a blank of pH 7.4 phosphate buffer by UV spectrophotometer, and the percentage of drug permeated was calculated.

***In-vitro* Anti-inflammatory Activity:** The anti-inflammatory activity of nanosponge gel was studied using the inhibition of albumin denaturation technique. The reaction mixture (5 ml) consisted of 4.5 ml of bovine serum albumin (5% aqueous solution) and 0. 5 ml of Nanosponge gel; pH was adjusted to 6.3 using a small amount of 1N Hydrochloric acid. The samples were incubated at 37°C for 20 minutes and then heated at 57°C for 3 minutes. After cooling samples, 2.5 ml of phosphate buffer solution was added to each test tube. Turbidity was measured spectrophotometrically at 259 nm. For control, 0.5 ml of distilled water was used instead of Nanosponge gel. The percentage inhibition of protein denaturation was then calculated.

**Release Kinetics:** A kinetic study was carried out by fitting the *in-vitro* drug release data into Zero order, First order, Higuchi model, Hixon-Crowell Cube Root Law model, and Korsmeyer- Peppas models. The best outfit model was confirmed by the value of $R^{2,}$ which is near to 1.

**Stability Studies:** Stability studies were carried out on the optimized formulation according to ICH guidelines. The optimized formulation was packed in a tightly closed container and was stored in the ICH-certified stability chamber maintained at 40 ± 2ºC and 75% ± 5% RH for 6 months. The formulation was evaluated before and after at periodic intervals for 3 months for changes in

appearance, pH, drug content, and *in-vitro* drug release. The work will be continued for 6 months.

**RESULT AND DISCUSSION:** An organoleptic evaluation of Aceclofenac was carried out. It was found to be white or almost white in colour. It was odourless or almost odourless and appearance was crystalline powder. The melting point determination of the drug was performed and the value observed was 153℃ which was within the standard melting point range of Aceclofenac, that is 149-153℃. The solubility of the drug was determined by dissolving the drug in different solvents.

The drug was very slightly soluble in water, freely soluble in methanol and in acetone, phosphate buffer saline 7.4 and chloroform. Analytical methods like determination of λmax, preparation of calibration curve and compatibility studies were performed for the determination of Aceclofenac. When scanned between 200-400 nm, the drug showed maximum absorption at 276 nm. A standard graph of Aceclofenac was plotted by taking absorbance on the y-axis and concentration (µg/ml) on the x-axis. The y-intercept and $R^2$ values were found to be 0.073, 0.995, respectively.

**Identification of Drug:**

**FTIR:** FTIR studies were carried out for compatibility evaluation. The FTIR spectrum of Aceclofenac exhibited peak signals at 3167 $cm^{-1}$, 2862 $cm^{-1}$, 1730 $cm^{-1,}$ and 2976 $cm^{-1}$ due to stretching vibrations of N-H, C-H, C=O, C- C bonds. There were no significant changes in the frequency of the functional groups of Aceclofenac. So, the drug was compatible with Ethyl Cellulose, Polyvinyl Alcohol, Dichloromethane, Methyl Paraben, Propylparaben, and Carbopol.

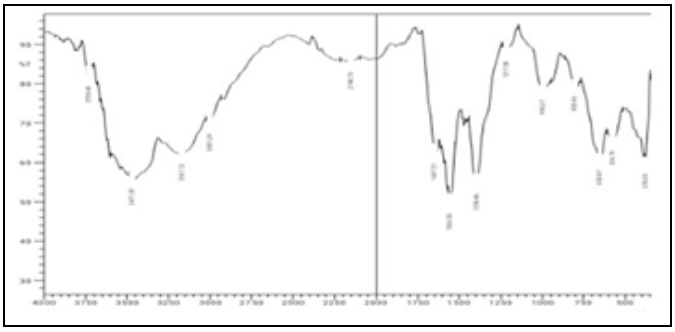

**FIG. 1: FTIR SPECTRA OF ACECLOFENAC (SAMPLE)**

**TABLE 2: FUNCTIONAL GROUPS AND THEIR OBSERVED PEAK VALUES**

| Sl. no. | Drug | Functional Groups ($cm^{-1}$) | | | | |
|---|---|---|---|---|---|---|
| | | N-H stretching | C-H stretching | C=O stretching | C-C stretching | C-Cl stretching |
| 1 | Reference Aceclofenac | 3400-3250 | 2963-2669 | 1850-1650 | 1500-1400 | 852-550 |
| 2 | Sample Aceclofenac | 3167.2 | 2862.19 | 1730.15 | 1556.55 | 653.87 |

**TABLE 3: % YIELD, DRUG ENTRAPMENT AND ZETA POTENTIAL OF NANOSPONGE FORMULATION**

| | Percentage Yield (%) | % drug entrapment (Mean±S.D)* | Zeta Potential (meV) |
|---|---|---|---|
| $F_1$ | 87.19 | 88.28±0.623 | -4.4 |
| $F_2$ | 92.65 | 90.76±1.091 | -4.8 |
| $F_3$ | 95.45 | 94.45±0.256 | -5.2 |
| $F_4$ | 96.15 | 96.15±0.366 | -5.4 |
| $F_5$ | 98.76 | 98.88±1.239 | -5.6 |
| $F_6$ | 85.76 | 86.76±0.555 | -5.9 |
| $F_7$ | 78.2 | 85.32±0.524 | -6.1 |
| $F_8$ | 81.39 | 81.39±0.781 | -6.3 |
| $F_9$ | 74.34 | 78.42±1.173 | -7.0 |

**Evaluation of Nanosponge:** The percentage yield was minimum for formulation F9 (75.31%) and maximum for formulation F5 (98.76%). The entrapment efficiency was found to be highest for F5 formulation, which is 98.88% and the lowest entrapment of drug was found for F9 formulation. The prepared nanosponges possess high drug entrapment efficiency and were found to be in the range of 78.42% - 98.88%. For Aceclofenac nanosponges using ethyl cellulose, the zeta potential was found to be -5.6 mV with a peak area of 100% intensity. These values indicate that the formulated Aceclofenac nanosponges (F5) are stable.

**Preparation of Nanosponge Gel:** From the drug content, drug entrapment, and drug release study, it is found that F5 is the best formulation. So it was selected and formulated to gel.

**FIG. 3: ACECLOFENAC LOADED NANOSPONGE GEL**

**Scanning Electron Microscopy (SEM):** The SEM images of formulations F5 are shown in Fig. 4. SEM images showed the nanosponge was porous with a smooth surface morphology and spherical shape.

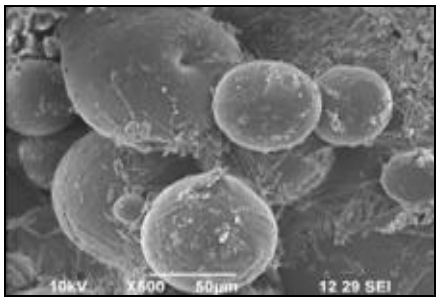

**FIG. 4: SEM IMAGE OF NANOSPONGE**

**Evaluation of Aceclofenac Nanosponge Gel:** The formulated Aceclofenac gel was visually assessed and found to be homogenous. The pH was 5.7, which states that the values were within the range near that of skin pH. The viscosity of the optimized Nanosponge gel was found to decrease as the rpm was increased and pseudo plastic behaviour was noted. Drug content of the gel formulation was found to be 98.3%. The spreadability of the Aceclofenac gel formulation was found to be 11.13 g cm/sec.

**TABLE 4: PH, VISCOSITY, DRUG CONTENT AND SPREADABILITY OF ACECLOFENAC NANOSPONGE GEL**

| pH | 5.7 |
|---|---|
| Viscosity | 8600-24490 |
| Drug content | 98.3% |
| Spreadability | 11.13gcm/sec |

***In-vitro* Drug Release Study of Drug Loaded Nanosponge Gel:** It was found that F5 formulation shows the drug release of 19.8 % in an initial 1 hr and up to 97.73 % in 12 hr. Carbopol 934, when taken in medium amount, provides good viscosity to the gel which further shows good spreadability. An increase or decrease in carbopol percent (0.2% and 0.4%) leads to decreased drug release.

**TABLE 5: %CDR OF DRUG LOADED NANOSPONGE GEL**

| Time (hrs) | %CDR | Drug-loaded plain gel |
|---|---|---|
| 0 | 0 | 0 |
| 1 | 19.8 | 20.21 |
| 2 | 29.4 | 36.49 |
| 3 | 36.65 | 52.42 |
| 4 | 45.34 | 70.98 |
| 5 | 52.27 | 83.1 |
| 6 | 56.6 | 96.56 |
| 7 | 63.59 | - |
| 8 | 70.56 | - |
| 9 | 75.53 | - |
| 10 | 81.12 | - |
| 11 | 89.64 | - |
| 12 | 97.73 | - |

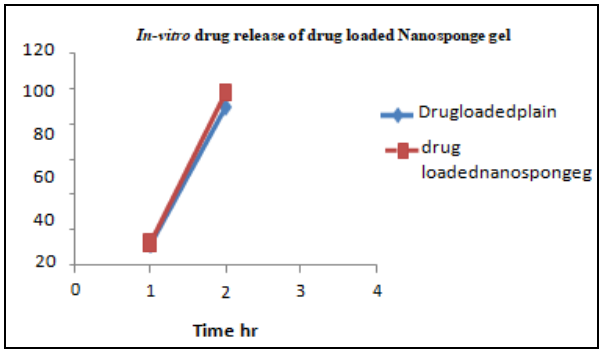


**FIG. 5: COMPARISON OF *IN-VITRO* % CDR PROFILE OF NANOSPONGE GEL AND PLAIN GEL**

***Ex-vivo* Skin Permeation Study:** The gel prepared using optimized nanosponge loaded gel was used for *ex-vivo* permeation study using goat's ear skin and showed 97.53% permeation through the skin.

**TABLE 6: *EX-VIVO* PERMEATION STUDYOF NANOSPONGE GEL**

| Time (hours) | Cumulative % drug release |
|---|---|
| 0 | 0 |
| 1 | 16.7 |
| 2 | 25.5 |
| 3 | 39.65 |
| 4 | 46.34 |
| 5 | 52.27 |
| 6 | 59.64 |
| 7 | 66.59 |
| 8 | 71.56 |
| 9 | 76.53 |
| 10 | 84.12 |
| 11 | 90.64 |
| 12 | 97.53 |

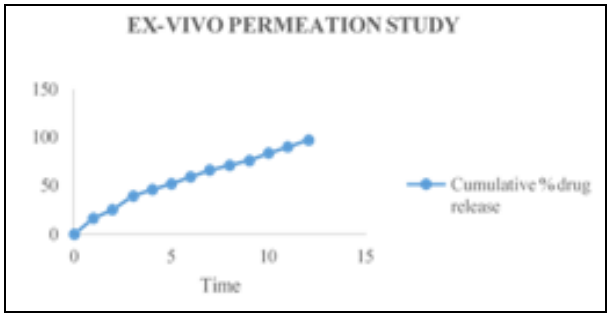


**FIG. 6: *EX-VIVO* PERMEATION STUDY OF NANOSPONGE GEL OF OPTIMIZED**

***In-vitro* Anti-Inflammatory Activity:** The Nanosponge gel was analyzed for its anti inflammatory activity. Denaturation of proteins is a well documented cause of inflammation. From the results of present study it can be stated that the aceclofenac gel is effective in inhibiting heat-induced albumin denaturation. The percentage inhibition was found to be 89.67%.

**Kinetic Study of Aceclofenac Loaded Nanosponge Gel:** To determine the drug release mechanism, the *in-vitro* release data were fitted to zero-order, first-order, Hixson Crowell equation and Higuchi matrix model. The release data were also kinetically analyzed using the Korsmeyer–Peppas model.

The release kinetics data indicates that the release of drug from Nanosponge best fits to zero order release kinetics. The data was fitted with the Higuchi equation, which gave almost a linear plot with the highest $R^{2,}$ indicating the mechanism of drug release was diffusion.

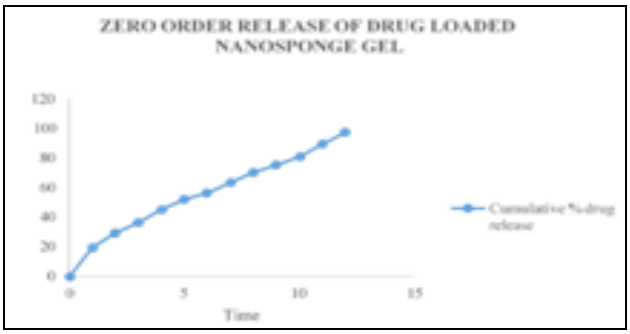


**FIG. 7: ZERO ORDER PLOT OF NANOSPONGE GELNANOSPONGE GEL**

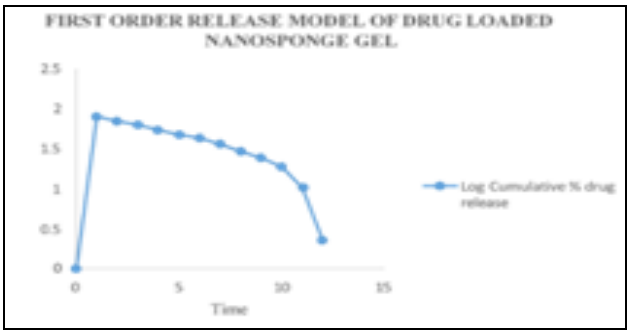


**FIG. 8: FIRST ORDER PLOT OF NANOSPONGE GELNANOSPONGE GEL**

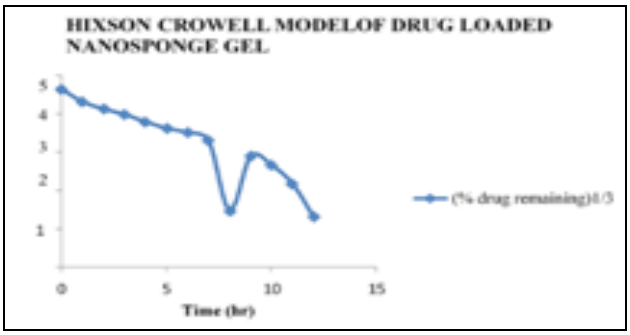


**FIG. 9: HIGUCHI PLOT OF NANOSPONGE GELNANOSPONGE GEL**

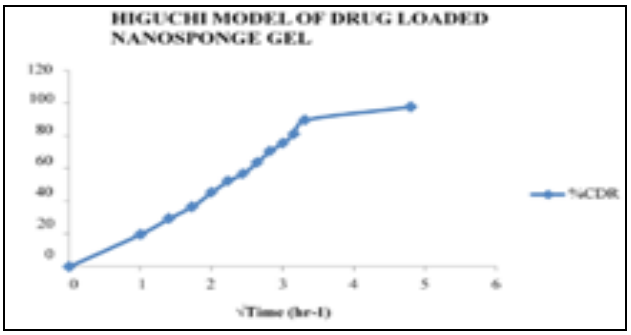


**FIG. 10: HIXON CROWELL PLOT OF NANOSPONGE GELNANOSPONGE GEL**

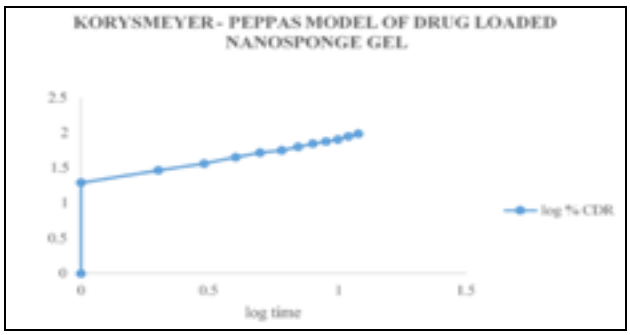


**FIG. 11: KORSMEYER-PEPPAS PLOT OF NANOSPONGE GEL**

The accuracy and prediction ability of the models were compared by calculation of $R^{2,}$ as given in **Table 7.** The model giving $R^2$ close to unity was taken as the best-fit model. The value of 'n' indicates the drug release mechanism. The 'n' value is used to characterize different release mechanisms, concluding that value n=0.5 indicates fickian diffusion and values of n between 0.5 and 1.0 or n=1.0 indicate non-fiction mechanism. The release kinetics data indicates that the drug release from Nanosponge best fits zero-order release kinetics. $R^2$ values of zero-order kinetic equations were found to be close to unity, indicating that the release from the films was not dependent on the concentration of the drug present in the formulation. The data was fitted with the Higuchi equation, which gave almost a linear plot with the highest $R^{2,}$ indicating the mechanism of drug release was diffusion. The dissolution data was also plotted in accordance with Hixon- Crowell cube root law. Data was analyzed using the Korsmeyer Peppas equation to determine whether fickian or non-fickian diffusion existed. The n value determined lies above 1.0, indicating it follows non-fickian diffusion. These observations showed that the mechanism of drug release for the formulations was non- fickian diffusion following the Higuchi model of drug release.

**TABLE 7: KINETIC PROFILE OF DRUG-LOADED NANOSPONGE GEL**

| Model | Value |
|---|---|
| Zero-order | $r^2 = 0.9777$ |
| First order | $r^2 = 0.0567$ |
| Higuchi | $r^2 = 0.949$ |
| Hixon Crowell | $r^2 = 0.819$ |
| Korsemeyer-Peppas | $r^2 = 0.6721$ n = 1.147 |

**Stability Study:** pH, Drug content and drug release values are analyzed periodically as per ICH guidelines through accelerated stability studies for optimized gel formulation.

**TABLE 8: STABILITY STUDY OF NANOSPONGEGEL**

| Time | pH | Drug content (%) | Drug release (%) |
|---|---|---|---|
| Initial | 5.7 | 98.83 | 97.69 |
| 3 months | 5.7 | 98.22 | 97.11 |

**CONCLUSION:** Nanosponges are one of the best carriers in the localized delivery of drugs to the target site. They are known to play a role in the development of Rheumatoid arthritis. These nanosponges offer a promising alternative to current treatments for Rheumatoid arthritis. Nanosponges were prepared using the emulsion solvent diffusion technique. Nine Formulations of Nanosponges were prepared and evaluated in this work. The optimized Nanosponge formulation was incorporated into 1% Carbopol gel base and produced a drug-loaded Nanosponge gel formulation, which is further evaluated. The drugs were identified by analyzing the lambda max, FTIR spectra, and DSC reports. FTIR and DSC studies showed that the drug combined with excipients is compatible and will not alter the properties and nature when combined. The formed nanosponges were homogenous and opaque white in colour. The sizes of the particles were determined by Malvern Zeta sizer. All the vesicle sizes were in the nanometric scale and had a low Poly dispersity index, indicating the homogeneity of the particle size.

The particle size of the optimized Nanosponge formulation was 268.6 nm, which met the criteria for topical drug delivery. The percentage yield of Nanosponges was between 75.31 - 98.76%. The concentration of polymer increases, the percentage yield decreases. Zeta potential was found to be -5.6 mV with a peak area of 100% intensity. These values indicate that the formulated Aceclofenac nanosponges (F5) are stable.

The *in-vitro* release data found that formulation F5 showed the best release of 98.88% at the end of 12 hrs among all nine formulations. The Kinetic study of Nanosponge indicated that it fits the Higuchi model and follows zero-order Kinetics. The optimized formulation F5 was incorporated into a 1% Carbapol gel base to form Aceclofenac-loaded Nanosponge gel. The kinetic data of drug-loaded Nanosponge gel indicated that it fits the Higuchi model and follows Zero-release kinetics.

The mechanism of drug release from the drug-loaded Nanosponge followed Anomalous (non-fickian) transport. All the above studies prove that phenospongee of Aceclofenac can be given to patients to manage inflammation and pains associated with arthritis and cancer due to its improved bioavailability and prolonged drug action.

This formulation can prevent the gastrointestinal side effects associated with the drug. This delivery system has the potential to overcome the drawbacks associated with the formulations in the market.

**ACKNOWLEDGEMENT:** Nil

**CONFLICTS OF INTEREST:** Nil

## REFERENCES:


1. Choy EHS and Panayi GS: Cytokine Pathways and Joint Inflammation in Rheumatoid Arthritis. New Engl J Med 2001; 344: 907-16.
2. Patel Ek and Oswal RJ: Nanosponge And Micro Sponges:A Novel Drug Delivery System. IJRPC 2012; 2(2): 237-44.
3. Swaminathan S, Darandale S and Vavia PR: Nanosponge-Aided Drug Delivery. A Closer Look. Pharm Formul Qual 2012; 2(7): 12-15.
4. Shinde G, Rajesh Ks, Bhatt D, Bangale G, Umalkar D and Virag G: Current status of colloidal system (nano range). Int J Drug Formul Res 2011; 2(6): 39-54.
5. Salunkhe A, Kadam S, Magar S and Dangare K: Nanosponges: A modern formulation approach in drug delivery system. World J Pharm Pharm Sci 2018; 7(2): 575-92.
6. Van der Ende AE, Kraviz EJ and Harth E: Approach to Formation of multifunctional polyester particles in controlled nanoscopic dimensions. J Am Chem Soc 2008; 130: 8706-13.
7. Swaminathan S, Vavia PR, Trotta F and Torne S: Formulation of betacyclodextrin based nanosponges of Itraconazole. J Incl Phenom Macrocyl Chem 2017; 57: 89-94
8. Indian Pharmacopoeia 2018. 2nd ed; 2: 29.
9. Verma N and Deshwal S: Design and *in-vitro* evaluation of transdermal Patches containing Ketoprofen. World J Pharm Res 2014; 3(3): 3930- 44.
10. Available from: https://en.wikipedia.org/wiki/Nonsteroidal anti-inflammatory drug [Last accessed on July 2021 25th].
11. Kumar AS, Sheri PS and Kuriachan MA: Formulation and Evaluation of Antifungal Nanosponge Loaded Hydrogel for Topical Delivery. Int J Pharm Pharm Res 2018; 13 (1): 362-79.
12. Abbas N, Parveen K, Hussain A, Latif S, Zaman SU, Shah PA and Ahsan M: Nanosponge-based hydrogel preparation of fluconazole for improved topical delivery. Trop J Pharm Res 2019; 18(2): 215-22.
13. Joshi B and Singh G: Development and characterization of Clarithromycin emulgel for topical delivery. Int J Drug Dev & Res 2012; 4(3): 310-323.


**How to cite this article:**
Koshy S, George C and Abraham S: Development and characterization of aceclofenac loaded nanosponge gel for the management of rheumatoid arthritis. Int J Pharm Sci & Res 2024; 15(3): 763-70. doi: 10.13040/IJPSR.0975-8232.15(3).763-70.