AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Formulation and Evaluation Of Roxithromycin Nanosponge Gel For Antibacterial Activity

Krithika CV*[1], Kishori [1]
1.Department of Pharmaceutics, Shree Devi College of Pharmacy, Kenjar, Mangaluru, Karnataka -574142, India.

ABSTRACT

This investigation examined a Roxithromycin-loaded nanosponge gel intended for topical delivery, to enhance the drug's solubility in an aqueous medium and maintaining its presence in the intended area of treatment. Roxithromycin is categorized within BCS category II compound, combining low water solubility with high permeability. Seven distinct formulations were produced using ethyl cellulose by the emulsion–solvent diffusion technique and assessed using physicochemical tests. Preliminary analysis identified a wavelength of maximum absorption (λmax) of 210 nm; the calibration response was linear from 1–5 µg/mL (R^2 = 0.9989). FTIR findings supported suitability of the polymer for use with the drug. Formulation F5 had a Particle size average 382.1 nm, a polydisperse index of 0.483, and with a corresponding zeta potential value of −41.9 mV; its nanosponge dispersion released 86.0% by 7 h. The nanosponges were subsequently dispersed in Carbopol 934 gel. The optimized F5 gel contained 89.10% drug and showed diffusion rising from 21.46% at 1 h to 83.2% at 7 h. Its release profile fitted the first-order model most closely (R^2 = 0.9977). Against *Staphylococcus aureus*, the gel produced a 3.4 cm inhibition zone. No visible irritation was reported during the 14-day observation period, and the measured stability parameters showed no notable change under the storage conditions tested. Taken together, the findings support further investigation of this nanosponge gel as a topical formulation with sustained Roxithromycin release and antibacterial activity.

Keywords: Roxithromycin, nanosponges, ethyl cellulose, polyvinyl alcohol, formulation.

*Corresponding Author Name: Krithika CV
Received 12 September 2026, Accepted 06 October 2026

Please cite this article as: Krithika CV P *et al*., Formulation and Evaluation Of Roxithromycin Nanosponge Gel For Antibacterial Activity. American Journal of PharmTech Research 2026.

INTRODUCTION

Delivering a medicine to the intended site while controlling how quickly it becomes available remains an important formulation challenge. If drug release is too rapid or poorly regulated, exposure may not be maintained for the desired period. Nanosponges are porous carrier systems being explored to address these limitations by accommodating active substances and allowing their release to occur over time. Their potential role in drug delivery has therefore attracted interest as an approach for improving formulation performance.[1]

Nanosponges are small, porous particles, generally discussed in the submicrometre size range, that can accommodate drug molecules within their structure. Depending on the carrier and formulation, this arrangement may help localize drug availability and moderate its release. Their internal pores and large available surface can be useful for compounds showing inadequate solubility in water, although improved bioavailability depends upon the drug and delivery route. Nanosponge systems are even investigated for protecting incorporated substances and for achieving a more consistent release profile. These properties have supported their study as alternatives to conventional dosage forms where local tolerability, duration of action, or delivery efficiency may be limiting factors.[2] The carrier should not be assumed to target a particular tissue automatically; its performance depends on composition, particle attributes, and how the finished product is applied.

Unlike carriers surrounded by a continuous membrane, nanosponges have a porous network in which an incorporated active ingredient can move between the carrier and the surrounding vehicle. Transfer occurs when conditions favour release of the drug from the carrier system and the vehicle is not already saturated. After a topical preparation is spread over the skin, evaporation or absorption of the vehicle can alter this balance and encourage further drug partitioning from the nanosponges into the remaining formulation and skin surface. Drug transfer may continue while particles remain at the application site, depending on the formulation and local conditions.[3,4]

Many conventional dermatological preparations make the active ingredient available quickly, and their effect may decline as the ingredient is removed, absorbed, or degraded. A nanosponge-based vehicle is designed to moderate this process and may support more prolonged availability while potentially reducing abrupt exposure. Nanosponges can be incorporated into diverse drug delivery formulations, including gels, creams, lotions, ointments, liquids, and powders. Gel and cream vehicles are particularly for topical use because they can be applied directly to a defined skin area. Any improvement in skin delivery depends on drug solubility, carrier properties, the vehicle, and the formulation's polydispersity.[5] For topical products, the practical aim is often to retain the drug near the intended application area rather than to maximize passage into systemic circulation.

Consequently, surface retention, local availability, tolerability, and release duration are relevant considerations when choosing a nanosponge gel vehicle.

Bacterial skin and soft-tissue infections develop when microorganisms affect the skin or underlying tissues. Their presentation ranges from relatively superficial conditions, including impetigo, folliculitis, furuncles, and carbuncles, to deeper infections such as cellulitis, erysipelas, and necrotizing fasciitis. Common clinical signs include swelling, warmth, redness, and tenderness; systemic symptoms may occur in more extensive disease. *Staphylococcus aureus* and *Streptococcus pyogenes* are important causative organisms, while *Pseudomonas aeruginosa* and other Gram-negative bacteria may be involved in certain wound-associated or healthcare-related infections.[6]

Roxithromycin is a semisynthetic macrolide antibiotic containing a 14-membered ring. Modification of the erythronolide A lactone structure was intended to improve its stability in the gastric environment. Published *in-vitro* studies describe antibacterial activity broadly comparable to that of other macrolides. Its reported spectrum includes Gram-positive cocci and bacilli, as well as selected Gram-negative organisms. Roxithromycin has structural similarities to erythromycin and has been reported to act against organisms such as *Staphylococcus aureus, S. pyogenes, S. epidermidis, Streptococcus pneumoniae, Chlamydia trachomatis, Branhamella catarrhalis, Legionella pneumophila, Gardnerella vaginalis, Mycoplasma pneumoniae, and* some anaerobes.[7,8]

MATERIALS AND METHOD

Materials

Roxithromycin was supplied by Yarrow Chemical, Mumbai. Ethyl cellulose and Carbopol 934 were procured from Hi-Media Laboratories Pvt. Ltd., Mumbai, while polyvinyl alcohol was sourced from Loba Chemie Products, Mumbai. Dichloromethane was obtained from Hi-Media Laboratories Pvt. Ltd.

Animals

The Wister rats weighing between 150-200 gm were procured from Animal house of Shree Devi college of Pharmacy, Mangalore and maintained under constant conditions (temperature 25+ 2C, Humidity 40-60%, 12 h light/ 12 h dark cycle). During maintenance the animals received a diet of food pellet supplied from animal house and water ad libitum. These experiments were approved by the Institutional Animal Ethics Committee, Shree Devi college of pharmacy of, Mangalore (IAEC registration no. SDCP/IAEC/21/2025)

Methods

Pre-formulation study

Organoleptic Properties:

Preformulation testing was undertaken before formulation to document the drug's basic physical and analytical characteristics. Such information helps guide selection of ingredients and processing conditions and supports the development of a reproducible dosage form. The assessment included identification and observation of the drug, its solubility in selected media, and measurement of its melting point. Physical features such as colour, odour, crystalline or amorphous appearance, and moisture sensitivity were also considered.[8]

The colour of the Roxithromycin sample was recorded by direct visual inspection. The odour of the sample was assessed by observation without altering the material.[9]

Determination of melting point:

The capillary method was utilized to measure the melting point. A small sample of finely powdered Roxithromycin was placed into a glass capillary having one end tightly sealed. The capillary was secured alongside a thermometer and placed in a Thiele tube. The apparatus was heated gradually, and the thermal melting point of the powder was determined and recorded.[10]

Solubility Studies:

For the solubility assessment, an excess quantity of Roxithromycin was added separately to 10 ml portions of ethanol, methanol, water, chloroform, and phosphate-buffered medium maintained at pH 7.4. Each sample was agitated in a water-bath shaker at 37 ± 0.5 °C for 24 h. The solutions were then filtered, diluted as required, and examined by spectrophotometry at the relevant absorption maximum.[11]

UV Spectrophotometric Method Development:

A 10 mg quantity of roxithromycin was placed into to a 100 ml volumetric flask. It was first dissolved in a small volume of ethanol, and phosphate buffer (pH 7.4) was added to volume to produce a 100 µg/ml primary stock. A 10 mL portion of this solution were introduced into a second 100 mL volumetric flask and brought to the final volume using the same buffer solution, giving a secondary stock solution of 10 µg/ml.

Standard plot for Roxithromycin

The prepared Roxithromycin solution was subjected to spectral analysis over the 200–400 nm wavelength range on a UV–visible spectrophotometer, using phosphate buffer at pH 7.4 as the reference blank. The wavelength at which Roxithromycin showed peak absorbance was identified as 210 nm.

Calibration Curve:

To prepare the calibration standards, 1, 2, 3, 4, and 5 ml portions of the 10 µg/ml secondary stock

were placed separately in individual 10 ml volumetric flasks. Each flask was made up to volume with phosphate buffer (pH 7.4), producing standards at 1–5 µg/ml.

The absorbance was measured at 210 nm using pH 7.4 phosphate buffer as the blank.[12]

Fourier transform infrared spectroscopy

FTIR analysis was carried out to identify the characteristic absorption bands of Roxithromycin, ethyl cellulose, and drug-loaded nanosponges to evaluate drug–polymer compatibility. The sample was finely triturated with potassium bromide (KBr) in a ratio of approximately 1:100 and compressed into a pellet using a KBr press. The spectral measurements extended from 4000 to 400 cm^{-1}.[13]

Particle size, size distribution and zeta potential

The Zeta sizer was employed to characterize particle dimensions, size distribution, and surface charge through dynamic light scattering (DLS). Zeta potential represents the electrical potential at the particle surface relative to the surrounding dispersion medium and provides an indication of the colloidal stability of the formulation. Its magnitude can provide an indication of electrostatic repulsion between particles and is therefore used as one measure when assessing dispersion stability.[14] Zeta potential is an indirect indicator and should be interpreted alongside the measured size distribution and visual observations rather than treated as a standalone stability result.

Preparation of Roxithromycin nanosponges

The emulsion–solvent diffusion process was used to prepare Roxithromycin nanosponges. Roxithromycin and ethyl cellulose, in the quantities specified for each batch, were dissolved in 20 ml dichloromethane to form the organic phase. This phase was added into an aqueous phase containing the required polyvinyl alcohol in 150 ml water. Continuous agitation of the mixture was performed with a magnetic stirrer at 1200 rpm for 30 minutes. The resulting particles were recovered by filtration and subsequently dried in an oven.[15]

Formulation chart of Nanosponges

Table 1: Different Formulations of Roxithromycin Nanosponges

Ingredients	F1	F2	F3	F4	F5	F6	F7
Roxithromycin (mg)	100	100	100	100	100	100	100
Ethyl Cellulose (mg)	100	100	300	400	500	400	400
Polyvinyl Alcohol (mg)	100	100	100	100	100	100	100
Dichloromethane (mL)	20	20	20	20	20	20	20
Distilled Water (mL)	150	150	150	150	150	200	300

Development of Roxithromycin-Loaded Nanosponge Gel

To prepare the gel base, Carbopol 934 was dispersed in distilled water and mixed with a magnetic stirrer at 600 rpm for 1 h until a uniform base was obtained. Then 2% triethanolamine was used to

adjust the pH. Roxithromycin-loaded nanosponges were incorporated into the prepared base and mixed to distribute them throughout the gel.[16]

Characterization of Roxithromycin-Loaded Nanosponges:

Percentage Yield:

Overall production yield was calculated using the was expressed as the percentage of the theoretical material recovered after preparation. Percentage yield was calculated using the following relationship:

percentage yield = (actual yield ÷ theoretical yield) × 100.[17]

Determination of Drug Entrapment Efficiency:

To determine entrapment efficiency, 10 mg of Roxithromycin-loaded nanosponges was suspended in 10 mL of phosphate buffer (pH 7.4) and kept for 24 hours. The dispersion was subsequently stirred at 1000 rpm for 30 minutes using a Remi magnetic stirrer and filtered. The absorbance of the filtered sample was subsequently quantified with a Shimadzu UV–visible spectrophotometer.[15]

Particle Size Analysis:

Mean particle diameter was measured using a Malvern Zetasizer. Initially each sample was diluted with water as appropriate. The average diameter was determined at a fixed scattering angle of 90°.

SEM (Scanning Electron Microscopy) Analysis:

For SEM imaging, the nanosponge sample was fixed to the adhesive surface of a specimen stub and coated with a thin gold/palladium layer to make the surface conductive. The prepared Roxithromycin nanosponges were then examined by scanning electron microscopy to document particle appearance and morphology.[18]

***In Vitro* Drug Release Studies:**

Drug release from the Roxithromycin nanosponge batches was examined in triplicate with the USP paddle apparatus. Each test used 100 mg of nanosponges in 900 ml phosphate buffer (pH 7.4), maintained at 37 ± 0.2 °C and stirred at 50 rpm. Aliquots were collected at hourly intervals for 7 h and analyzed at 210 nm by spectrophotometry. The withdrawn sample volume was restored using fresh buffer after each collection to maintain a constant dissolution volume.[19] The sampling schedule and replacement of withdrawn medium were kept consistent across the formulations so that release profiles could be compared using the same experimental approach. The reported values represent the measured release under the specified *in-vitro* conditions and should not be equated directly with drug release in living skin.

Evaluation of Roxithromycin-Loaded Nanosponge Gel

Physical Examination:

The formulated gels were visually examined for appearance, colour, consistency, uniformity, and any perceptible grittiness. These observations were used to describe their physical and cosmetic acceptability.

Viscosity:

The viscosity of the nanosponge gels was measured with a Brookfield viscometer operated at 20 rpm using spindle number 64.[20]

pH:

The pH of the Roxithromycin loaded nanosponge gel formulations was determined using a digital pH meter. The mean pH was reported for each batch.[21]

Spreadability:

A weighed 1 g portion of the formulation was sandwiched between two glass plates and applied a 125 g weight for 1 minute. The spreadability was then calculated using the standard equation:

$S=ML/T$

Where:

S = Spreadability

M = Weight applied on the upper slide

L = Length

T = Time taken to completely separate the slides

Drug content:

A 100 mg quantity of the nanosponge-based gel was distributed in 10 ml phosphate buffer at pH 7.4. The resulting sample was analyzed by UV–visible spectrophotometry at 210 nm, using a blank for comparison.

***In Vitro* Drug Diffusion:**

The drug release profile of the gel formulation was investigated using a Franz diffusion apparatus equipped with a cellophane membrane. The donor compartment was loaded with 1 g of the formulated gel, while phosphate buffer (pH 7.4) was added to the receptor compartment. The receptor medium was maintained at 37 ± 0.5 °C with continuous stirring. Aliquots were removed at regular time intervals from the receptor compartment and replenished using an equal amount of fresh buffer medium to maintain a constant volume. Roxithromycin concentration was quantified at 210 nm by spectrophotometry.[22] The cellophane membrane served as a separating barrier for the in-vitro diffusion setup. This test provides a comparative assessment of drug movement from the gel into the receptor medium; it does not reproduce the full barrier properties of human skin.

Therefore, the findings are useful for formulation screening but require confirmation in a suitable skin-based model if skin permeation is the intended claim.

Release Kinetics:

The *in-vitro* diffusion data analysis was performed using four commonly applied release models: zero-order, first-order, Higuchi, and Korsmeyer–Peppas. The correlation coefficients (R^2) obtained for the plots were compared, and the model with the largest R^2 was taken as the best statistical fit to the observed data.[23]

Antimicrobial Activity by Zone of Inhibition Method:

Antibacterial activity was tested by measuring the growth-inhibition zone against Staphylococcus aureus. A 20 ml portion of sterilized broth was placed in a Petri dish and inoculated with the organism. After the inoculated medium had been spread over the solidified nutrient agar, wells measuring 6 mm in diameter were made and filled with Roxithromycin nanosponge gel. The prepared plates were kept under incubation at 35–37 °C for 24 h. The diameter of the clear zone around wells were subsequently recorded.[15]

Skin irritation test:

A 0.5 g quantity of the formulation was applied to a 2 cm^2 area of closely clipped skin on each of two rats. The skin regions were covered using cotton gauze and secured using a semi-occlusive dressing. One rat served as the test animal, while the other was designated as the control. After 4 hours, the dressings were removed, and the treated areas were gently wiped with moist gauze to remove any remaining formulation. The skin surfaces were observed for visible signs of irritation or sensitivity, and observations were documented at 1, 24, and 72 hours after patch removal, as well as on days 7 and 14.[24]

Stability Study:

The optimized Roxithromycin nanosponge gel was stored under the reported warm condition of 25 ± 2 °C/60 ± 5% relative humidity and under refrigeration at 8 ± 2 °C. Drug content and in-vitro diffusion were monitored during the study period in accordance with the stated ICH-based approach.[15]

RESULTS AND DISCUSSION

Organoleptic Characteristics:

Visual assessment demonstrated that the Roxithromycin sample was a white, odourless powder with an amorphous appearance.

Determination of Melting Point:

The measured melting point was 112 °C, within the reported interval of 111–120 °C. This finding

was in agreement with the cited range, although melting point alone does not establish drug purity.

Determination of Solubility:

Roxithromycin dissolved in acetone, methanol, and alcohol, whereas it was insoluble in chloroform and water under the conditions tested. The solubility observations were used to help select a medium for the release experiments. Phosphate-buffered saline at pH 7.4 was chosen because it gave the more suitable solubility response in the study.

Determination of Absorption Maximum (λ-max):

The prepared drug solution was subjected to spectral scanning over 200–400 nm. The maximum absorbance for Roxithromycin was recorded at 210 nm.

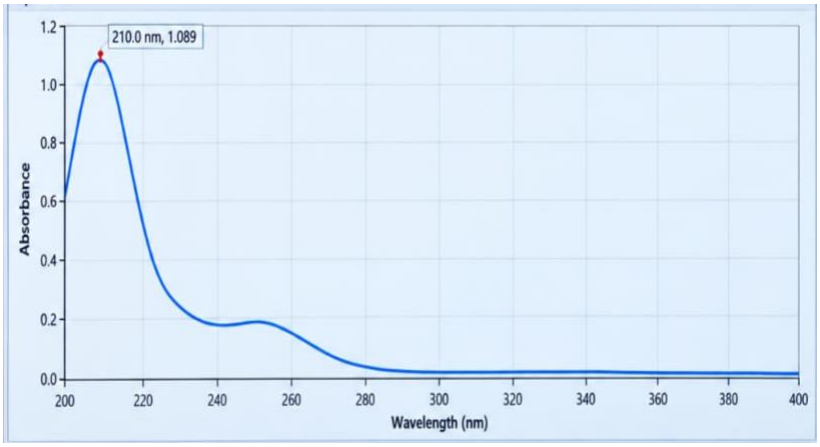


Figure 1: Standard plot of Roxithromycin in phosphate buffers pH 7.4

Standard graph of Roxithromycin

Table 2: Calibration data of Roxithromycin

Concentration (µg/ml)	Absorbance at 210 nm
0	0
1	0.107
2	0.197
3	0.309
4	0.394
5	0.508

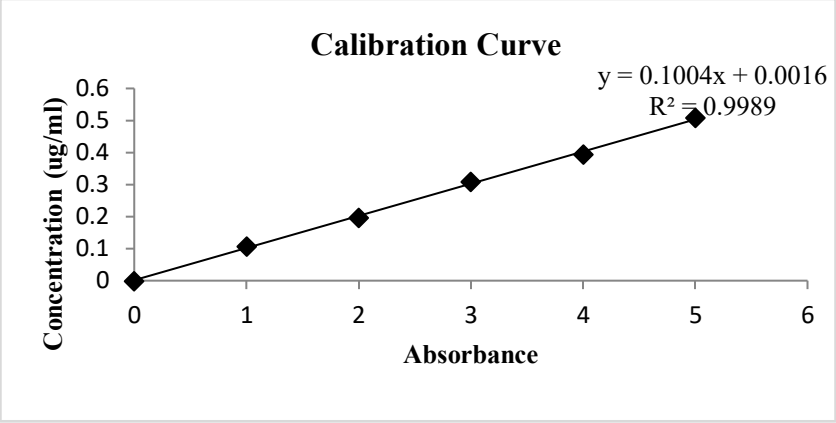


Figure 2: Standard calibration curve of Roxithromycin

The calibration plot was used to relate measured absorbance to Roxithromycin concentration. A linear regression equation (y = mx + c) was obtained, and the response across 1–5 µg/ml was highly linear (R^2 = 0.9989), consistent with Beer–Lambert behaviour over the tested range.

Drug-polymer compatibility studies

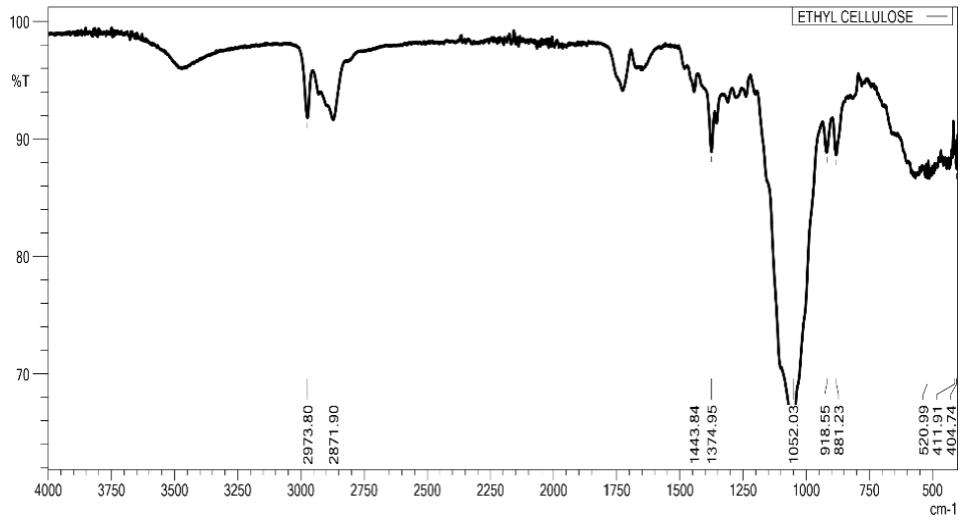


Figure 3: FTIR spectra of Ethyl Cellulose

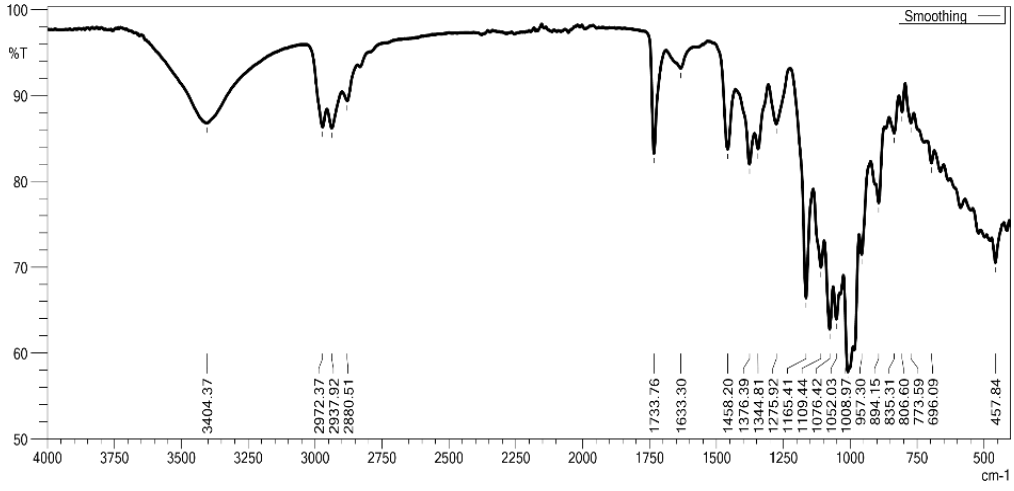


Figure 4: FTIR Spectrum of Roxithromycin

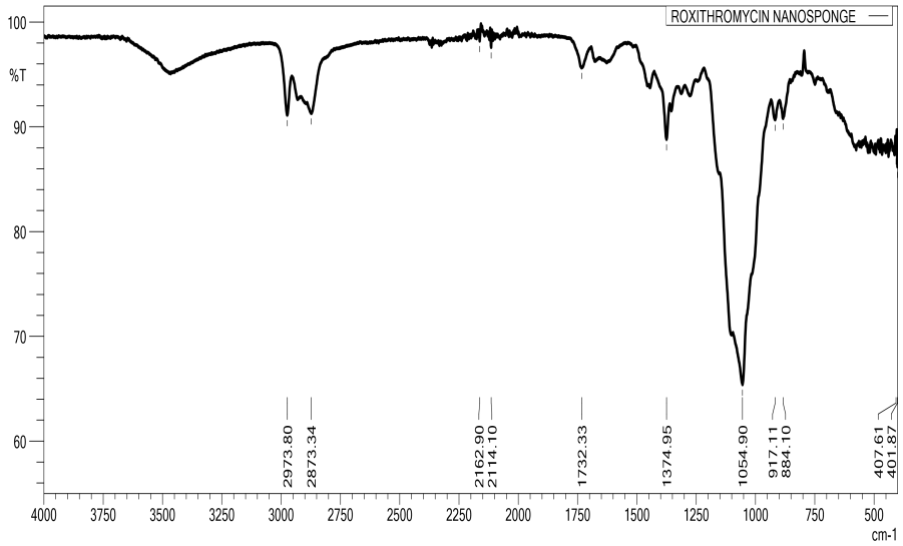


Figure 5: FTIR Spectrum of Roxithromycin Nanosponges

FTIR spectra of the pure drug, ethyl cellulose, and Roxithromycin-loaded nanosponges were compared to assess the characteristic functional groups and possible drug–polymer interactions. Roxithromycin showed bands at 3404.37 cm^{-1} (O–H), 2972.37 cm^{-1} (C–H), and 1733.75 cm^{-1} (C=O). The ethyl cellulose spectrum contained bands at 3500 cm^{-1} (O–H), 2973.80 cm^{-1} (C–H), and 1052.03 cm^{-1} (C–O–C). For the loaded nanosponges, bands were observed at 3500 cm^{-1} (O–H), 2973.80 cm^{-1} (C–H), 1732.33 cm^{-1} (C=O), and 1054.90 cm^{-1} (C–O–C).

Evaluation of Roxithromycin nanosponges

Percentage yield

Table 3: Percentage yield of Roxithromycin Nanosponges

Formulation code	% Yield
F1	64
F2	72
F3	74
F4	75
F5	83
F6	68
F7	63

The recovered yield of the seven Roxithromycin nanosponge batches ranged from 63% to 83%. F5 gave the greatest yield, suggesting that this composition supported effective particle formation and recovery with less loss during processing. The result may be related to the ethyl cellulose level in F5, which appeared favourable for polymer precipitation and nanosponge formation.

Table 4: Entrapment Efficiency of Nanosponges (F1-F7)

Formulation code	% Entrapment Efficiency
F1	68.70 ±0.3
F2	70.85± 0.2
F3	75.4±0.4
F4	84.1±0.2
F5	89.32±0.3
F6	32.42±0.4
F7	29.35±0.4

Across F1–F7, entrapment efficiency values varied from 29.32% to 89.32%. F5 achieved the highest value (89.32%), which may reflect a suitable ethyl cellulose concentration for retaining Roxithromycin within the carrier matrix. Lower values for F6 and F7 coincided with the larger aqueous-phase volumes used in those batches. Under these conditions, changes in dispersion and particle formation may have contributed to irregular particles and aggregation, reducing drug retention.

Average particle size and size distribution

Particle size can affect the available surface area, drug-release behaviour, and contact between a topical preparation and the skin. The evaluated nanosponge sample had a mean diameter of 382.1 nm and a PDI of 0.483, indicating a moderately broad size distribution. This nanoscale size may support contact with the skin surface; however, improved skin deposition would require direct evidence from an appropriate skin-distribution study.

Zeta potential

Zeta potential indicates the electrical charge at the particle–liquid interface and is commonly considered alongside other measures of dispersion stability. A larger absolute value may increase electrostatic repulsion between particles and limit their tendency to aggregate. F5 had a zeta potential of −41.9 mV, a result consistent with favourable electrostatic stability under the measurement conditions.

Surface morphology

SEM images showed particles that were mainly spherical and had a porous-looking surface. A degree of clustering was also visible and could have arisen during specimen preparation or drying. Overall, the findings supported the successful development of the nanosponge delivery system.; the images alone do not establish the release mechanism, but the porous morphology may be relevant to drug incorporation and diffusion.

***In Vitro* Drug Release Studies (Dissolution studies)**

Table 5: *In-vitro* drug release study of nanosponges

Time (hr)	Cumulative percentage drug release(%)						
	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	10.8	14.2	12.5	15.1	22.4	14.8	10.2
2	18.5	22.6	20.9	24.3	38.6	23.9	19.1
3	29.4	32.8	30.5	35.6	49.8	34.8	28.7
4	36.8	43.5	41.2	44.8	59.7	43.9	38.2
5	45.7	51.2	49.0	55.7	68.5	54.2	47.1
6	53.8	60.7	59.2	68.4	77.8	66.9	56.8
7	62.1	69.3	71.0	79.2	86.0	77.5	66.1

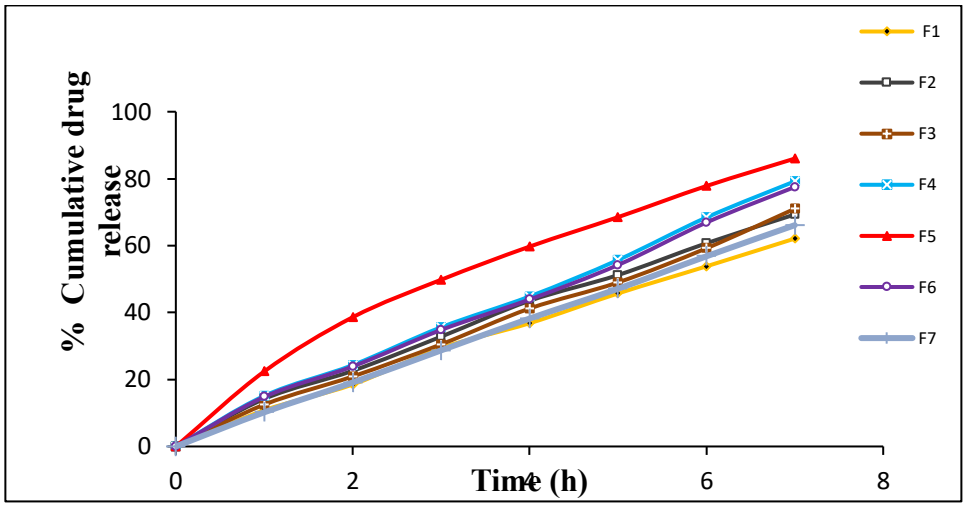


Figure 6: *In Vitro* drug release of Roxithromycin nanosponge

Drug release from the nanosponge batches increased progressively throughout the 7 h test. At the final sampling point, cumulative release values ranged from 62.1% to 86.0%, with F5 reaching the highest value (86.0%). Among the tested compositions, F5 showed the most favourable release result, potentially reflecting the balance between polymer content and the structure formed during preparation.

Physical Examination

Table 6: Physical characteristics of Roxithromycin nanosponge gel

Formulation Code	Appearance	Viscosity (cPs)	pH	Spread ability(gm s.cm/sec)	Consistency	Drug Content
F1	Translucent	9850±125	6.5±0.5	14.20±0.35	Poor	68.7±0.48
F2	Translucent	10504±120	6.08±0.03	13.35±0.32	Fair	70.85±0.42
F3	Translucent	11540±130	6.38±0.02	12.10±0.30	Good	79.4±0.49
F4	Translucent	12053±135	6.18±0.03	11.58±0.38	Good	61.2±0.42
F5	Translucent	12540±140	6.29±0.03	10.85±0.28	Very good	89.1±0.45
F6	Translucent	11320±145	6.31±0.03	11.03±0.34	Good	52.42±0.48
F7	Translucent	10580±125	6.45±0.03	11.23±0.32	Fair	68.7±0.52

Formulation of Nanosponge Gel

Each of the seven nanosponge batches (F1–F7) was dispersed in Carbopol 934 to prepare a gel. Carbopol 934 served as the gel-forming polymer and was intended to provide body, consistency, and even distribution of the carrier particles. 2% triethanolamine was added to adjust the pH of prepared topical gel.

pH

Measured pH values extended from 6.08 to 6.50 across the gel batches. The values were relatively close to one another and lie within a range commonly considered compatible with topical products; tolerability still depends on the complete formulation and requires appropriate testing.

Viscosity

The recorded viscosity values ranged from 9850 to 13540 cPs. The results varied across batches, suggesting that formulation composition affected gel consistency. The observed pattern appeared to be associated with the ethyl cellulose concentration. Although viscosity can also be influenced by dispersion and gel structure. The viscosity result is important to interpretation because a thicker gel may remain in place more readily but can also be harder to spread. Accordingly, viscosity and spreadability were evaluated collectively when comparing the batches, rather than treating either parameter in isolation.

Spreadability

Spreadability measurements were between 10.85 and 14.20 g·cm/sec. F1 had the largest value, whereas F5 had the smallest, indicating that F5 resisted spreading more than F1 under the test conditions. This difference may be associated with the higher viscosity measured for F5.

Drug Content

Drug content varied from 52.42% to 89.10% among the prepared gels. F5 gave the highest measured content at 89.10%, suggesting that this batch retained a greater measured quantity of Roxithromycin and/or had a more uniform distribution in the sampled gel.

***In-vitro* drug release study for F5 nanosponge gel (diffusion studies)**

Table 7: *In-vitro* drug release study for F5 nanosponge gel

Time(hrs)	%CDR (F5)
0	0
1	21.46
2	36.94
3	51.73
4	63.85
5	73.26
6	79.56
7	83.2

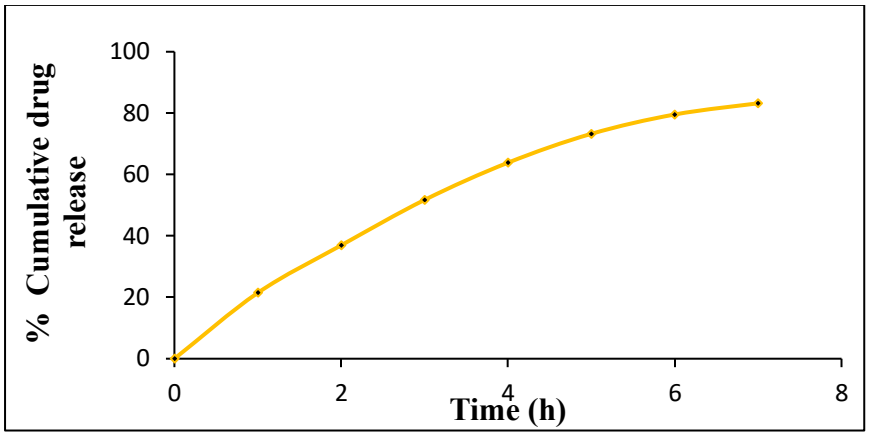


Figure 7: *In Vitro* drug release for F5 nanosponge gel

The diffusion profile for the optimized F5 gel increased over the 7 h observation period. The reported cumulative diffusion rose from 21.46% at 1 h to 83.2% at 7 h. Compared with the nanosponge dispersion, the gel vehicle may add resistance to drug movement, while the polymer matrix and nanosponge structure can together influence the rate at which Roxithromycin reaches the receptor medium. F5 gave the strongest overall release result among the tested formulations; the data support prolonged diffusion during the test period but do not alone prove a clinical controlled-release effect. Because the experiment used an artificial membrane and a defined buffer medium, the curve should be understood as an in-vitro diffusion profile. It is not direct evidence of the amount reaching deeper skin layers or of clinical duration of action.

Kinetics of drug release for F5 Nanosponge gel

Table 8: Kinetic release study for F5 Nanosponge gel

Time(hr)	Log Time	Sq. Root Time	% Cumulative Release	Logl% Release	%Drug remaining	Log% Drug remaining
0	0	0	0	0	100	2
1	0.000	1.000	21.46	1.332	78.54	1.895
2	0.301	1.414	36.94	1.5675	63.06	1.800
3	0.477	1.732	51.73	1.7137	48.27	1.684
4	0.602	2.000	63.85	1.8052	36.15	1.558
5	0.699	2.236	73.26	1.8649	26.74	1.427
6	0.778	2.449	79.56	1.9007	20.44	1.310
7	0.845	2.646	83.2	1.9201	16.8	1.225

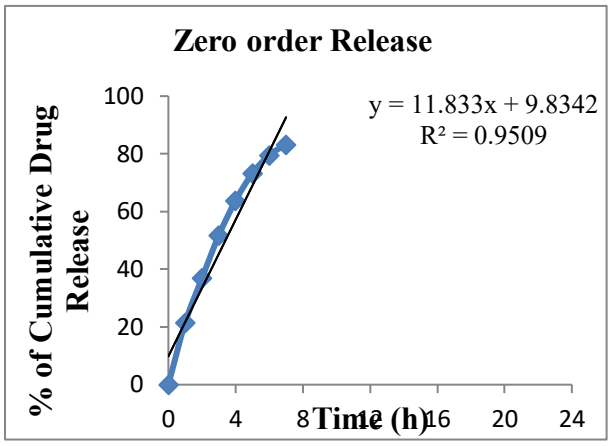


Figure 8: Zero order kinetics

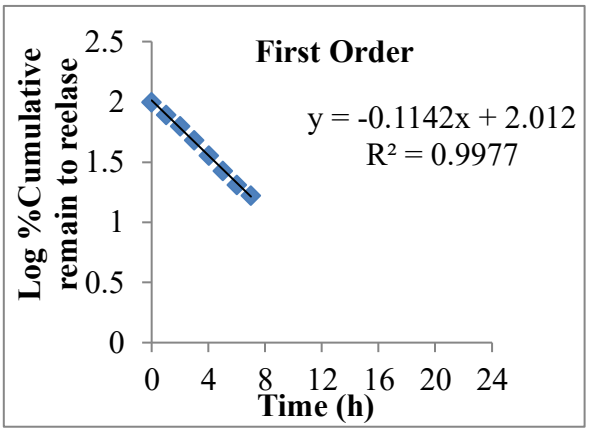


Figure 9: First Order Kinetics

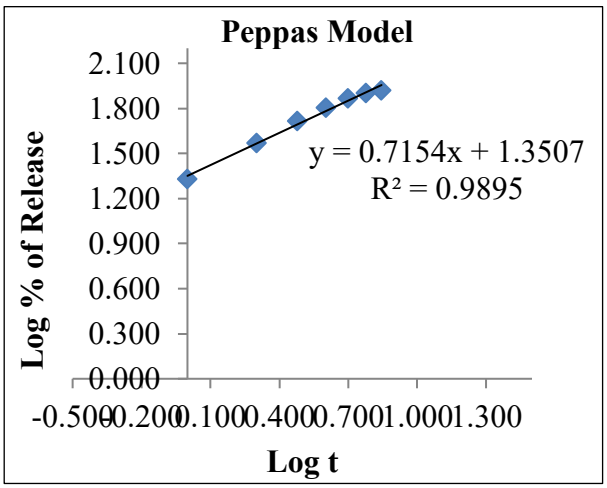


Figure 10: Peppas Model

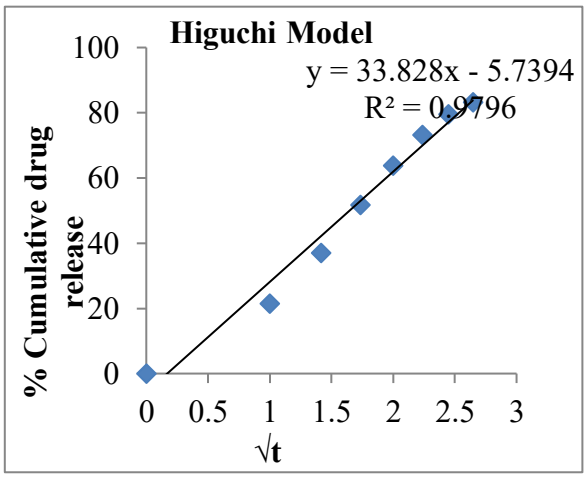


Figure 11: Higuchi Model

To compare the release behaviour mathematically, the in-vitro diffusion data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The corresponding R^2 values are provided in the kinetics table. Comparison of these coefficients was used to identify which model described the measured F5 profile most closely.

For F5, the first-order plot gave the largest correlation coefficient ($R^2 = 0.9977$). A first-order fit indicates that the release rate is related to the quantity of drug remaining in the dosage form. This is compatible with release occurring progressively over time, although the kinetic fit should be interpreted as a description of the observed data rather than proof of a single release mechanism.

Antimicrobial activity for F5 nanosponge gel

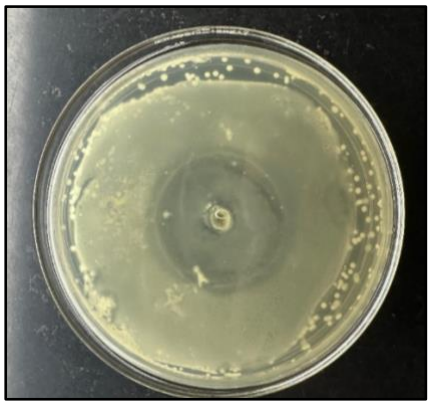


Figure 12: Antimicrobial activity by zone inhibition method

The antibacterial performance of the F5 Roxithromycin nanosponge gel was examined against Staphylococcus aureus using an agar-well inhibition test. A clear zone measuring 3.4 cm was recorded around the formulation well. The result demonstrates inhibition of this test organism under the study conditions. Roxithromycin's known action involves inhibition of bacterial protein synthesis; a comparison with a standard antibiotic or marketed product was not reported in this experiment.

Skin irritation test for F5 nanosponge gel

The skin assessment was intended to identify visible local reactions following exposure to the formulation. No redness or other obvious changes were recorded during the 14-day observation period. This observation suggests that visible irritation was not seen under the specific study conditions.

Stability Studies for F5 nanosponge gel

Table 9: stability study (8±2 ^{o}C)

Evaluation parameters	Time (days) 8±2 ^{o}C			
	0 day	30 days	45 days	60 days
Appearance	Translucent	Translucent	Translucent	Translucent
Drug content (%)	89.1	88.22	86.36	86.1
In-vitro diffusion in 07 hr(%)	83.2	80.1	78.2	77.5

Table 10: stability study (25±2 ^{o}C)

Evaluation parameters	Time (days)			
	Accelerated condition 25±2 ^{o}C at (60±5%RH)			
	0 day	30 days	45 days	60 days
Appearance	Translucent	Translucent	Translucent	Translucent
Drug content (%)	89.1	88.50	87.30	87.0
In-vitro diffusion in 07 hr(%)	83.2	88.50	80.20	80.34

Stability testing was performed using the optimized gel stored at 25 ± 2 °C/60 ± 5% RH and at 8 ±

2 °C. The parameters considered included visual appearance, drug content, and in-vitro diffusion behaviour, allowing the formulation to be monitored under the two reported storage conditions. No meaningful differences were noted in the parameters measured during the study period. On these observations, the best gel appeared unchanged under the tested storage conditions and over the period assessed.

CONCLUSION

This work involved preparing and evaluating a Roxithromycin-loaded nanosponge gel as a topical formulation designed to extend drug release. Nanosponges were produced by emulsion–solvent diffusion, with ethyl cellulose as the carrier polymer and polyvinyl alcohol (PVA) as the stabilizing agent. Seven batches (F1–F7) were made by changing formulation variables, after which the prepared particles were introduced into Carbopol 934 gel for further evaluation.

The preliminary tests provided basic information relevant to formulation development. Roxithromycin appeared as an amorphous, white and odourless powder and had a measured melting point of 112 °C. It dissolved in acetone, methanol, and alcohol but was insoluble in water and chloroform in the conditions tested. Phosphate buffer at pH 7.4 was selected for release testing, and the measured λmax was 210 nm. The calibration response was linear over 1–5 µg/mL, with $R^2 = 0.9989$, supporting its use for concentration measurements within this range.

The FTIR spectra retained the main peaks associated with Roxithromycin and ethyl cellulose after nanosponge preparation. No substantial loss of the reported bands or new major bands was observed. These findings suggest that no major drug–polymer interaction was detectable by the FTIR method used and support the compatibility of the selected materials in the prepared formulation.

Considering the overall evaluation, F5 was selected as the most promising of the seven nanosponge batches. It had the highest production yield and entrapment efficiency, suggesting efficient recovery and drug incorporation. Its mean particle size was 382.1 nm, PDI was 0.483, and zeta potential was −41.9 mV. SEM images showed mainly spherical particles with porous surface features, alongside some aggregation.

Across the nanosponge formulations, cumulative drug release after 7 h ranged from 62.1% to 86.0%. F5 reached 86.0%, the highest value among the batches. The result may be associated with the ethyl cellulose concentration and particle structure obtained in this formulation, which together influenced the movement of Roxithromycin into the dissolution medium.

All seven nanosponge batches were incorporated into Carbopol 934P gel and assessed for topical formulation properties. The gel pH ranged from 6.08 to 6.50, viscosity from 9850 to 13540 cPs,

and spreadability from 10.85 to 14.20 g·cm/sec. These findings describe the measured physical characteristics of the batches. F5 had the highest reported drug content, 89.10%, indicating a greater measured content in the tested gel sample than in the other formulations.

In the F5 gel diffusion test, cumulative drug diffusion increased from 21.46% at 1 h to 83.2% at 7 h. The progressive increase indicates that Roxithromycin continued to pass from the gel into the receptor medium throughout the test. The gel base, together with the nanosponge carrier, may have contributed resistance to diffusion and thereby extended the release profile.

Kinetic modelling showed the strongest fit for F5 with the first-order equation ($R^2 = 0.9977$). This model relates the release rate to the amount of drug remaining in the formulation and describes the observed profile well. It supports a time-dependent release pattern, but further mechanistic studies would be required to establish the processes governing release.

The optimized F5 gel produced a 3.4 cm zone of inhibition against Staphylococcus aureus in the test performed. This observation supports antibacterial activity against the organism under the assay conditions. Since a marketed formulation or standard antibiotic control was not included, the result does not establish superiority over existing products.

No visible redness, discomfort, or other obvious skin changes were recorded in the irritation assessment during the 14-day observation period. The result suggests that the formulation was tolerated in the limited test conducted; additional safety assessment would be necessary before human topical use.

The optimized gel was monitored at 25 ± 2 °C/60 ± 5% RH and 8 ± 2 °C. The measured appearance, drug content, and in-vitro diffusion profile showed no significant changes during the stated period. Thus, the formulation remained apparently stable under the conditions and duration examined.

In summary, F5 was the most promising Roxithromycin nanosponge gel among the formulations examined, based on its production yield, particle characteristics, drug content, entrapment efficiency, and *in-vitro* release profile. The gel showed a pH and spreadability range recorded during the evaluation, progressive diffusion over 7 h, and an inhibition zone against Staphylococcus aureus. No visible irritation or major change in the measured stability parameters was observed under the study conditions. These results justify further investigation of the formulation, including more extensive safety, efficacy, and comparative testing, before any conclusion about clinical suitability can be made. The present work has limitations: the antibacterial assessment was performed against one test organism, no standard positive control or marketed product was included, and the skin irritation observations do not replace comprehensive

safety testing. Additional studies should evaluate reproducibility, longer-term stability, performance in relevant skin models, and comparative antibacterial efficacy.

ACKNOWLEDGEMENT

The author wishes to convey heartfelt appreciation to the research guide, Mrs. Kishori, M.Pharm., Associate Professor, Department of Pharmaceutics, Shree Devi College of Pharmacy, Mangaluru, for her valuable mentorship, continuous encouragement, dedicated involvement, and guidance throughout the research work. Her assistance and insightful suggestions played an important role in the successful completion of this study.

The author extends sincere gratitude to Dr. V. Felix Joe, M.Pharm., Ph.D., Professor and Head, Department of Pharmaceutics, Shree Devi College of Pharmacy, Mangaluru, for his constructive guidance, consistent encouragement, and support throughout the research period. The author is grateful to the Principal, Dr. Jagadish V. Kamath, M.Pharm., Ph.D., Shree Devi College of Pharmacy, Mangaluru, for providing the opportunity and essential facilities required to carry out this research work.

The author also expresses sincere thanks to Mrs. Smitha Shetty, M.Pharm., Associate Professor, Department of Pharmaceutics, Shree Devi College of Pharmacy, Mangaluru, for her valuable assistance, cooperation, and encouragement during the course of this study.

REFERENCES

1. Krishnamoorthy K, Rajappan M. Nanosponges: a novel class of drug delivery system--review. J. Pharm. Pharm. Sci: a publication of the Canadian Society for Pharmaceutical Sciences, Societe canadienne des sciences pharmaceutics. 2012;15(1):103-11.
2. Goel V, Nautiyal U, Raina D. Development and evaluation of nanosponge loaded hydrogel of Ceftriaxone for the treatment of anti-bacterial infections. Biomed Eng Commun. 2025;4(3):19.
3. Alongi J, Poskovic M, Frache A, Trotta F. Role of β-cyclodextrin nanosponges in polypropylene photooxidation. Carbohydrate Polymers. 2011;86(1):127-35
4. Patel B, Bagade O, Ramteke K, Patel R, Awsarkar V. An assessment on preparations, characterization, and poles apart appliances of nanosponge. Int. J. Pharm.Tech. Res. 2014;6(7):2092-101
5. Trotta F, Zanetti M, Cavalli R. Cyclodextrin-based nanosponges as drug carriers. Beilstein J. Org. Chem. 2012;8(1):2091-9

6. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: a review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can. J. Infect. Dis. and Med. Microbiol. 2008;19(2):173-84.
7. Bryskier A. Roxithromycin: review of its antimicrobial activity. The Journal of antimicrobial chemotherapy. 1998 Mar 1;41(suppl_2):1-21.
8. Young RA, Gonzalez JP, Sorkin EM. Roxithromycin: a review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. Drugs. 1989 Jan; 37:8-41
9. Hingmire LP, Deshmukh VN, Sakarkar DM. Development and evaluation of sustained release matrix Tablets using natural polymer as release modifier. 2008;1(3):193-6.
10. Arun DK, Kishanta PK, Ranjita D. Murthy PN, Amithesh PK. Method development, validation and stability study of Repaglinide in bulk and pharmaceutical dosage form by spectro photometric method. IJBPR 2011: 2(1):7-10
11. Sahu M, Bhowmick M, Rathi J. Preformulation screening of repaglinide for transdermal anti-diabetic therapy. J. Drug. Del. Ther. 2017;7(4):103-9
12. Jain NA, Lohiya RT,Umekar MJ. Spectro photometric determination of naproxen and esomeprazole in a laboratory mixture by Simultaneous equation, absorption correction, absorption ratio and area curve methods. Int. J. Pharm. Sci. Res. 2011;2(5):130-4.
13. Solunke RS, Borge UR, Murthy K, Deshmukh MT, Shete RV. Formulation and evaluation of gliclazide nanosponges. Int J Appl Pharm. 2019:181-9.
14. Kasliwal RH, Thakre AR, Gholse YN. Nanosponges: a novel approach of drug delivery system. J. Med. Pharm. Allied. Sci. 2016;78(92):78.
15. Sujitha YS, Muzib YI. Formulation and optimization of quercetin loaded nanosponges topical gel: Ex vivo, pharmacodynamic and pharmacokinetic studies. Int. J. Appl. Pharm. 2019;11(5):156-65.
16. Mamtha DP, Viresh KC, Shabaraya AR. Nanosponges: an overview about the novel class of drug delivery system. World J Pharm Pharm Sci. 2021;10(6):1014-1027
17. Sowmya shree, ShripathyD, Shabaraya AR. Nanosponges- a novel nanocarrier approach for targeted drug delivery a brief review. World J. Pharm. Pharm. Sci. 2021; 10(5): 417-35.
18. Viresh KC, Gopika S, Shabaraya AR. Comparative characterization of gel loaded oxiconazole nitrate nanosponges for topical delivery. Eur J Pharm Med Res. 2023;10(1):364-372
19. Solunke RS, BORGE UR, Murthy K, Deshmukh MT, SHETE RV. Formulation and evaluation of gliclazide nanosponges. Int. J. Appl. Pharm. 2019;181-9.

20. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi pharm. J. 2012;20(1):63-7.
21. Manyam N, Budideti KK, Mogili S. Formulation and *in-vitro* evaluation of nanosponge loaded extended release tablets of trimethoprim. UPI J. Pharm. Med. Health Sci. 2018:78-86.
22. Iriventi P, Gupta NV, Osmani RA, Balamuralidhara V. Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis. DARU J. Pharm. Sci.. 2020;28(2):489-506
23. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta. Pol. Pharm. 2010;67(3):217-23.
24. Yadav V,Jadhav P, Dombe S, Bodhe A, Salunkhe P. Formulation and evaluation of microsponge gel for topical delivery of antifungal drug. Int. J. Appl. Pharm. 2017;9:30-7.

