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Formulation and Evaluation of Beta Cyclodextrin Based nanosponges Cream Formulation Containing Mometasone Furoate for Skin Disease

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ABSTRACT

The objective of this study was to develop and evaluate β-cyclodextrin (β-CD) nanosponges for the topical delivery of Mometasone furoate, a corticosteroid used for skin diseases. The nanosponges were synthesized using the hot melt method, with varying ratios of β-CD and diphenyl carbonate (DPC) as the cross-linker. Mometasone furoate was successfully loaded into the nanosponges via the freeze-drying technique. The physicochemical properties of the formulations were characterized by UV spectroscopy, FTIR, particle size analysis, zeta potential, scanning electron microscopy (SEM), and entrapment efficiency. The particle size of the formulations ranged from 131.1 nm to 217.8 nm, with formulation F5 exhibiting the smallest particle size. Zeta potential values indicated good stability, with F5 showing the highest charge (97.3 mV). The entrapment efficiency ranged from 65.4% to 96.2%, with F5 showing the highest efficiency. The formulated nanosponges were incorporated into a cream, which showed favorable characteristics such as optimal viscosity (1784 cps), pH (6.5), and spreadability (10.42 g.cm/s). The antimicrobial activity was evaluated against *E. coli* and *S. aureus*, showing significant antimicrobial effects. The formulation was also found to be non-irritant upon skin application. These results suggest that Mometasone furoate-loaded β-CD nanosponges cream could be an effective and safe formulation for the treatment of skin diseases.

Keywords: *Mometasone furoate, β-cyclodextrin nanosponges, topical delivery, hot melt method, freeze-drying, drug entrapment, antimicrobial activity, skin irritation, particle size, zeta potential.*

1. INTRODUCTION

Skin diseases, ranging from inflammatory conditions to infections and allergies, represent a significant global health burden. Among these, dermatological disorders such as eczema, psoriasis, and atopic dermatitis are common, requiring effective treatments to manage symptoms and reduce the severity of the conditions. Mometasone furoate (MF), a potent corticosteroid, is widely used for the treatment of such inflammatory skin diseases due to its anti-inflammatory, anti-pruritic, and vasoconstrictor properties (Sahoo et al., 2019). However, the application of mometasone furoate on the skin faces challenges, primarily related to poor skin penetration and limited bioavailability due to its lipophilic nature (Bhagat et al., 2017). To overcome these limitations, novel drug delivery systems such as nanosponges, formulated with cyclodextrins, are gaining attention for their ability to enhance the solubility, stability, and permeation of poorly water-soluble drugs. Beta-cyclodextrins (β-CD) are cyclic oligosaccharides made up of seven glucose units and are widely employed in the pharmaceutical industry for their ability to form inclusion complexes with hydrophobic drugs (Liu et al., 2018). β-CD-based nanosponges (NSs) are a new class of drug delivery systems characterized by their three-dimensional network structure, which allows them to entrap a variety of hydrophobic drugs, enhancing their stability, solubility, and controlled release. The use of β-CD nanosponges in transdermal drug delivery offers significant advantages over conventional formulations, as they can improve the drug's percutaneous absorption, thus enhancing therapeutic efficacy (Vora et al., 2015). Nanosponges can be incorporated into a cream formulation, allowing for easy application and improved drug penetration through the skin. This formulation type is particularly useful for localized treatment of skin disorders, as it ensures better drug release at the site of action. The incorporation of β-CD-based nanosponges into mometasone furoate formulations aims to increase the drug's stability, enhance its skin penetration, and reduce systemic side effects by targeting the drug to the affected area. The objective of this study is to formulate and evaluate a β-cyclodextrin-based nanosponges cream formulation containing

mometasone furoate for the effective treatment of skin diseases. The study will focus on optimizing the formulation to achieve the desired release profile, stability, and skin permeability of the drug. The physicochemical properties of the nanosponges, such as size, morphology, and zeta potential, will be characterized, and the cream's performance will be evaluated in vitro for its release and skin penetration abilities.

2. MATERIALS AND METHODS

Materials

The formulation of mometasone furoate-based nanosponges cream involves various chemicals such as mometasone furoate (Sigma-Aldrich), propylene glycol, methyl paraben, and triethanolamine (Loba Chemie), as well as solvents like petroleum ether and chloroform (Merck). Other reagents, including glacial acetic acid (Researchlab), sodium hydroxide (Fizmerck), ethanol (Molychem), and ammonia (Clorofiltind), are used for pH adjustment and solubilization. Additionally, stabilizers like carboxymethyl cellulose (Narang Chemical) and testing materials such as NAM media (Himedia) contribute to the formulation process.

Methods

Determination of Lambda Max

To determine the lambda max of Mometasone furoate, 10 mg of the drug was dissolved in 10 mL of methanol. From the resulting stock solution, 0.2 mL of Mometasone furoate was transferred into a 10 mL volumetric flask and the volume was adjusted to the mark with methanol to prepare a 20 µg/mL concentration. The working standard solution was then scanned in the UV range of 200 to 400 nm in normal mode, using distilled water as the blank. The peaks were observed, and the absorption maxima were determined (Kumbhar and Salunkhe, 2013).

Functional Group Identification by FTIR

Fourier Transform Infrared (FTIR) spectroscopy is a critical technique employed in academic and pharmaceutical research to analyze molecular structures and identify functional groups within samples. FTIR utilizes modulated mid-infrared energy to probe the vibrational energy of atoms within a molecule. When the vibrational energy of a bond aligns with the energy of the infrared light, absorption occurs, producing unique absorption bands that serve as a molecular "fingerprint." FTIR spectra for the nanosponges were recorded using the KBr pellet method, scanning from 400 to 4000 cm-1. To prepare the KBr disc, 1 mg of Mometasone furoate was mixed with 100 mg of spectroscopic-grade KBr, which was then dried under an IR lamp. The mixture was pressed under hydraulic pressure to form a disc, which was placed in the FTIR chamber for analysis.

Formulation of β-Cyclodextrin Nanosponges

β-Cyclodextrin nanosponges were synthesized using the 'hot melt method'. Various ratios of Diphenyl carbonate (DPC) cross-linker and β-cyclodextrin (β-CD) polymer were selected for the preparation, as outlined in Table 4. Anhydrous β-CD and DPC were finely homogenized and then heated gradually to 90–100 ºC with magnetic stirring for 6 hours. The substrate mixture (β-CD and DPC) was allowed to react for 6 hours to ensure complete cross-linking. This reaction led to the formation of nanosponges. After the reaction, the mixture was cooled to ambient temperature. The solid product was washed repeatedly with double-distilled water to remove unreacted β-CD, then dried at 40 ºC and stored in a desiccator until further use (Kumar et al., 2021).

Table 1: Composition of nanosponge's formulation

Ingredients	Formulation Code				
	F1	F2	F3	F4	F5
Mometasone furoate (mg)	100	100	100	100	100
DPC cross linker (Ratio)	100	100	100	100	100
Beta-cyclodextrin	50	100	150	200	250
Temperature	800 C	850 C	900 C	950 C	1000 C
Distilled water	q.s	q.s	q.s	q.s	q.s

DPC - Diphenyl carbonate

Loading of Mometasone Furoate in Nanosponges

Mometasone furoate was loaded into the prepared nanosponges using a freeze-drying technique. A placebo nanosponges (1 g) was dispersed in 50 mL of double-distilled water with the assistance of a magnetic stirrer. Approximately 100 mg of the drug was added to the dispersion, and the mixture was sonicated for 10 minutes. The dispersion was then kept under stirring for 24 hours. Afterward, the suspension was centrifuged at 2000 rpm for 10 minutes to separate the unentrapped drug, leaving the residue beneath the colloidal supernatant. The supernatant was lyophilized at -81°C and 0.0010 mbar pressure. The resulting drug-loaded nanosponges powder was stored for future use (Kumar et al., 2018).

Evaluation Parameters of Drug-Loaded Nanosponges Formulation

Physical Properties

The physical properties of the formulation, including color, odor, appearance, and homogeneity, were evaluated to ensure the material's suitability for its intended application.

Entrapment Efficiency (EE)

The percent entrapment efficiency (% EE) was estimated by collecting the filtrate from the dispersion after centrifuging the drug-loaded nanosponges at 30 minutes in a REMI Ultra Centrifuge. The supernatant was filtered and analyzed by UV spectroscopy at 247 nm to determine the concentration of Mometasone furoate. The % EE was calculated using the following formula (MMA, 2020):

%EE = (Initial amount of drug added - Drug amount in supernatant) × 100 Initial amount of drug added

Determination of Particle Size

The particle size of the drug-loaded nanosponges was determined using a Malvern Zetasizer (Malvern Instruments) based on dynamic light scattering (DLS). A diluted suspension of the nanosponges in a suitable liquid medium was prepared to avoid multiple scattering effects. The sample was transferred to a cuvette or specialized holder and placed in the Zetasizer. The Zetasizer software analyzed the Brownian motion of particles to determine the hydrodynamic diameter and polydispersity index (PDI), providing valuable insights into particle size distribution and formulation stability.

Zeta Potential

The zeta potential, which indicates the particle charge and the velocity of particle movement in an electric field, was measured using the Zetasizer Malvern device. The nanosponge suspension was diluted ten times with distilled water for analysis, and all samples were subjected to sonication for 5–15 minutes before measurement (Volić et al., 2022).

SEM Analysis

Scanning electron microscopy (SEM) was employed to assess the surface morphology of the prepared nanosponges. The nanosponges were mounted on a double-sided adhesive tape and attached to a metal slab for analysis under the scanning electron microscope. Photomicrographs were captured, and the nanosponges' spongy structure was examined at an acceleration voltage of 15.00 kV (Dora et al., 2016).

Preparation of Nanosponges Cream Formulations

Nanosponges-loaded Mometasone furoate cream formulations were prepared using the conventional oil-in-water (o/w) cream preparation method. In brief, the excipients for the continuous and dispersed phases were dissolved accordingly. The dispersed phase was prepared by heating glycerol monostearate, isopropyl myristate, cetyl alcohol, stearic acid, propyl parahydroxybenzoate, triethanolamine, and liquid paraffin at 70°C. Similarly, the continuous phase was prepared by blending dexpanthenol, glycerol, methyl parahydroxybenzoate, and purified water, also at 70°C. Mometasone furoate was dissolved in the dispersed phase. Both phases were then mixed and homogenized for a specified time at 70°C. The type of blending and homogenization equipment was selected based on preliminary studies, with a mechanical blade impeller providing a more homogeneous and reproducible product. The final cream was stored in suitable containers and evaluated for drug content, pH, viscosity, spreadability, and stability to ensure it met the desired therapeutic and quality standards. This nanosponge-based cream formulation offers improved drug delivery, prolonged action, and reduced side effects compared to conventional formulations (Crowley, 2006).

Evaluation Parameters of Nanosponges Cream Formulation

Physical Properties of Creams

To evaluate the physical properties of the cream, several key tests were conducted to assess its quality and stability. These included the evaluation of appearance and color for uniformity, pH measurement to ensure compatibility with skin, texture and consistency analysis using viscometers, and spreadability tests to ensure easy application. The cream's viscosity was also measured to determine its thickness, and stability tests were performed to detect any phase separation. Additionally, the cream's odor was assessed to ensure it was pleasant and free from signs of degradation. These evaluations ensured the cream's

effectiveness and safety for use.

Determination of pH

The pH of the formulated cream was measured using a digital pH meter. One gram of the formulated cream was dissolved in 10 mL of distilled water, and the pH was determined, with results recorded in Table 16 (Thakur et al., 2012).

Viscosity Determination

The rheological properties of the Mometasone furoate nanosponges-loaded cream were assessed at 37°C ± 2°C, at a speed of 100 rpm, using a Brookfield viscometer (DV-III Programmable) with spindle no. S-6.

Determination of Spreadability

The spreadability of the prepared Mometasone furoate nanosponges cream was measured using the horizontal slide method. A 1-gram sample of cream was placed between two slides, one adhered to a wooden surface and the other placed on top. A 125 g weight was applied to the upper slide for 5 minutes to remove excess cream and ensure a uniform layer. Spreadability was calculated using the following equation (Baibhav et al., 2012):

Spreadability = (M × L) / T

Where M is the weight on the top slide (125 g), L is the length the glass slide moved, and T is the time.

Test for Skin Irritancy

The skin irritancy test was performed by applying 0.5 g of the prepared nanosponge cream onto the skin for a duration of four hours. During this period, the skin was carefully monitored for any signs of erythema or edema. Observations were recorded at four, eight, and twelve hours after application, with the results documented in Table 18 (Bothiraja et al., 2014).

In Vitro Antimicrobial Activity

Culture Collection

The microbial strains used for the antimicrobial study were sourced from the Pinnacle Biomedical Research Institute, Bhopal. The pure cultures were preserved on nutrient agar for further growth and were stored at 4°C in a refrigerator until required.

Preparation of Nanosponges Cream Dilutions

To prepare the required dilutions of the nanosponge cream, 2 mg, 4 mg, and 8 mg of the cream were separately weighed out. Each weighed amount was transferred to three separate clean and dry test tubes. To each test tube, 1 mL of double-distilled water was added. The contents were thoroughly mixed until the nanosponge cream was completely dispersed or dissolved. Gentle agitation (such as stirring or vortexing) was used if necessary to ensure uniform dispersion. Each test tube was labeled according to its respective concentration for further use.

Agar Well Diffusion Method

Preparation of Media

The antimicrobial activity of the drug-loaded nanosponges cream was assessed using the agar well diffusion method. For this, 100 mL of nutrient agar media was prepared by dissolving 2.8 grams of nutrient agar in 100 mL of distilled water in a clean flask. The media was then sterilized by autoclaving at 121°C for 15-20 minutes to eliminate any microbial contamination. After autoclaving, the nutrient agar was allowed to cool slightly (without solidifying) before being poured into sterile Petri dishes.

Culture Inoculation and Well Preparation

Lawn cultures of *E. coli* and *S. aureus* were spread evenly on the surface of the nutrient agar plates using a sterile spreader. Using a sterile cork borer, four wells were created in each agar plate. The drug-loaded cream, prepared in various concentrations, was then introduced into the wells. The plates were incubated at 37°C for 24 hours. After incubation, the zones of inhibition surrounding each well were measured. A larger zone of inhibition indicates stronger antimicrobial activity, while the absence of a zone suggests no antimicrobial effect (Bauer, 1996).

3. RESULTS AND DISCUSSION

The results obtained from the various characterization tests and evaluations of the Mometasone furoate-loaded β-cyclodextrin (β-CD) nanosponges cream formulations offer a comprehensive understanding of the formulation's properties and its potential for effective skin delivery. The UV absorption maximum for Mometasone furoate was found at 247.0 nm (Figure 1), which corresponds to the characteristic absorbance of the drug. The FTIR study (Figure 2) of Mometasone furoate revealed specific peaks corresponding to functional groups within the molecule, confirming its chemical identity and stability in the nanosponges formulation. The particle size analysis of the various formulations (F1 to F5) revealed that the particle sizes ranged from 131.1 nm (F5) to 217.8 nm (F4), as shown in Figure 3 and Table 2. The particle size plays a crucial role

in the stability and bioavailability of the formulation. A smaller particle size, as observed in formulation F5, generally indicates better drug release and absorption. The polydispersity index (PI) values also indicated a relatively narrow distribution in most formulations, suggesting uniformity in particle size. Zeta potential measurements (Figure 4 and Table 3) indicated the charge stability of the nanosponge formulations. The zeta potential of formulations F1 (64.8 mV), F2 (90.8 mV), and F5 (97.3 mV) were significantly higher compared to formulations F3 (19.4 mV) and F4 (92.2 mV). The higher the zeta potential, the greater the repulsion between particles, ensuring better stability and preventing aggregation. Formulations F1, F2, and F5 exhibited excellent stability due to their high zeta potential values.

The entrapment efficiency of the nanosponge formulations was determined to be highest in formulation F5 (96.2%), followed by F3 (87.3%), F1 (76.8%), F2 (70.5%), and F4 (65.4%) (Table 4). A higher entrapment efficiency indicates that a larger portion of the drug is successfully incorporated into the nanosponges, which is critical for achieving optimal therapeutic effects and prolonged drug release. The SEM analysis (Figure 5) provided insights into the surface morphology of the nanosponges, showing a spongy and porous structure. This porous nature is beneficial for drug loading and sustained release, as it allows for the encapsulation of a substantial amount of drug while providing a controlled release profile. The physical properties of the prepared Mometasone furoate nanosponges cream were evaluated, revealing that the cream had a white color, was odorless, had a creamy appearance, and exhibited uniform homogeneity (Table 5). These characteristics are essential for the formulation's aesthetic and sensory appeal, which are important factors for patient compliance. The cream's viscosity, pH, spreadability, and irritancy were also evaluated (Table 6). The viscosity of the cream was found to be 1784 cps, which is suitable for topical application. The pH value of 6.5 indicates that the formulation is compatible with the skin, as it is within the normal pH range of the skin. The spreadability of 10.42 g.cm/s suggests that the cream spreads easily over the skin, enhancing patient comfort. No irritation was observed upon application, indicating the formulation's safety for dermatological use. The antimicrobial activity of the Mometasone furoate-loaded nanosponges cream was assessed against *E. coli* and *S. aureus* using the agar well diffusion method. The results (Figure 6 and Table 7) demonstrated that the cream exhibited a dose-dependent antimicrobial activity, with higher concentrations resulting in larger zones of inhibition. At 8 mg/mL (C2), the cream showed inhibition zones of 9 mm for *E. coli* and 7 mm for *S. aureus*, suggesting its potential as a therapeutic agent for skin infections.

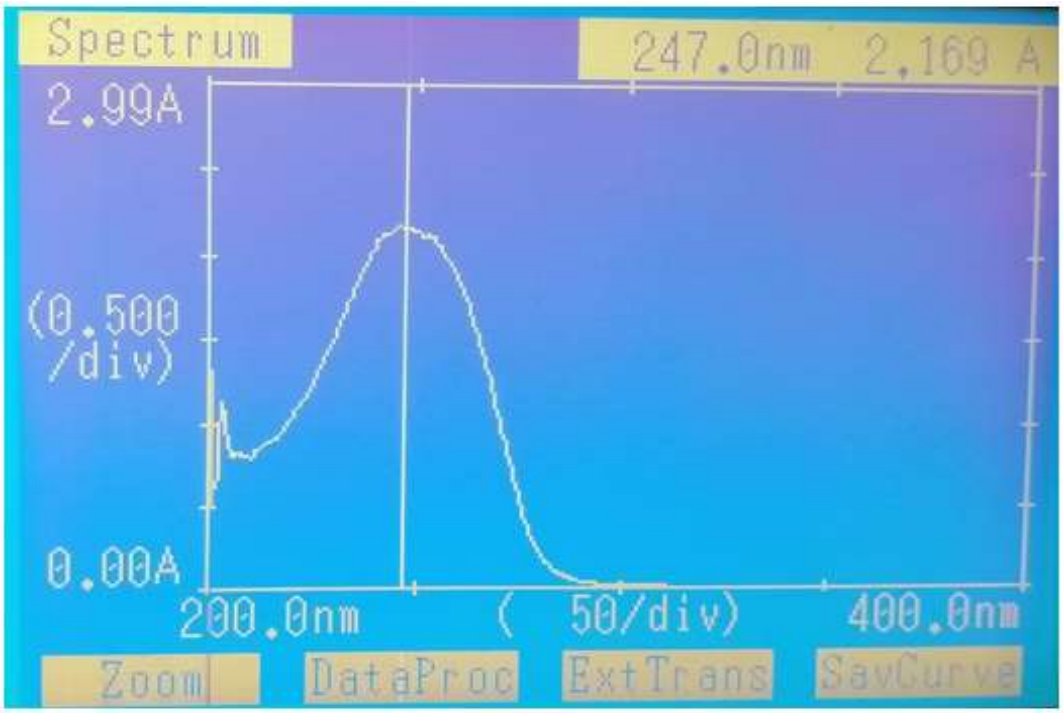


Figure 1: UV graph of Mometasone furoate (247.0nm)

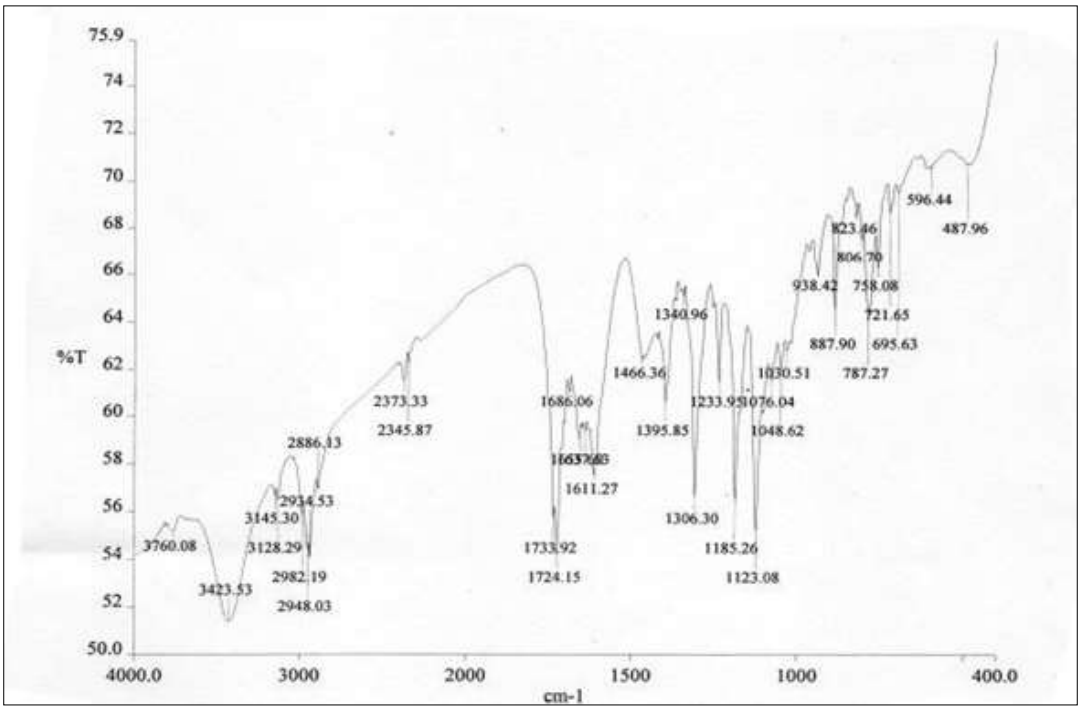
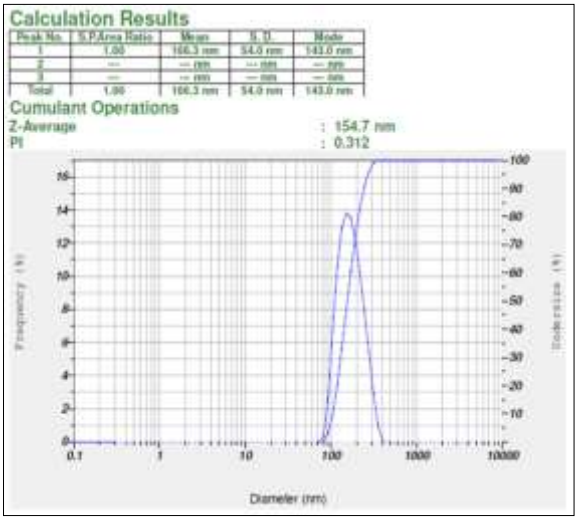
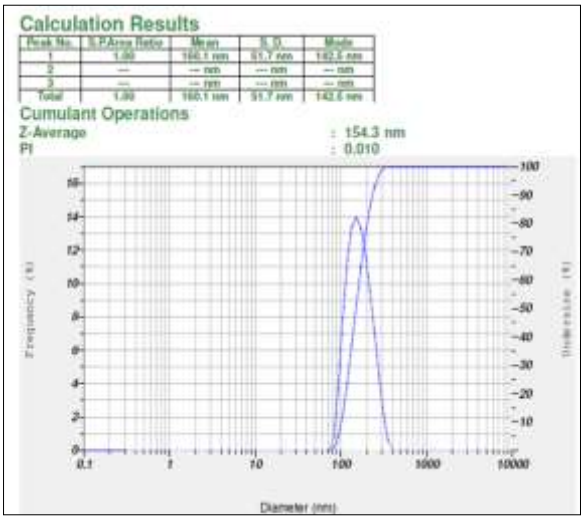


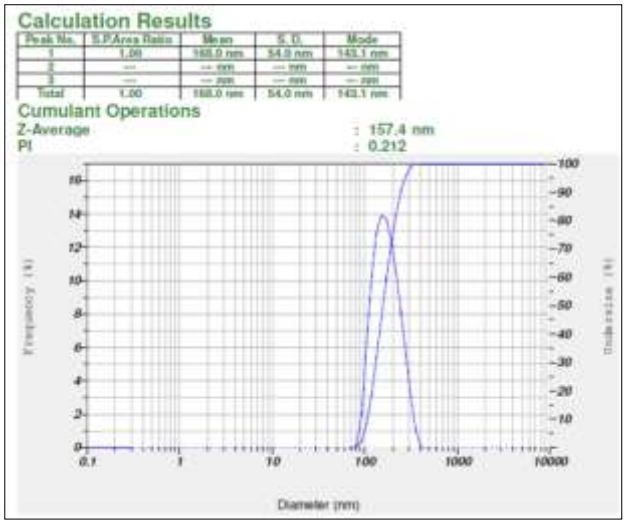
Figure 2: FTIR Study of Mometasone furoate

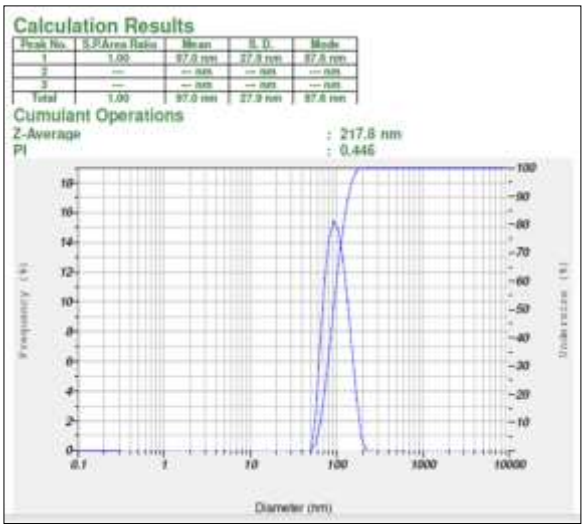
Characterization of formulation



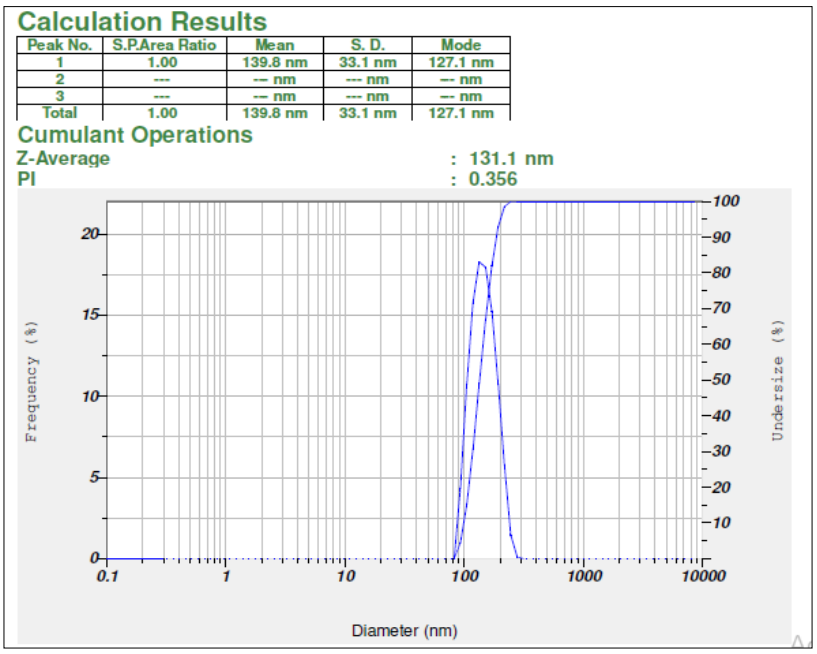


F1 **F2**





F3 **F4**



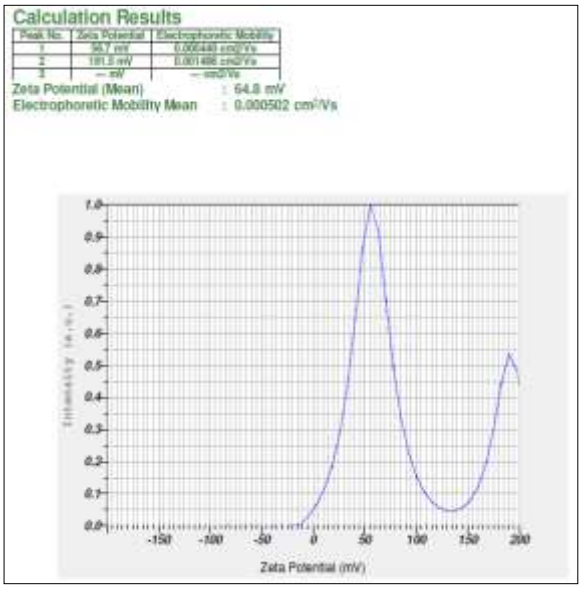
F5

Figure 3: Particle Size of formulation F1 to F5

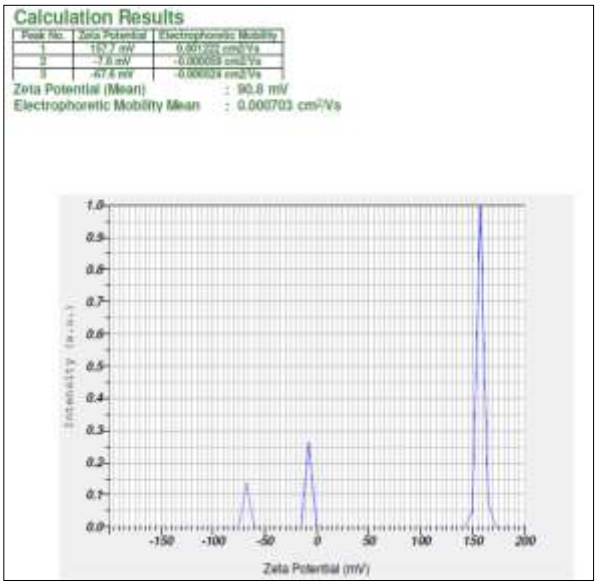
Table 2: Results of Particle size

S. No	Formulation	Particle size	PI Value
1.	F1	154.3	0.010
2.	F2	154.7	0.312
3.	F3	154.4	0.212
4.	F4	217.8	0.446
5.	**F5**	**131.1**	**0.356**

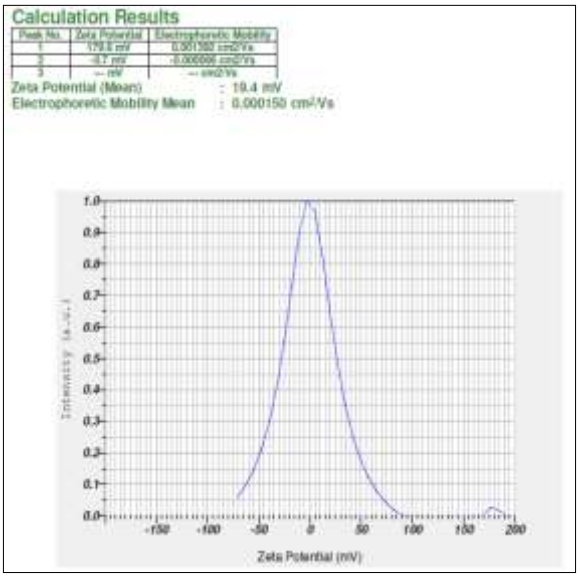
Zeta potential of nanosponge formulation



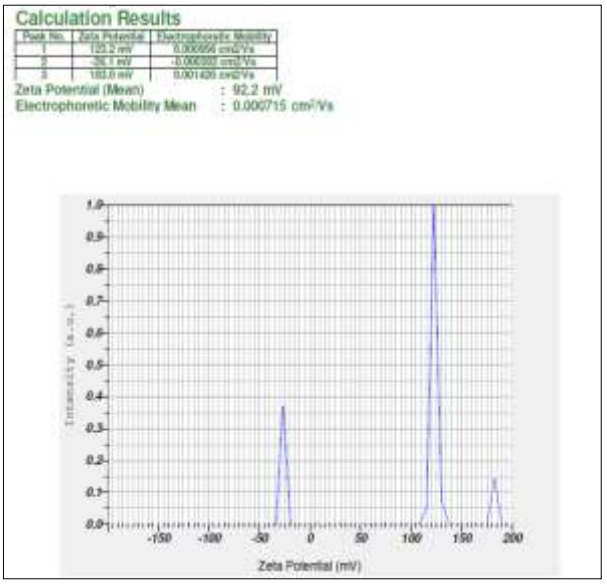
F1



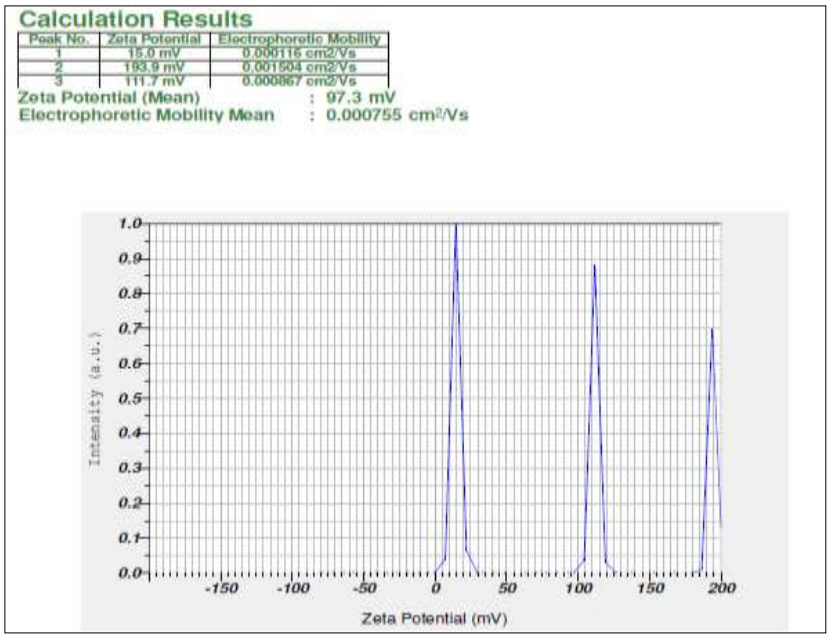
F2



F3



F4



F5

Figure 4: Graphs of Zeta potential

Table 3: Results of Zeta potential

S. No	Formulation	Zeta potential
1.	F1	64.8 Mv
2.	F2	90.8 Mv
3.	F3	19.4 Mv
4.	F4	92.2 Mv
5	**F5**	**97.3 Mv**

Table 4: Results of Entrapment efficacy

S. No.	Formulations	Entrapment efficacy
1.	F1	76.8 %
2.	F2	70.5 %
3.	F3	87.3 %
4.	F4	65.4 %
5.	F5	**96.2 %**

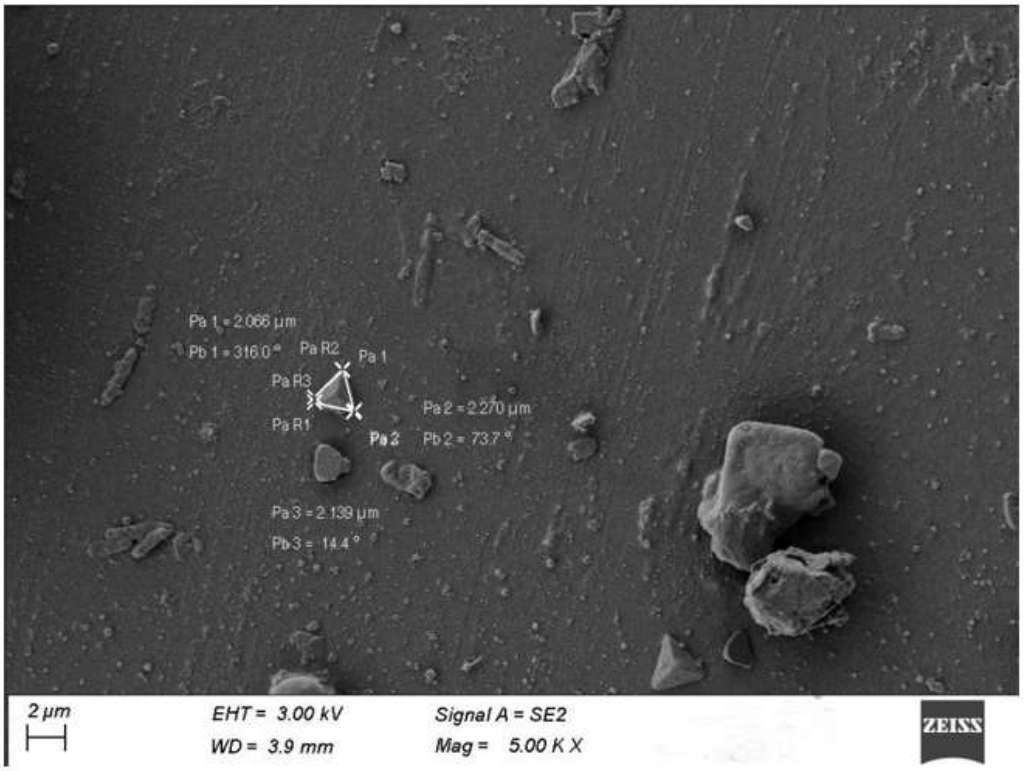


Figure 5: Scanning electron microscope (SEM)

Table 5: Results of Physical appearance of cream

S. No	Parameter	Result
1.	Colour	White
2.	Odour	Odourless
3.	Appearance	Creamy
4.	Homogeneity	Uniform

Table6: Results of evaluation of cream formulation

S. No.	Formulation	Viscosity (Cps)	pH	Spreadability (g.cm/s)	Irritancy
1	Nanosponges cream	1784 cps	6.5	10.42 g-cm/sec	No irritation observed

Figure 6: Results of Antimicrobial activity against *E.coli* and *S.aureus*

Table 7: Antimicrobial activity of Formulation against *E.coli* and *S.aureus*

S. No.	Sample Name (mg/ml)	Zone of Inhibition (mm) of *E.coli*	Zone of Inhibition (mm) of *S.aureus*
1.	C1 (control)	0mm	0mm
2.	C2 (8mg/ml)	9mm	7mm
3.	C3 (4mg/ml)	5mm	3mm
4.	C4 (2mg/ml)	3mm	2mm

4. CONCLUSION

The Mometasone furoate-loaded β-cyclodextrin nanosponges cream formulation exhibited promising characteristics for effective topical drug delivery. The results of the particle size, zeta potential, entrapment efficiency, and antimicrobial activity support the hypothesis that nanosponges can enhance drug stability, control release, and provide effective antimicrobial activity. The formulation showed good physical properties, safety, and efficacy, making it a suitable candidate for dermatological applications. Further studies, including in vivo testing and stability studies, are recommended to validate the clinical potential of the formulation.

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