International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

QUALITY BY DESIGN (QBD) FORMULATION, DEVELOPMENT AND OPTIMIZATION OF POLYMERIC NANOSPONGES GEL CONTAINING BETA SITOSTEROL FOR TOPICALLY DELIVERY BOX-BEHNKEN DESIGN APPROACH

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***Article History:**

Received: 01/02/2025
Revised: 17/02/2025
Accepted: 22/03/2025

ABSTRACT

The aim of this study was to develop and optimize a polymeric nanosponges gel formulation containing Beta-sitosterol for topical delivery using the Box-Behnken design. Beta-sitosterol was characterized for its organoleptic properties, solubility, pH, and melting point. The nanosponges were prepared by the inclusion complexation method using Beta-cyclodextrin (β-CD) as a polymer and diphenyl carbonate (DPC) as a crosslinker. Various formulation parameters such as polymer concentration, crosslinker concentration, stirring time, and drug loading were optimized. The particle size and entrapment efficiency were analyzed, and the optimized formulation exhibited a particle size of 321.5 nm and an entrapment efficiency of 94.6%. The release kinetics study revealed a zero-order release pattern, ensuring sustained drug release. The formulation was further evaluated for its physical properties, including viscosity, pH, and spreadability. Stability studies showed that the formulation remained stable over a period of 90 days under both controlled and accelerated conditions. These findings suggest that the developed Beta-sitosterol nanosponges gel formulation is a promising candidate for efficient topical drug delivery, with sustained release and good stability.

Keywords: Polymeric Nanosponges, Beta-sitosterol, Topical Delivery, Box-Behnken Design, Optimization, Entrapment Efficiency, Drug Release, Stability Study, Nanosponges Gel, Beta-cyclodextrin, Crosslinker.

INTRODUCTION

The concept of Quality by Design (QbD) is a systematic approach to pharmaceutical development that aims to ensure product quality by understanding the process and product, focusing on design, optimization, and control. In the field of topical drug delivery, QbD plays a pivotal role in the formulation of drugs to achieve enhanced bioavailability, efficacy, and safety (Patel *et al.,* 2020). Polymeric nanosponges (NS), a class of nanocarriers, have emerged as promising systems for topical drug delivery due to their ability to encapsulate hydrophobic drugs, improve stability, enhance skin penetration, and provide controlled release over prolonged periods (Bhatia *et al.,* 2019). The unique characteristics of nanosponges, such as their small size, high surface area, and flexibility, allow for better permeation through the skin, making them ideal for topical applications (Saini *et al.,* 2020).

Beta-sitosterol, a plant-derived phytosterol, has gained significant attention in the pharmaceutical and cosmetic industries due to its antioxidant, anti-inflammatory, and skin-

healing properties. It has been reported to possess therapeutic potential for conditions such as eczema, psoriasis, and wound healing, making it an ideal candidate for incorporation into topical formulations (Nugraha *et al.,* 2021). However, due to its poor solubility in water and low bioavailability when administered through conventional delivery systems, Beta-sitosterol often requires innovative delivery strategies to enhance its therapeutic potential (Sharma *et al.,* 2019).

Incorporating Beta-sitosterol into polymeric nanosponges presents an effective solution to overcome these challenges. Nanosponges can provide a stable environment for hydrophobic drugs, facilitating their encapsulation, enhancing solubility, and ensuring targeted delivery to the skin, thereby improving therapeutic outcomes (Choudhary *et al.,* 2021). The use of nanosponges in QbD formulation allows for a detailed understanding of the relationships between formulation variables, the properties of the nanoparticles, and their performance in the desired application.

To optimize the formulation process, a Box-Behnken Design (BBD), which is a powerful tool in response surface methodology (RSM), can be employed. BBD is specifically designed for evaluating and optimizing multiple factors simultaneously, which is essential in the preparation of a complex formulation such as a nanosponges gel. By varying critical formulation factors such as the concentration of polymer, surfactant, and the drug, and their interactions, BBD allows for the identification of the optimal formulation conditions with minimal experimental runs (Verma *et al.,* 2020). This design ensures that the final formulation meets the required quality attributes, such as particle size, drug release profile, stability, and skin permeability, ultimately leading to a product that is safe, effective, and reproducible.

The aim of this study is to design, develop, and optimize polymeric nanosponges gel containing Beta-sitosterol for topical delivery using the Box-Behnken Design approach under the Quality by Design (QbD) framework. This research will focus on formulating a stable and effective gel that ensures the sustained release of Beta-sitosterol while maximizing its therapeutic effect. The physical characteristics of the gel, including drug encapsulation efficiency, particle size, morphology, *in-vitro* release, and stability, will be evaluated, along with an assessment of the skin permeation ability.

MATERIALS AND METHODS

Pre-formulation studies

Organoleptic Properties

Organoleptic properties of Beta sitosterol were observed by visual observation. The organoleptic studies of Beta sitosterol like general appearance like color, odor, state, etc. were performed.

Solubility study

Qualitative solubility of Beta sitosterol in different solvents was determined according to USP NF, 2007. Approximately 1 mg of Beta sitosterol was weighed and transferred into a 10 ml test tube and dissolved in the respective solvents (1 ml each of methanol, ethanol, DMSO, chloroform and water) (Jain and Verma, 2020).

pH determination

pH was determined by Electrochemical method. Digital pH meter is used to determine the pH of Beta sitosterol. After the meter has

been turned on, allowed to stabilize as necessary and properly calibrated, begin by rinsing the probe with deionized or distilled water and blotting the probe dry with lint-free tissue paper. Immerse the sensing tip of the probe in the sample and record the pH reading and Rinse the probe, blot dry and repeat step 2 on a fresh portion of sample. The two readings should agree to within the accuracy limits of the meter.

Melting Point

Melting point was analyzed by open Capillary method using Thiele's tube. Few quantity of the Beta sitosterol was placed in a thin walled capillary tube 10-15 mm long, about 1mm inside diameter, and closed at one end. Liquid paraffin oil was filled in the thieles tube and placed in the contact of flame. The capillary was suspended into the thiele's tube and heat the sample slowly; thermometer was attached to check the temperature. The temperature at which the sample starts to melt was taken as the melting point of the sample (Chowk, M. I. 2020).

Determination of Lambda max and calibration curve:

Preparation of standard stock solution:

About 5mg of Beta sitosterol was weighed and transferred into 5ml volumetric flask. The volume was made up to 5ml using methanol to obtain a solution that has a concentration 1000 µg/ml. 1ml of this stock solution was taken and then diluted up to 10 ml using methanol to obtain a solution that has a concentration 100 µg/ml which is standard stock solution**.**

λ_{max}

From the above stock solution 2 ml of sample was transferred into a 10 ml volumetric flask and the volume was made up to mark with methanol to prepare a concentration of 20 µg/ml. The sample was scanned by Double beam UV-VIS Spectrophotometer (Shimadzu - 1700) in the range of 200- 400 nm, using methanol as a blank. The maximum absorbance (λ_{max}) of the sample was noted (Kumbhar and Salunkhe, 2013).

Linearity (Calibration curve)

Aliquots of 10, 20, 30, 40, 50, 60 and 70µg/ml were prepared from the solution of 100 µg/mL Beta sitosterol working standard stock solution were accurately transferred into a series of 5 mL calibrated flask and volume was made up to the mark with methanol. The absorbance of the resulting solutions was measured at 250.0 nm against methanol blank. Calibration curve was prepared by plotting the absorbance vs concentration of drug. Seven points calibration curve were obtained in a concentration range from 10-70µg/ml of Beta sitosterol (Behera *et al.,* 2012).

Fourier transmission Infra-Red Spectroscopy

FT-IR spectrum of Beta sitosterol was recorded over the range of 4000 to 400 cm−1 by KBr pellet method using a FT-IR spectrophotometer. The KBr disc was prepared using 1 mg of each Beta sitosterol in 100 mg of spectroscopic grade KBr which has been dried using IR lamp. Both KBr and drug was mixed and subjected to hydraulic pressure to form disc. This disc was placed in FT-IR chamber. Infrared spectrum was recorded in the 4000 - 400 cm-1 region.

Formulation of β-cyclodextrin Nanosponges

Beta-cyclodextrin nanosponges were prepared by 'hot melt method'. Various ratios comprising Diphenyl carbonate (DPC cross-linker) and Beta- cyclodextrin (β-CD

polymer) (Ratios of DPC and β-CD are given in table no.4) were chosen for the nanosponges preparation. Anhydrous polymer (β-CD) and crosslinker (DPC) (finely homogenised) were gradually heated (90 to 100 ºC) with magnetic stirring for 1to 3 hours. The substrate mixture (β-CD and DMC) was allowed to react for 1 to 3h so as to ensure completion of cross linking reaction amongst them; resulting in formation of nanosponges. The obtained reaction mixture was subsequently cooled at ambient temperature. The solid thus obtained was washed repeatedly using double distilled water (to remove unreacted β-CD). Finally, the placebo nanosponges obtained were dried (at 40 ºC) and stored in a desiccator, till further use.

Loading of drug in nanosponges

The precisely weighed amounts of prepared NS (1g) were suspended in water (20 mL) and sonicated for few minutes to avoid the formation and presence of any aggregates. In this aqueous suspension, excess amount of drug (100 mg) mixture was dispersed. The resultant solution was maintained under constant stirring for 1 to 4 h for allowing complexation between CD NS and incorporated drugs. After complexation reaction, the uncomplexed drug was separated out from nanosuspension via centrifugation for 10 min. The obtained colloidal supernatant was then freeze dried to get drug loaded NS; which were then stored into covered vacuum desiccator at ambient temperature till further studies (Kumar *et al.,* 2018, Ahmed *et al.,* 2021).

Design of experiment

Design of experiment for the formulation of nanosponges was performed by Design Expert (Version 12.0.1.0) software. The quadratic response surfaces were represented by the second- order polynomial model. The independent and dependent variables selected are presented in Table 2.

Evaluation parameters of nanosponge

Zeta potential

The zeta potential was measured for the determination of the movement velocity of the particles in an electric field and the particle charge. In the present work, the nanosponges was diluted 10 times with distilled water and analyzed by Zetasizer Malvern instruments. All samples were sonicated for 5-10 minutes before zeta potential measurements (Kumar *et al.,* 2018, Penjuri *et al.,* 2016).

Particle size

The size of nanosponges was measured using Malvern Zeta sizer (Malvern Instruments). The dispersions were diluted with Millipore filtered water to an appropriate scattering intensity at 25°C and sample was placed in disposable sizing cuvette. The size data is documented in Table 25 (Sharma and Pathak 2011).

Entrapment efficiency

% Entrapment efficiency was determined by indirect estimation. Drug -loaded nanosponges were centrifuged at 15,000 rpm for 30 min using REMI Ultra Centrifuge. The non-entrapped drug (free drug) was determined in the supernatant solution using UV spectrophotometer. The peak area was determined and amount of free drug is determined by extrapolating the calibration curve. And drug entrapment calculated by using below equation (Solunke *et al.,* 2019).

Entrapment efficiency % = Total drug conc. - Supernatant drug conc. / total drugconc.*100

Scanning Electron Microscopic (SEM)

The electron beam from a scanning electron microscope was used to attain the morphological features of the optimized Beta sitosterol loaded nanosponges were coated with a thin layer (2–20 nm) of metal(s) such as gold, palladium, or platinum using a sputter coater under vaccum. The pre-treated specimen was then bombarded with an electron beam and the interaction resulted in the formation of secondary electrons called auger electrons. From this interaction between the electron beam and the specimen's atoms, only the electrons scattered at 90° were selected and further processed based on Rutherford and Kramer's Law for acquiring the images of surface topography (Anwer *et al.,* 2019).

Formulation of Nanosponges loaded Gel

Initially carbopol-934 was immersed in 50 mL of warm water (A) for 2 hr and was homogeneously dispersed using magnetic stirrer at 600 rpm. In separate container carboxymethyl cellulose and methyl paraben was added into 50 ml warm water (B) and stirredcontinuously to make stiff gel. Both the mixtures A and B were mixed with the continuous stirring. Then tri-ethanol amine (Drop wise) was added to neutralize the pH and nanosponges of optimized formulation were incorporated into the dispersion to obtained Gel. At this stage, permeation enhancer was added. The final dispersion was agitated until smooth gel was formed without lumps (Abbas *et al.,* 2019).

Characterization of nanosponges loaded Gel

Physical appearance

The prepared Gel formulation was evaluated for appearance, Color, Odor, and homogeneity by visual observation (Kumar and Eswaraiah, 2020).

pH

pH of the formulation was determined by using Digital pH meter (EI). The meter was allowed to stabilize as necessary and properly calibrated, begin by rinsing the probe with de-ionized or distilled water and blotting the probe dry with lint-free tissue paper. Immerse the sensing tip of the probe in the sample and record the pH reading and Rinse the probe, blot dry and repeat step 2 on a fresh portion of sample. The two readings should agree to within the accuracy limits of the meter. The samples were analyzed in triplicate. If slight deviations in pH were noted, it was adjusted to skin pH using drop wise addition of tri-ethanolamine solution (Kumar *et al.,* 2018).

Viscosity

The viscosity of the gel formulations was determined using Brookfield viscometer with spindle no. 61 at 100 rpm at the temperature of 25^0C (Monica and Gautami, 2014).

Spreadability

An ideal topical gel should possess a sufficient spreading coefficient when applied or rubbed on the skin surface. This was evaluated by placing about 1g of formulation on a glass slide. Another glass slide of the same length was placed above that, and a mass of 50 mg was put on the glass slide so that the gel gets sandwiched between the two glass slides and spreads at a certain distance. The time taken for the gel to travel the distance from the place of its position was noted down. Spreadability was determined by the following formula:

$$S= M*L/T$$

Where, S-Spreadability, g.cm/s M-Weight put on the upper glass L-Length of glass slide T-Time for spreading gel in sec (Sandeep, 2020).

In-vitro drug release

The *in-vitro* drug release study of Nanospoges loaded Gel formulations were studied by dialysis bag diffusion method. Nanosponges loaded Gel was dispersed into dialysis bag and the dialysis bag was then kept in a beaker containing 100 ml of pH 7.4 phosphate buffer. The beaker was placed over a magnetic stirrer and the temperature of the assembly was maintained at 37 ± 2 °C throughout the experiment. During the experiment rpm was maintained at 100 rpm. Samples (2 ml) were withdrawn at a definite time intervals and replaced with equal amounts of fresh pH 7.4 phosphate buffers. After suitable dilutions the samples were analyzed using UV–Visible spectrophotometer at 250.0 nm. To analyze the *in vitro* drug release data various kinetic models were used to describe the release kinetics.

To analyze the *in vitro* release data various kinetic models were use to describe the release kinetics. The zero order rate Eq. (2) describes the systems where the drug release rate is independent of its concentration. The first order Eq. (3) describes the release from system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. The results of *in vitro* release profile obtained for all the formulations were plotted in modes of data treatment.

Stability studies

The nanosponges loaded gel formulation was packed and were placed in the stability test chamber and subjected to stability studies at accelerated testing ($25^0C \pm 2^0C$ and 60 ± 5% RH) and ($40^0C \pm 2^0C$ and 70 ±5% RH) for 3 months. The formulation was checked for evaluation parameter viscosity and pH at the interval of 30, 45, 60, 90 days (3 month) months. The formulation was tested for stability under accelerated storage condition for 3 months in Accordance to International Conference on Harmonization (ICH) guidelines. Formulation was analyzed for the change in evaluation parameter viscosity and pH. All Results were compared against final formulation of 0 days as the reference.

RESULTS AND DISCUSSION

The results of this study highlight the successful development and optimization of a polymeric nanosponges gel formulation containing Beta-sitosterol using the Box-Behnken design approach. The organoleptic properties, solubility, and melting point studies confirmed the characteristics of Beta-sitosterol. Formulation trials demonstrated that the particle size and entrapment efficiency (EE) were significantly influenced by the polymer and crosslinker concentrations, with optimal values observed in formulations with higher polymer and crosslinker content. The zeta potential and SEM images indicated stable nanosponges with a uniform structure. The release kinetics study revealed that the optimized formulation followed zero-order release, ensuring sustained drug release. Additionally, stability studies showed that the formulation remained stable over 90 days under different storage conditions. These findings suggest that the developed nanosponges gel is a promising system for topical delivery of Beta-sitosterol with consistent drug release and excellent stability.

Table 1: Composition of nanosponges formulation

S. No	Polymer (B-Cyclodextrin) mg	Cross linker (DPC) mg	Stirring time (hrs)	Drug (mg)	Temperature (°C)
1	50	175	1	100	90
2	175	50	1	100	90
3	300	175	1	100	90
4	175	300	3	100	90
5	175	300	1	100	90
6	300	300	2	100	90
7	50	300	2	100	90
8	50	50	2	100	90
9	300	175	3	100	90
10	50	175	3	100	90
11	300	50	2	100	90
12	175	50	3	100	90

Table 2: Independent and Dependent variables

Independent variables	Dependent variables
(X1) Polymer (B-Cyclodextrin) (mg)	(Y1) Particle size (nm)
(X2) Cross-linker (DPC) (mg)	(Y2) Zeta potential (mV)
(X3) Stirring time (min.)	

Values of variables

Table 3: Values of variables

Factor	Name	Units	Type	Minimum	Maximum	Coded Low	Coded High	Mean	Std.Dev.
A	Polymer	mg	Numeric	50.00	300.00	-1 ↔50.00	+1 ↔300.00	175.00	106.60
B	Cross linker	mg	Numeric	50.00	300.00	-1 ↔50.00	+1 ↔300.00	175.00	106.60
C	Stirring time	hrs	Numeric	1.0000	3.00	-1 ↔1.00	+1 ↔3.00	2.00	0.8528

Table 4: Composition of gel formulation

S. No	Excipients	Quantity (gm)
1.	Carbopol 934	1.00 gm
2.	Carboxymethyl cellulose	1.00 gm
3.	Propylene glycol	0.5 ml
4.	Methyl paraben	0.2 ml
5.	Nanosponges	1.0 gm
6.	Tri-ethanolamine	q.s
7.	Water	100 ml

Table 5: Organoleptic properties of Beta sitosterol

Drug	Organoleptic properties	Observation
Beta sitosterol	Colour	White
	Odour	Odourless
	State	Fine powder
	Appearance	Solid powder

Table 6: Solubility study of Beta sitosterol

Drug	Solvents	Observation/Inference
Beta sitosterol	Water	Insoluble
	Ethanol	soluble
	Methanol	soluble
	Chloroform	Slightly soluble
	DMSO	Freely soluble

Table 7: pH of Beta sitosterol

S. No	Drugs	Observed
1.	Beta sitosterol	7.2

Table 8: Melting point of Beta sitosterol

Drugs	Observed	Reference
Beta sitosterol	163°C	160 to 164 °C

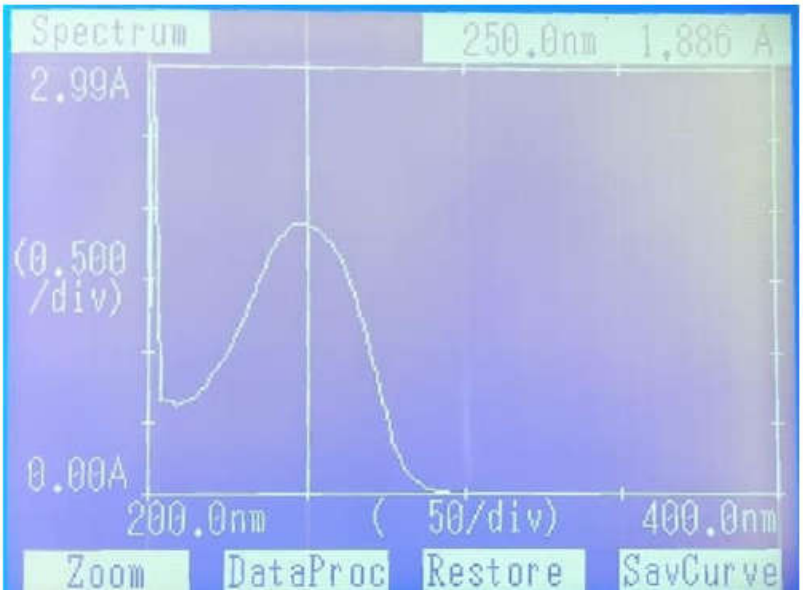

Figure 1: λ_{max} of Beta sitosterol

Figure 2: FTIR spectra of Beta sitosterol

Table 9: Formulation trials as per Box–Behnken design

S. No	Polymer (B-Cyclodextrin) mg	Cross linker (DPC) mg	Stirring time (hrs)	Drug (mg)	Temperature (°C)	Particle size (nm)	Entrapment efficiency (%)
1	50	175	1	200	90	853.2	72.3
2	175	50	1	200	90	456.8	74.6
3	300	175	1	200	90	321.5	69.1
4	175	300	3	200	90	597.6	94.6
5	175	300	1	200	90	489.1	88.2
6	300	300	2	200	90	538.9	96.8
7	50	300	2	200	90	976.8	97.1
8	50	50	2	200	90	812.5	90.7
9	300	175	3	200	90	218	78.5
10	50	175	3	200	90	751.2	89.3
11	300	50	2	200	90	347.2	68.3
12	175	50	3	200	90	572.6	65.8

Table 10: Variables operating range for nanosponges formulation

Name	Goal	Lower Limit	Upper Limit	Importance
A:Polymer	is in range	50	300	3
B:Cross linker	is in range	50	300	3
C:Stirring time	is in range	1	3	3
Particle size	none	218	976.8	3
EE	none	65.8	97.1	3

Final Equation in Terms of Coded Factors

Particle size = +577.95-246.01 A +51.66 B +2.35 C

Table 11: Predicted value and actual value of all formulations

Formulations	Actual Value	Predicted Value
NS 1	853.20	821.61
NS 2	456.80	523.94
NS 3	321.50	329.59
NS 4	597.60	631.96
NS 5	489.10	627.26
NS 6	538.90	383.60
NS 7	976.80	875.63
NS 8	812.50	772.30
NS 9	218.00	334.29
NS 10	751.20	826.31
NS 11	347.20	280.28
NS 12	572.60	528.64

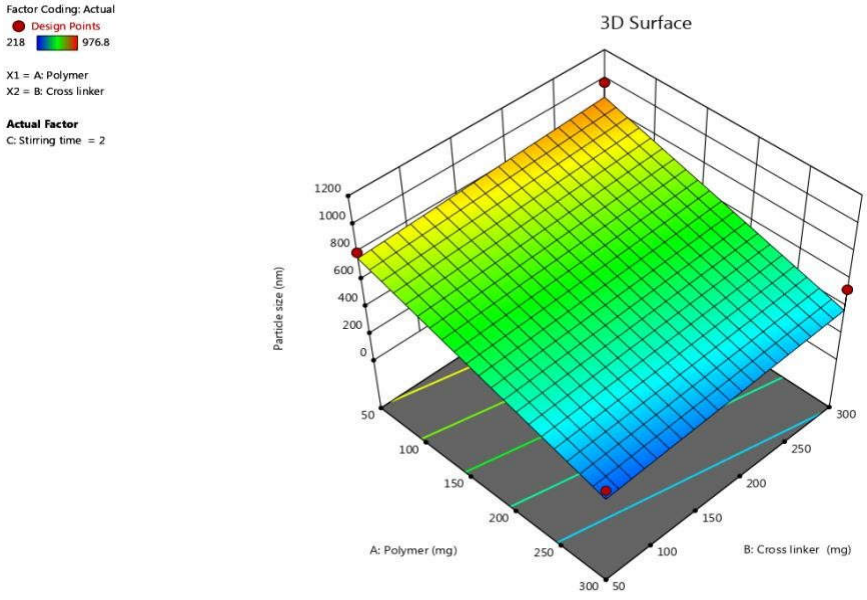

Figure 3: Response surface plot showing combined effect of polymer and cross linker on particle size of nanosponges

Table 12: Response 2: EE (ANOVA Linear model)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	987.27	3	329.09	4.67	0.0361	significant
A-Polymer	168.36	1	168.36	2.39	0.1607	
B-Cross linker	746.91	1	746.91	10.60	0.0116	
C-Stirring time	72.00	1	72.00	1.02	0.3416	
Residual	563.46	8	70.43			
Cor Total	1550.73	11				

Final Equation in Terms of Coded Factors

Entrapment efficiency = +82.11 -4.59 A +9.66 B +3.00 C

Table 13: Predicted and actual value of Entrapment efficiency

Formulation code	Actual Value	Predicted Value
NS 1	92.3	95.69
NS 2	74.6	74.04
NS 3	79.1	86.90
NS 4	94.6	98.15
NS 5	78.2	76.08
NS 6	86.8	82.40
NS 7	77.1	73.62
NS 8	70.7	71.58
NS 9	88.5	93.65
NS 10	89.3	96.12
NS 11	88.3	82.83
NS 12	82.3	87.33

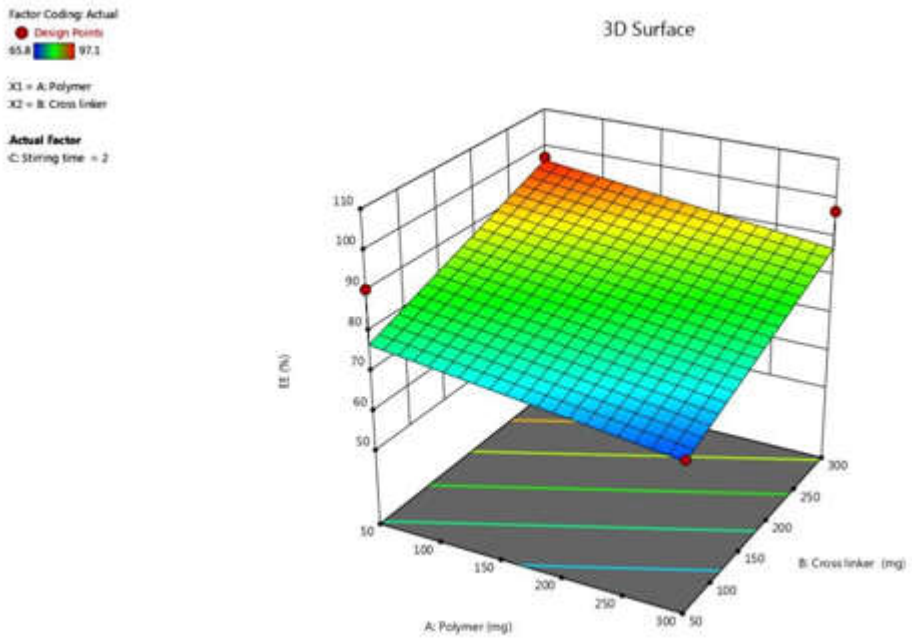

Figure 4: Response surface plot showing combined effect of polymer and cross linker on entrapment efficiency of nanosponges formulation

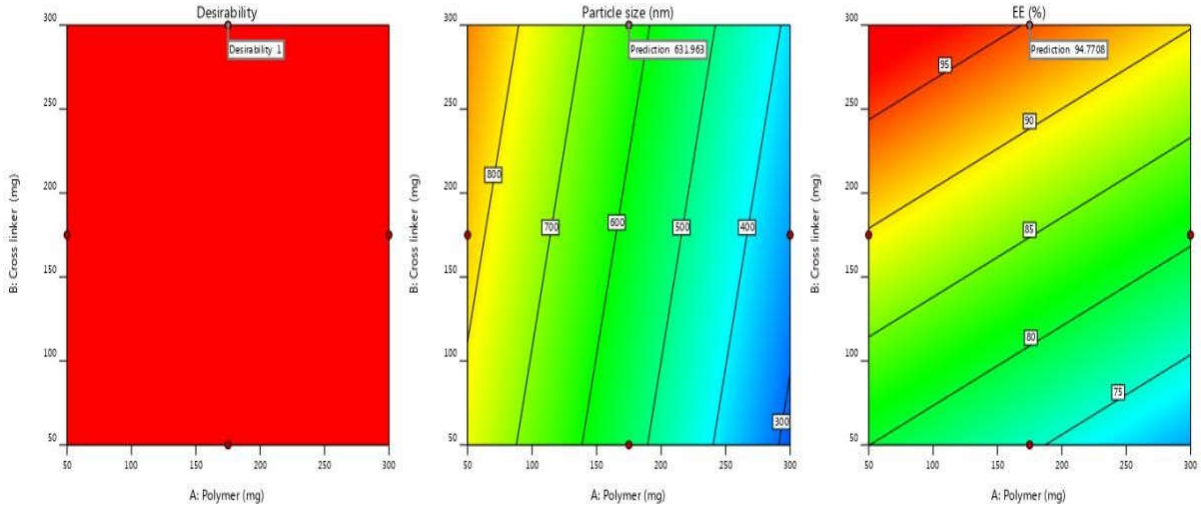

Figure 5: Response surface plot showing prediction data for optimization

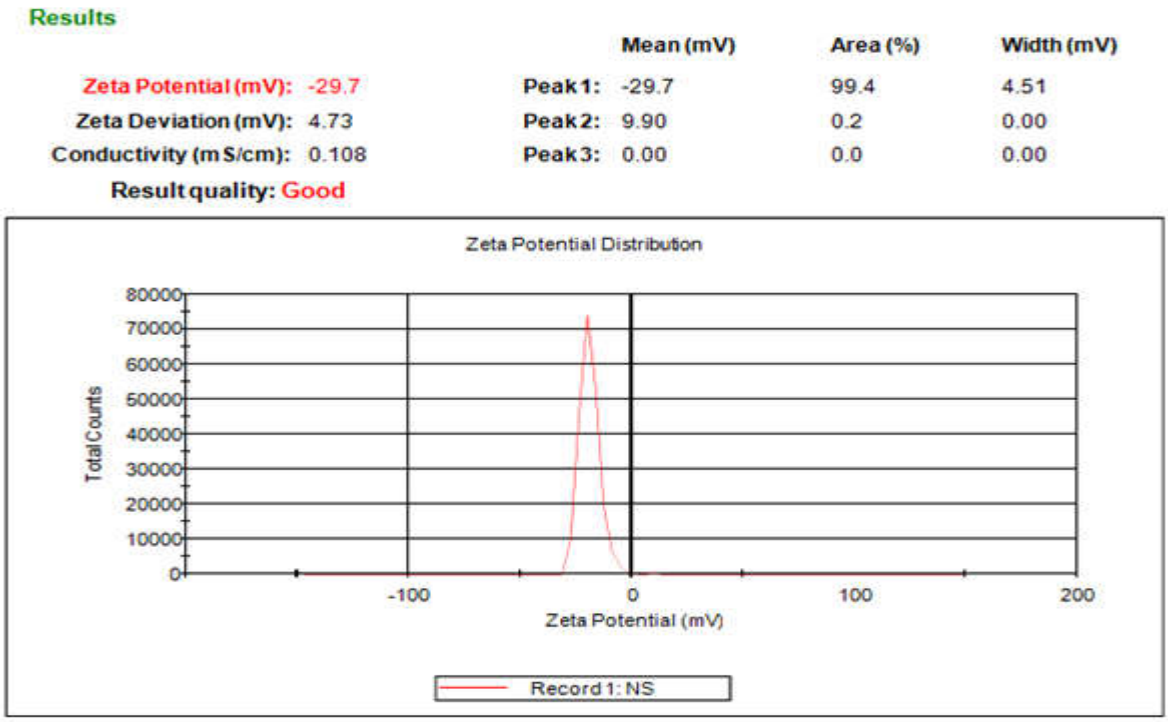

Figure 6: Zeta potential

Table 14: Zeta potential

S. No	Formulation	Zeta potential
1.	Nanosponges	- 29.7 mV

Table 15: Entrapment efficacy

S. No.	Formulations	Entrapment efficacy (Predicted value)	Entrapment efficacy (Actualvalue)
1.	Nanosponges	94.7 %	95.3 %

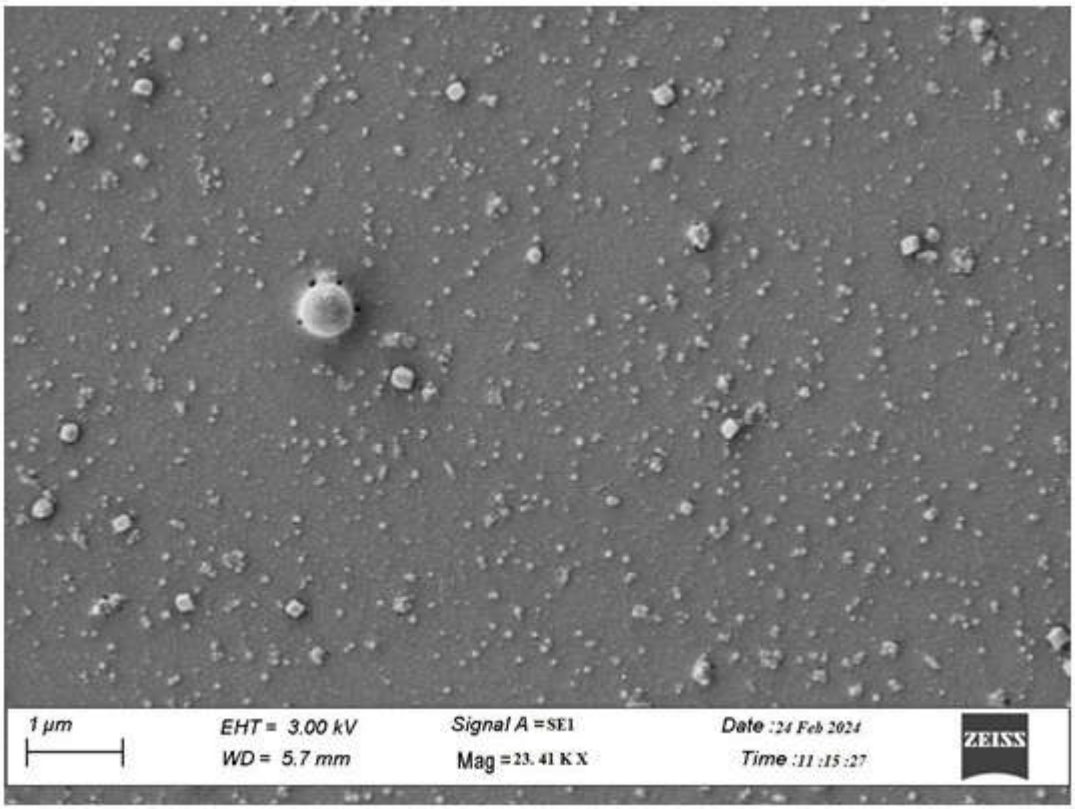

Figure 7: Scanning electron microscope (SEM)

Table 16: Physical appearance

S. No	Parameter	Result
1.	Colour	White
2.	Odour	Odourless
3.	Appearance	Transparent
4.	Homogeneity	Homogeneous

Table 17: Viscosity, pH and Spreadability (g.cm/s)

S. No	Formulation	Viscosity (cps)	pH	Spreadability (g.cm/s)
1.	Gel	6128±0.53	6.1	11.14

Table 18: Release kinetics study of optimized formulation

Time (Hr)	cumulative % s drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	Log cumulative %drug released
0	0	100	0.000	2.000	0.000	0.000
2	24.14	75.86	1.414	1.880	0.301	1.383
4	32.08	67.92	2.000	1.832	0.602	1.506
6	46.63	53.37	2.449	1.727	0.778	1.669
8	58.61	41.39	2.828	1.617	0.903	1.768
10	67.31	32.69	3.162	1.514	1.000	1.828
12	73.65	26.35	3.464	1.421	1.079	1.867
14	85.54	14.46	3.742	1.160	1.146	1.932
16	96.01	3.99	4.000	0.601	1.204	1.982

Table 19: Correlation value (R^2 value)

Formulation	Model	Kinetic parameter values
Nanosponges gel formulation	Zero Order	$R^2 = 0.979$
	First Order	$R^2 = 0.862$
	Higuchi	$R^2 = 0.970$
	Korsmeyerpeppas	$R^2 = 0.809$

Table 20: Stability Study of optimized formulation (Nanosponges gel)

S. No	Time (Days)	25^0C±2 ^{0}C and 60 ± 5% RH			40^0C±2 ^{0}C and 70 ±5% RH		
		Viscosity (cps)	pH	Drug release (%)	Viscosity (cps)	pH	Drug release (%)
1.	0	6128	6.1	96.01	6128	6.1	96.01
2.	30	6126	6.2	95.97	6311	6.3	96.00
3.	45	6339	6.4	95.95	6309	6.3	95.99
3.	60	6348	6.1	95.97	6308	6.4	95.91
4.	90	6385	6.0	95.94	6302	6.2	95.97

CONCLUSION

In conclusion, the polymeric nanosponges gel formulation containing Beta-sitosterol was successfully developed and optimized using the Box-Behnken design approach. The formulation demonstrated excellent entrapment efficiency, small particle size, and sustained drug release, making it a promising candidate for topical drug delivery applications. The optimized formulation showed stable physical properties, including appropriate viscosity, pH, and spreadability, which are crucial for topical applications. Furthermore, stability studies indicated that the formulation remained effective over time under various storage conditions. These results suggest that the Beta-sitosterol nanosponges gel formulation could offer a viable and efficient method for the controlled release of Beta-sitosterol, improving its therapeutic potential for topical treatments.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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