RESEARCH ARTICLE

Preparation, Evaluation and Optimization of Polymeric Nanoparticles of Eluxadoline for the Treatment of Irritable Bowel Syndrome

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ABSTRACT

Eluxadoline, exhibits potential as an irritable bowel syndrome treatment and management strategy. Eluxadoline, a mu-opioid receptor agonist and delta-opioid receptor antagonist, has shown efficacy in relieving IBS symptoms. However, its applications have been limited due to low water solubility, which causes a low dissolution rate and oral bioavailability. In this study, we aimed to enhance the therapeutic efficacy of eluxadoline by formulating polymeric nanoparticles of eluxadoline. Polymeric nanoparticles of chitosan loaded with eluxadoline were prepared using the ionic gelation method. The formulation parameters including concentration of chitosan, concentration of tripolyphosphate and volume of tripolyphosphate were systematically optimized using a Box-Behnken design to achieve nanoparticles (CNP1-CNP17) with optimal physicochemical properties. The optimized formulation based on particle size of (300.4 nm) with a low PDI value (0.305), zeta potential (41.2mV) and % entrapment efficacy (76.89%). The efficiency of the drug release from optimised formulation was studied in vitro by using a dialysis bag diffusion technique in buffer condition pH 6.8 intestinal condition and showed a sustained release behaviour with maximum drug release 80.23%. Thus, the findings demonstrated that the formulated chitosan-based polymeric nanoparticles present a promising strategy for efficiently delivering eluxadoline via oral administration, offering a potential solution for treating irritable bowel syndrome.

Keywords: Eluxadoline, Chitosan nanoparticles, Box-Behnken Design, Cross linking agent, Intestinal delivery.

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INTRODUCTION

Irritable bowel syndrome (IBS) ranks among the prevalent gastrointestinal disorders globally, affecting approximately 11–15% of the population. Persistent abdominal pain accompanied by alterations in stool frequency constitutes a primary symptom of IBS. The disorder is categorized as mixed or unclassified based on predominant stool patterns, with the former being the most common, accounting for approximately 45–50% of all IBS cases. Effective management of IBS-D poses a challenge, with conventional treatments typically involving anti-diarrheal medications alongside dietary and lifestyle adjustments. IBS-D substantially impacts patients' quality of life, surpassing declines observed in conditions such as gastrointestinal reflux disease, asthma, and even IBS with constipation.[1,2] Additionally, IBS is associated with various comorbidities, including depression, anxiety, fibromyalgia, migraines, and interstitial cystitis.[3] The increased healthcare utilization for IBS-D places a significant financial burden on both society and investors.[4] Eluxadoline, a pharmacological agent, exerts local action with a diverse range of effects, acting as both mu-opioid receptor and kappa opioid receptor agonists, while also functioning as a delta opioid receptor antagonist.[5,6] Despite its notably low oral bioavailability, the US Food and Drug Administration has officially approved its use for treating IBS-D. Eluxadoline's unique pharmacological profile leads to a significant decrease in intestinal motility and a reduced likelihood of drug-induced constipation issues. Studies, including those using animal models, have demonstrated that combining an agonist for the mu-opioid receptor with an antagonist for the delta-opioid receptor enhances therapeutic effects on visceral sensations while minimizing the risk of constipation. These distinguishing characteristics differentiate eluxadoline from peripherally acting mu-opioid receptor agonists such as Loperamide. Eluxadoline for the treatment of IBS-D is available in tablet form (75 and 100 mg), though capsules and liquid formulations for pediatric use are not commercially accessible.[7,8] Polymeric nanocarrier systems have garnered considerable attention and shown immense potential due to their numerous advantageous properties.[9,10] Nanoencapsulation has proven effective in delivering drugs by enhancing solubility, facilitating sustained release, providing physical protection, preventing chemical degradation, improving pharmacological activity and stability, and mitigating toxicity. Among various polymers utilized in creating drug-loaded polymeric systems, chitosan stands out as one of the most popular choices.[11,12] Chitosan exhibits versatility, offering protective attributes against environmental moisture and allowing precise

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Table 1: Factors and their levels

INDEPENDENT VARIABLE					
S. No	Factors	Unit	Low limit	Medium limit	High limit
1.	Conc of chitosan (X1)	mg	1.0	3.0	3.0
2.	Conc of NaTPP (X2)	mg	0.5	1.0	2.0
3.	Vol of NaTPP (X3)	ml	15	16	17

DEPENDENT VARIABLE		
S. No	Response variables	Level
1.	Particle size in nm (Y1)	Minimum
2.	PDI (Y2)	Maximum
3.	Zeta potential in mV(Y3)	Maximum
4.	Drug entrapment in % (Y4)	Maximum

formulation tailored to specific delivery requirements, including controlled, immediate, or continuous release mechanisms. Additionally, chitosan masks odors and flavors and is recognized for its pH-sensitive nature, demonstrating solubility variations across different pH levels.[13,14] The objective of this study is to enhance the targeted delivery of eluxadoline by encapsulating it within chitosan nanoparticles and to investigate the potential effectiveness of eluxadoline-loaded chitosan nanoparticles in treating irritable bowel syndrome (IBS). Utilizing Box-Behnken Design Expert software, formulations were optimized, taking into account variables such as chitosan concentration (X1), sodium tripolyphosphate concentration (X2), and sodium tripolyphosphate volume (X3). The factors and their levels illustrated in table 1. Subsequently, the optimized eluxadoline-loaded nanoparticles were evaluated for various pharmacological properties and their ability to enhance oral efficacy in combating irritable bowel syndrome.[15]

Table 2: Formulation batch codes and quantities of factors through Box-Behnken design

Batch	Conc. of chitosan (mg) (X1)	Conc. of NaTPP (mg) (X2)	Vol. of NaTPP (ml) (X3)
CNP1	2	2	15
CNP2	1	1.25	17
CNP3	2	1.25	16
CNP4	2	1.25	16
CNP5	2	1.25	16
CNP6	3	1.25	17
CNP7	2	2	17
CNP8	3	2	16
CNP9	3	0.5	16
CNP10	2	0.5	15
CNP11	2	0.5	17
CNP12	2	1.25	16
CNP13	3	1.25	15
CNP14	1	2	16
CNP15	2	1.25	16
CNP16	1	0.5	16
CNP17	1	1.25	15

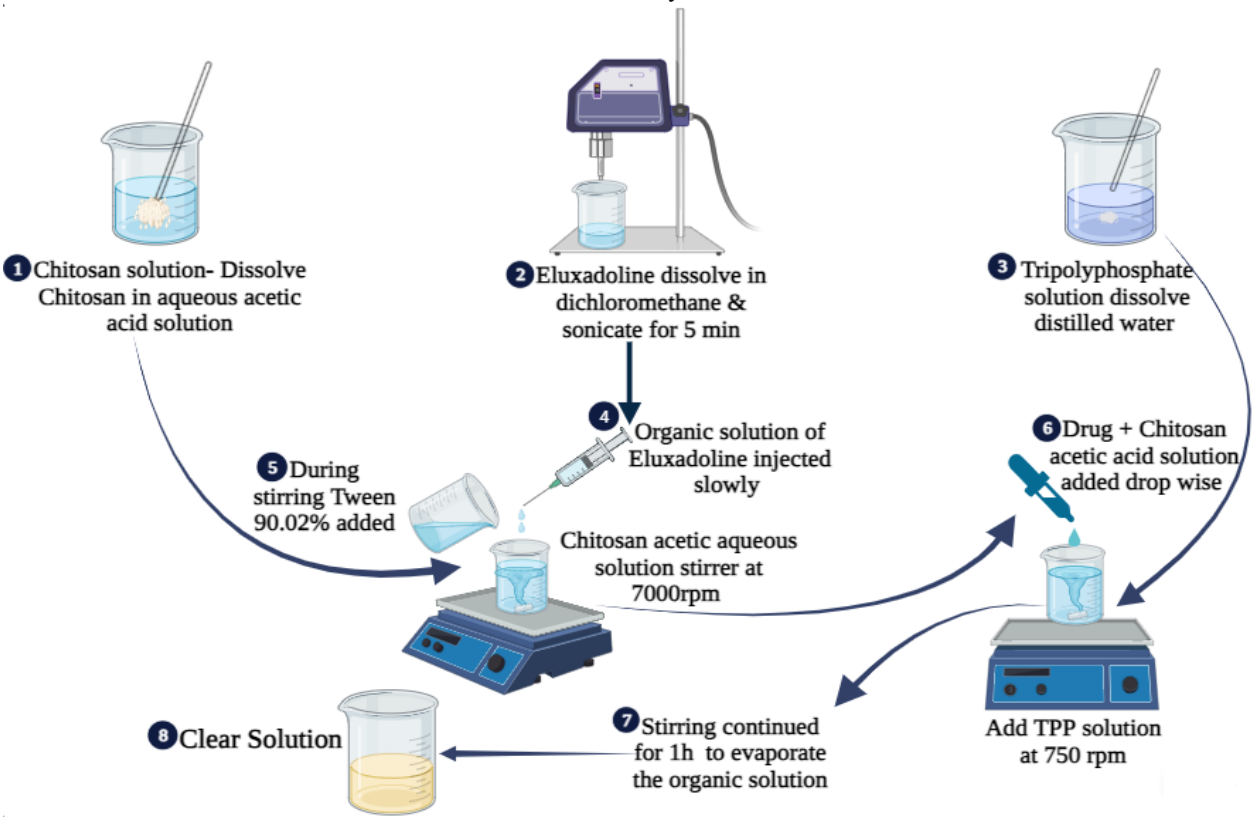

Figure 1: Preparation of eluxadoline loaded nanoparticles by ionic gelation technique

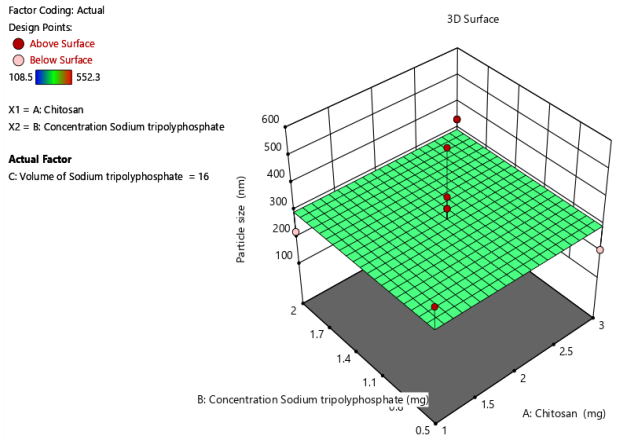

Figure 2: Response surface plot showing the effect of concentration of chitosan and concentration of sodium tripolyphosphate on Particle size of Eluxadoline loaded nanoparticles

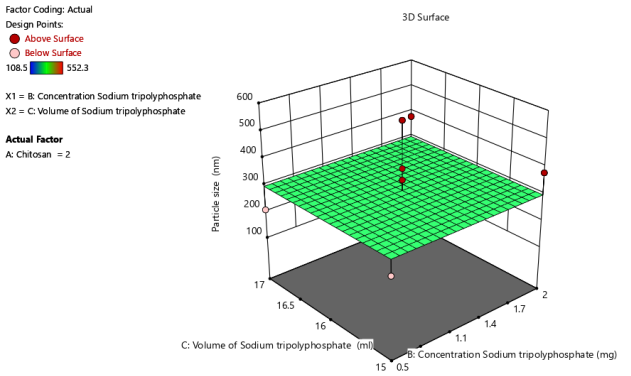

Figure 3: Response surface plot showing the effect of concentration of sodium tripolyphosphate and volume of sodium tripolyphosphate on Particle size of Eluxadoline loaded nanoparticles

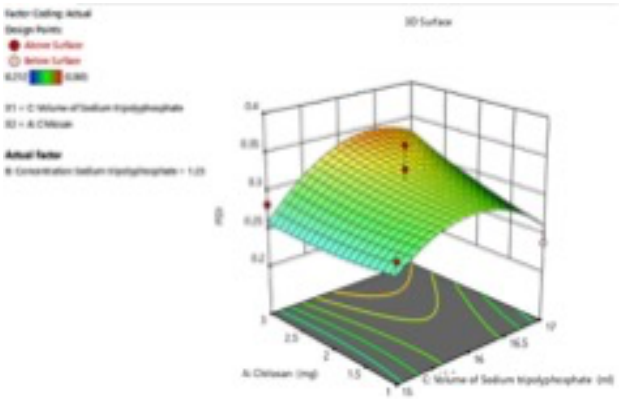

Figure 4: Response surface plot showing the effect of concentration of chitosan and volume of sodium tripolyphosphate on PDI of Eluxadoline loaded nanoparticles

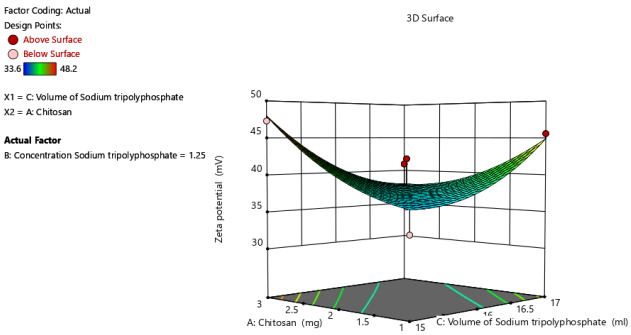

Figure 5: Response surface plot showing the effect of concentration of chitosan and volume of sodium tripolyphosphate on zeta potential of Eluxadoline loaded nanoparticles

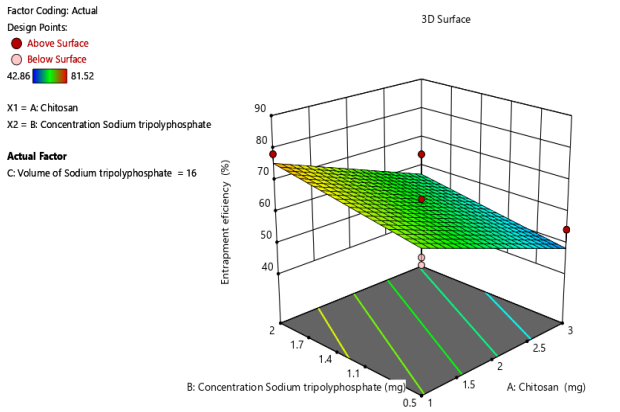

Figure 6: Response surface plot showing the effect of concentration of chitosan and concentration of sodium tripolyphosphate on entrapment efficiency Eluxadoline loaded nanoparticles

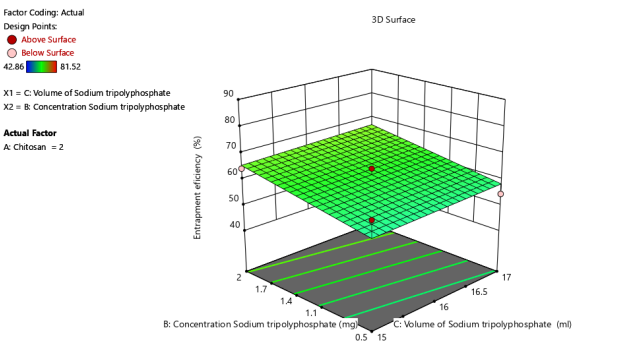

Figure 7: Response surface plot showing the effect of concentration of sodium tripolyphosphate and volume of sodium tripolyphosphate on entrapment efficiency of Eluxadoline loaded nanoparticles

MATERIALS AND METHODS

Materials

Eluxadoline was provided by Torrent Pharmaceuticals Limited, Ahmadabad, India. Chitosan, Sodium tripolyphosphate, Di- chloromethane, Tween 80 were purchased from S.K. Traders, M. P. India., All other chemicals used were of analytical grade.

Table 3: Summary of model fitting and statistical summary

Response	Suggested Model	Suggested P-Value	Suggested F- Value	Lack of Fit	R^2	Adjusted R^2	Predicted R^2	Adequate precision
Particle size (Y1)	Linear	0.8883	0.3915	-	0.0535	-0.1649	-0.4466	4.8941
Zeta Potential (Y2)	Quadratic	0.2671	1.93	0.2671	0.7514	0.4318	-1.5089	10.5345
PDI(Y3)	Quadratic	0.4010	1.26	0.4010	0.7750	0.4858	-0.9275	4.1556
Drug entrapment (Y4)	Linear	0.4576	1.22	0.4576	-	0.3481	0.1366	4.1411

Table 4: Polynomial equation for response variables.

Response variable	Polynomial equation
Particle size(Y1)	98.66A-1.12B-23.34C
PDI (Y2)	0.0420A -0.0282B-0.0115C
Zeta potential(Y3)	-0.2375A+4.83B-0.0125C
Drug entrapment(Y4)	-7.10A+5.33B+2.57C+3.36AB-1.96AC-6.31BC-0.8888A^2 -5.54 B^2 -6.25C^2

Box–Behnken Design (BBD) Optimization

To optimize eluxadoline-loaded chitosan nanoparticles, a Box–Behnken experimental design was employed using Design-Expert® Software. This design incorporated three factors, each with three levels, namely the concentration of chitosan (X1), the concentration of sodium tripolyphosphate (X2), and the volume of sodium tripolyphosphate (X3). These factors were varied at high, medium, and low levels to create 17 formulations detailed in table 2. The responses analysed included particle size (Y1), polydispersity index (Y2), zeta potential (Y3), and drug entrapment. Moreover, 3D response surface graphs were generated to depict how the specified factors influenced the measured responses. [1,15]

Eluxadoline Loaded Nanoparticles by Ionic Gelation Technique

Chitosan nanoparticles were fabricated through the Ionic gelation method. Initially, a solution of chitosan (ranging from 1.0 to 1.5 mg/ml) in acetic acid (1.5%) was prepared separately. Eluxadoline (10 mg) was dissolved in 8 ml of dichloromethane in a beaker using a bath sonicator for five minutes. To maintain the dichloromethane, the container was sealed during sonication, ensuring a uniform organic solution. Simultaneously, a solution of sodium tripolyphosphate (ranging from 0.5 to 1.5 mg/ml) was prepared in distilled water. Then, the organic solution of Eluxadoline was slowly introduced dropwise into the chitosan acetic acid solution (30 ml) using a syringe (5 ml) under high-speed stirring at 7000 rpm. Tween 90 (0.2% v/v) was incorporated as a stabilizer during stirring, which continued for 1 minute at 7000 rpm. Upon complete rotation, 25 ml of the prepared chitosan acetic acid solution containing the drug was gradually added dropwise into the sodium tripolyphosphate solution (15-17 ml) of varying concentrations using a needle under magnetic stirring conditions (750 rpm) at room temperature for 1 hour. This allowed for the evaporation of the remaining organic solution, resulting in nanoparticle suspension formation through ionic and electrostatic interactions between oppositely charged ions. Subsequently, the suspension underwent purification via centrifugation (20000 rpm, 30 min, 15°C) and freeze-drying to yield a free-flowing powder.[2] The method for preparing the formulation is shown in the figure 1.

Evaluation of Eluxadoline Loaded Nanoparticles

The morphological assessment of the optimized Eluxadoline Loaded Nanoparticles was carried out using Field Emission-Scanning Electron Microscopy (FE-SEM). Additionally, an analysis of mean particle size, polydispersity index, zeta potential, and entrapment efficiency were performed to characterize the properties of the optimized nanoparticles loaded with Eluxadoline.

Determination of particle size, PDI, and Zeta potential of Eluxadoline Loaded Nanoparticles

The Horiba SZ-100 particle size analyser was utilized to analyse the particle size, polydispersity index, and zeta potential of the optimized batches of Eluxadoline Loaded Nanoparticles. Figure 9 presents a graphical depiction of the particle size distribution of the optimized nanoparticles

Table 5: Predicted value and the practically observed value of variables of optimized Eluxadoline loaded nanoparticles.

Components		Quantity	
Conc of Chitosan (X1)		1.20 mg	
Conc of NaTPP (X2)		1.56 mg	
Vol of NaTPP (X3)		15.4ml	
Evaluation parameter	Predicted value	Practically observed value	Relative error
Particle size	297.2	300.4	1.07
PDI	0.316	0.305	3.4
Zeta Potential	36.16	41.2	13.9
Entrapment efficiency	70.48	76.89	9.09

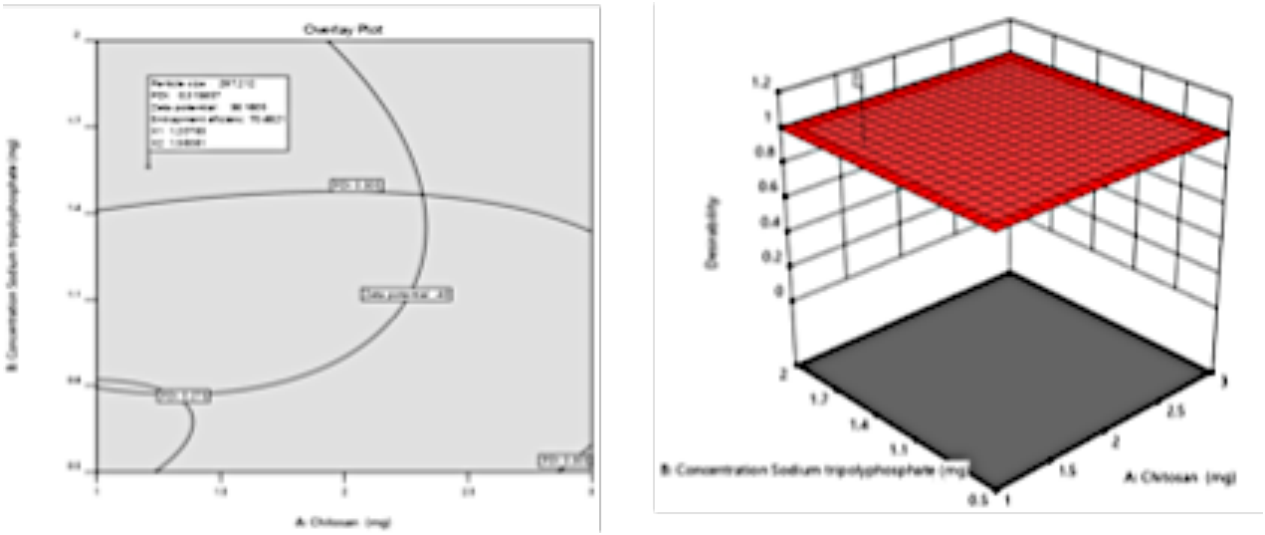

Figure 8: Response surface and contour plot of maximum desirability of Eluxadoline loaded nanoparticles

loaded with Eluxadoline. The particle size was determined employing the dynamic light scattering method, with a scattering angle of 90°, at a temperature of 25°C, and an electrode voltage of 3.3. Furthermore, the zeta potential of the optimized Eluxadoline Loaded Nanoparticles was measured to evaluate the stability of the nanoparticle suspension.

Entrapment efficiency and drug loading

The entrapment efficiency and drug loading within the pores of the Eluxadoline Loaded Nanoparticles were evaluated by dispersing the sample into 5 ml of ethanol and allowing it to stand for 24 hours. Following this, the dispersed solution underwent centrifugation, and the supernatant was analyzed using a UV/VIS spectrophotometer (Shimadzu 1800) at a wavelength of 243 nm. The entrapment efficiency of the drug was calculated using the following equation:

Entrapment efficiency was calculated by the formula

$$\%\text{Entrapment efficiency} = \frac{\text{Actual drug content}}{\text{Theoritical drug content}} \times 100$$

FTIR Studies

FTIR studies were carried out to evaluate potential interactions between the drug and the excipients. Initially, a blank sample of potassium bromide (KBr) was analyzed to eliminate background errors. Subsequently, samples including pure eluxadoline, chitosan, sodium tripolyphosphate, a physical mixture, and the optimized formulation were individually mixed with KBr, physically compressed to form a transparent film, and examined within a wavelength range of 4000–400 cm−1.

Morphology of Eluxadoline Loaded Nanoparticles

The morphological characteristics of the optimized Eluxadoline Loaded Nanoparticles were evaluated using both a polarizing microscope and Field Emission-Scanning Electron Microscopy (FE-SEM). Microscopic examination was conducted using a polarizing microscope (Leica) under an oil immersion lens at 100X magnification, while FE-

Table 6: Developed formulations and observed responses.

Batch	Response 1 Particle size nm	Response 2 PDI	Response 3 Zeta potential mv	Response 4 Entrapment efficiency
CNP1	378.6	0.314	42.7	64.2
CNP2	152.6	0.238	45.6	76.96
CNP3	336.2	0.290	35.7	42.86
CNP4	336.2	0.362	42.2	64.2
CNP5	552.3	0.290	37	58.16
CNP6	378.6	0.314	41	64.2
CNP7	378.6	0.314	41	64.2
CNP8	336.2	0.362	44.6	64.1
CNP9	207.5	0.365	40.8	54.41
CNP10	239.1	0.212	48.2	63.03
CNP11	207.5	0.365	40.8	54.41
CNP12	108.5	0.332	37	58.16
CNP13	177	0.282	47.3	44.63
CNP14	222	0.365	41	78.25
CNP15	378.6	0.314	35.7	54.41
CNP16	378.6	0.314	44.6	64.1
CNP17	284.5	0.282	33.6	81.52

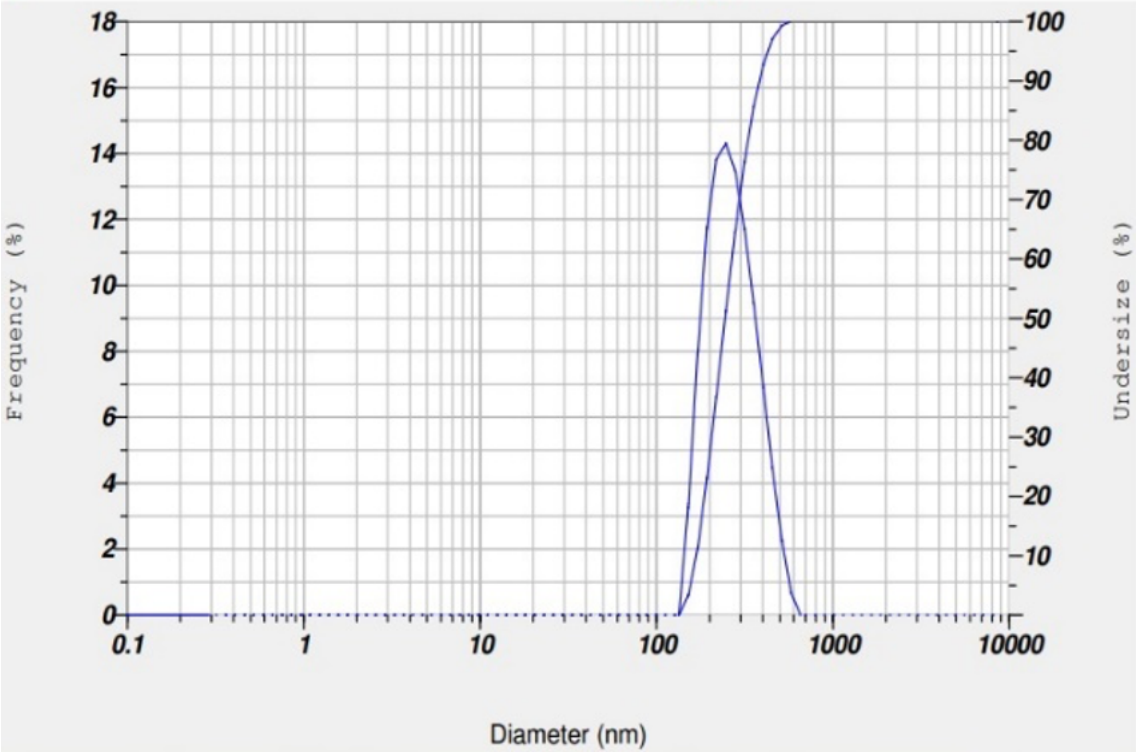

Figure 9: Particle size distribution of Eluxadoline loaded nanoparticles

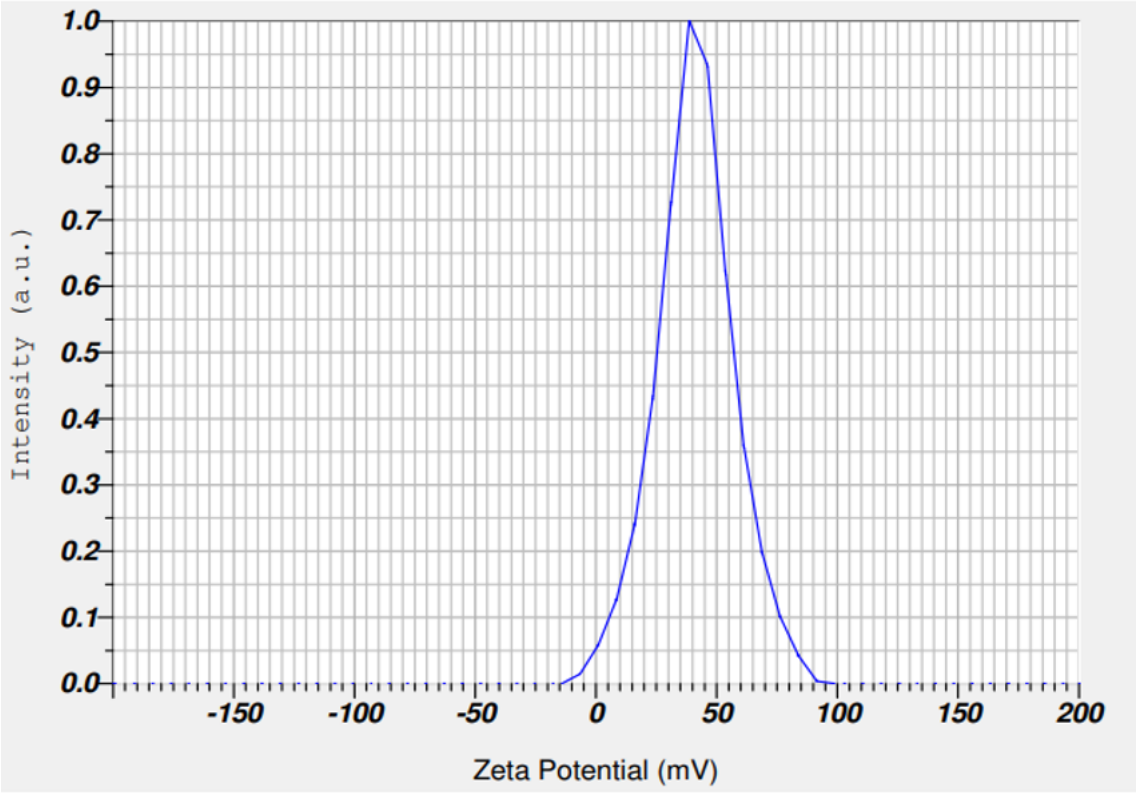

Figure 10: Zeta potential of Eluxadoline loaded nanoparticles

SEM analysis was performed utilizing a Supra 55 Zeiss microscope. The corresponding images from both microscopic and FE-SEM analyses are presented in Figure 17. For FE-SEM observation, the optimized Eluxadoline Loaded Nanoparticles were mounted onto a stub using double-sided adhesive carbon tape. Subsequently, the samples were coated with gold vapors and examined at an accelerated voltage of 16 kV and a magnification of 58.7 KX.

In-vitro drug release

To evaluate the release behavior and mechanism of the optimized formulation, in vitro drug release studies were

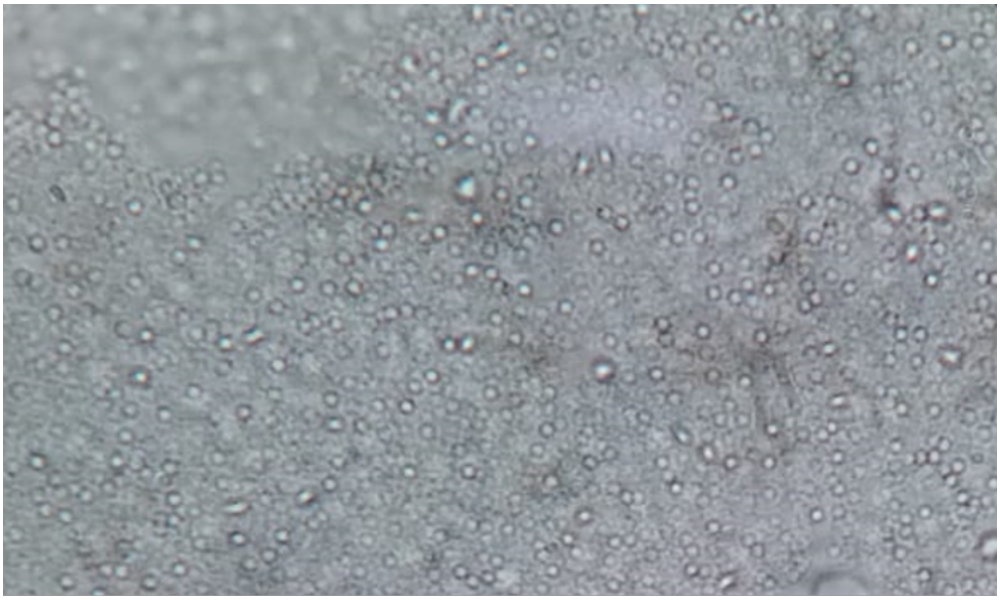

Figure 11: Microscopic image of optimized Eluxadoline loaded nanoparticles

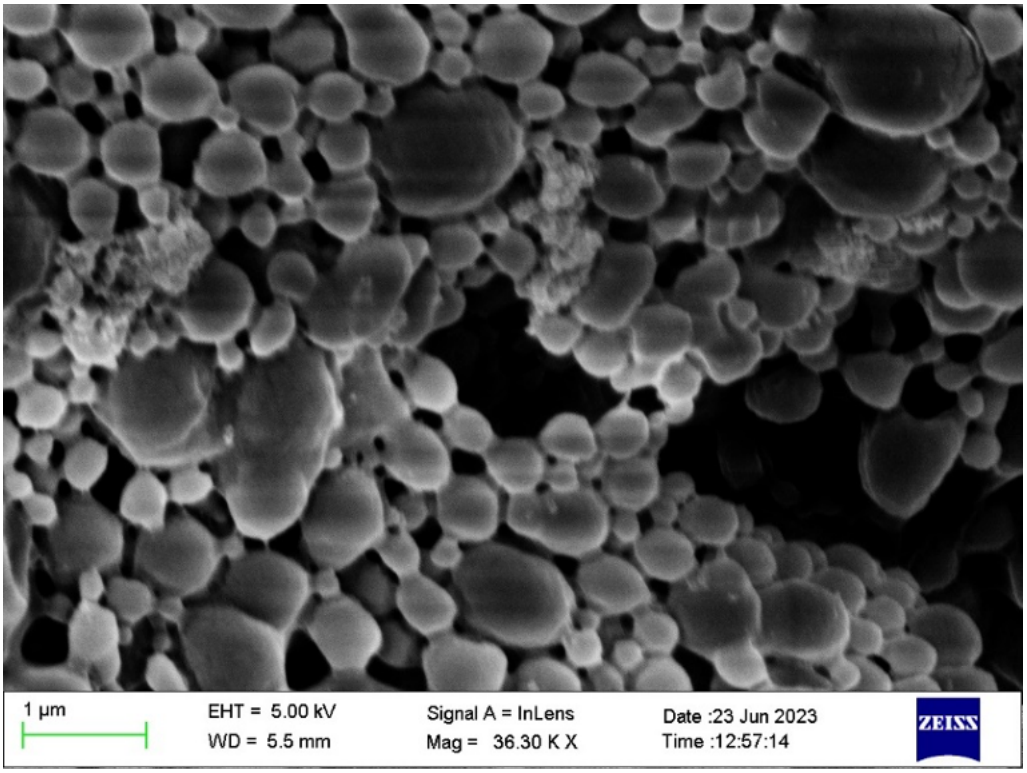

Figure 12: FE-SEM image of optimized Eluxadoline loaded nanoparticles

conducted utilizing the dialysis membrane method. The optimized formulation was enclosed within a dialysis bag, securely sealed at both ends. These bags were immersed in separate beakers containing 200 mL of dissolution media with pH values set at 1.2 and 6.8. The beakers were maintained at a constant temperature of 37.0±0.2°C and stirred at 100 rpm. At predefined intervals, 0.5 mL aliquots were withdrawn from each beaker, and fresh media was replenished to maintain sink conditions. The drug release was quantified by analyzing the samples at 243 nm using a Shimadzu 1700 UV Spectrophotometer.

RESULTS

Eluxadoline-loaded chitosan nanoparticles were prepared using the ionic gelation method, enabling electrostatic interaction between the cationic charge on chitosan and the anionic charge on sodium tripolyphosphate. The optimization of nanoparticle formulation was conducted through the Box–Behnken design approach. Key independent variables, including the concentration of chitosan, concentration of sodium tripolyphosphate, and volume of sodium tripolyphosphate, were fine-tuned based on response variables such as achieving minimal particle size, minimal polydispersity index (PDI), target zeta

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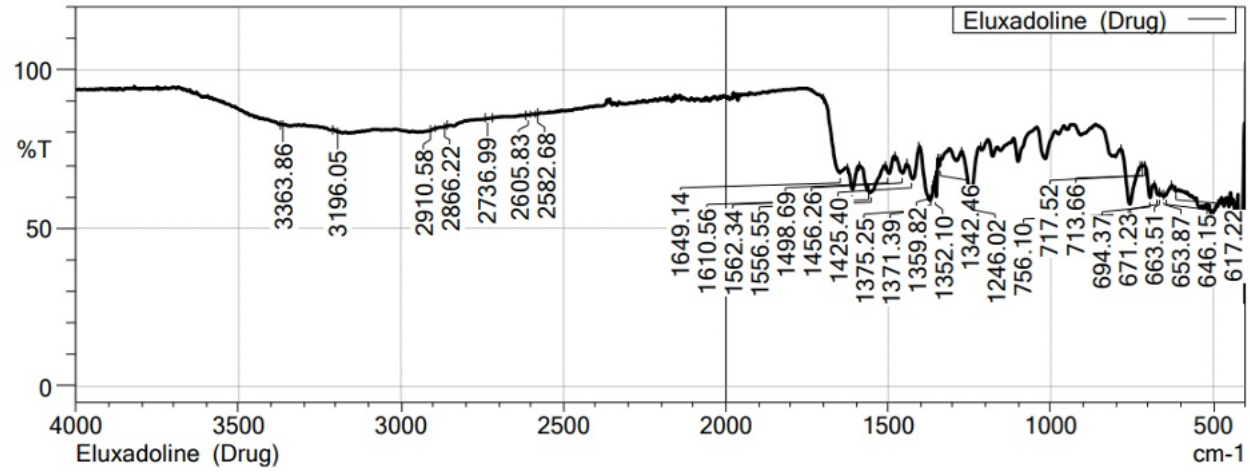


Figure 13: FTIR graph of Eluxadoline

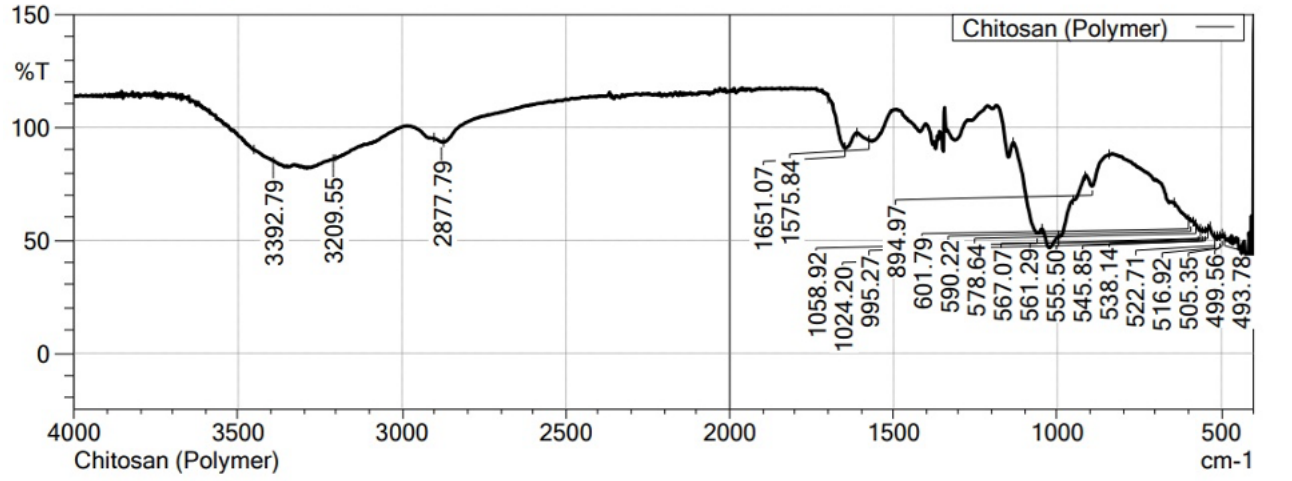


Figure 14: FTIR graph of Chitosan

potential, and optimal entrapment efficiency. In total, 17 formulations were generated for Eluxadoline-loaded chitosan nanoparticles. Figure 2-7 displays a response surface plot illustrating the impact of different factors on the response variable. The Design Expert software provided multiple potential solutions with varying desirability. By scrutinizing desirability contours and response surface plots, the formulation with the highest desirability score (0.991) was identified as the optimized formulation, guiding the subsequent nanoparticle synthesis. Utilizing statistical analysis within the Design Expert software, specific criteria for desired characteristics were established for the final formulation.

The polynomial equation derived from experimental data revealed intricate relationships among the formulation variables. Optimization of independent variables, including chitosan concentration, sodium tripolyphosphate concentration, and sodium tripolyphosphate volume was conducted within the ranges of 1-3 mg, 0.5-2.0 mg, and 15-17 ml, respectively. These optimizations aimed at achieving the desired outcomes for particle size, PDI, zeta potential, and entrapment efficiency.

Summary of model fitting and statistical summary shown in table 3 and the polynomial equation for the optimized Eluxadoline nanoparticles is provided in table 4, summarizing the relationships between the formulation variables.

Prediction of optimized formulation of Eluxadoline loaded nanoparticles

In this investigation, the software forecasted a peak desirability of 0.991 for the ultimate optimized batch, which consisted of 1.20 mg of chitosan, 1.56 mg of sodium tripolyphosphate, and 15.4 ml of sodium tripolyphosphate. Following this prediction, the optimized batch was synthesized and assessed for particle size, polydispersity index (PDI), zeta potential, and entrapment efficiency. The practical findings were subsequently compared with the projected results, as outlined in Table 5. Examining the main effects, considering both the direction and magnitude, provided insights into the relative impact of each factor on the response. The findings revealed that the encapsulation efficiency was at its peak with low levels of chitosan concentration, high levels of sodium tripolyphosphate concentration, and low levels of sodium tripolyphosphate volume. Conversely, the encapsulation efficiency was at its lowest with high levels of chitosan concentration, low

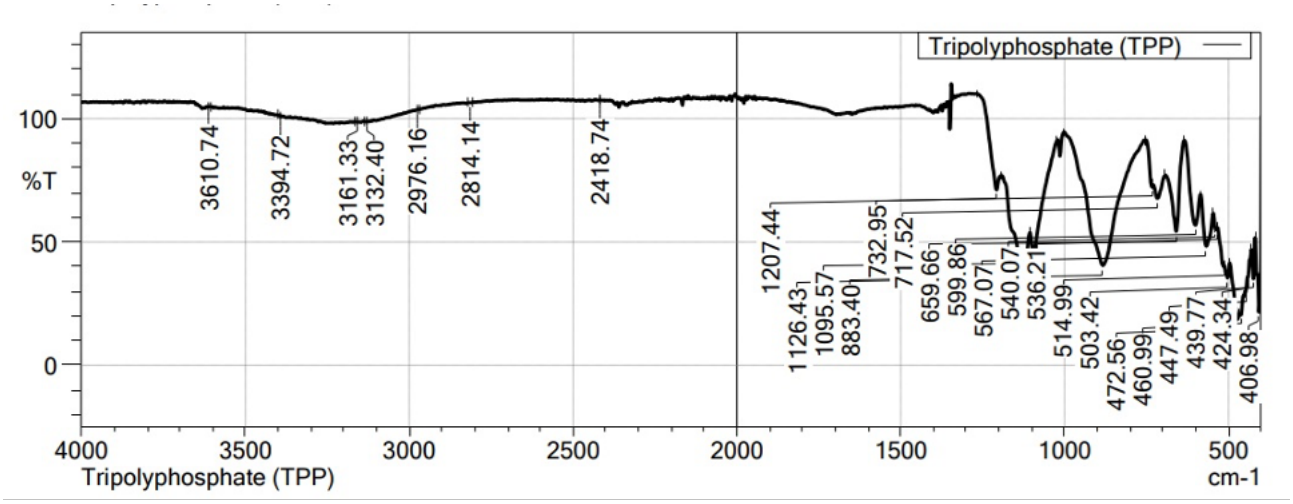


Figure 15: FTIR graph of Tripolyphosphate

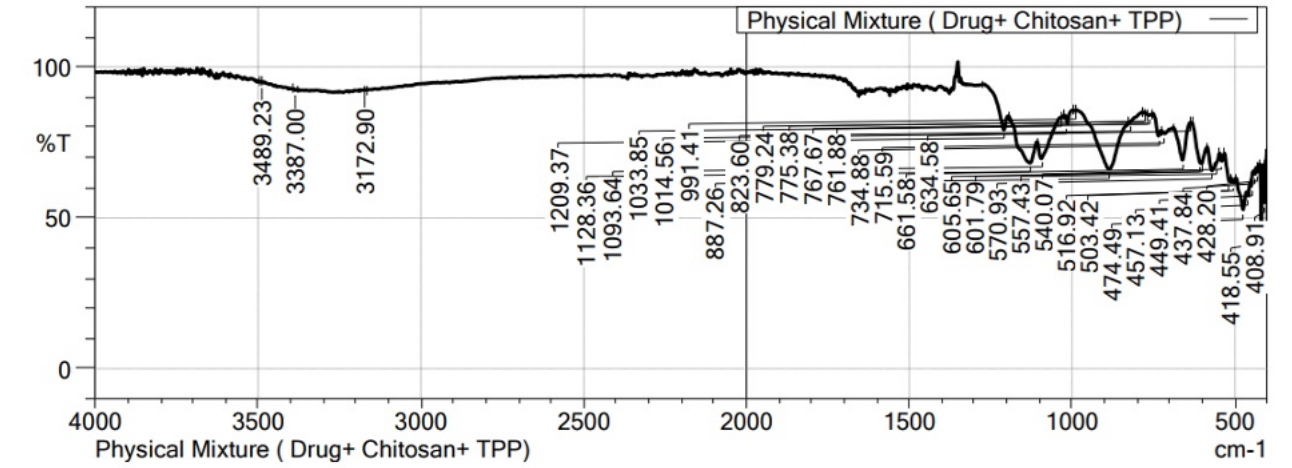


Figure 16: FTIR graph of Physical Mixture (Eluxadoline, Chitosan and Tripolyphosphate)

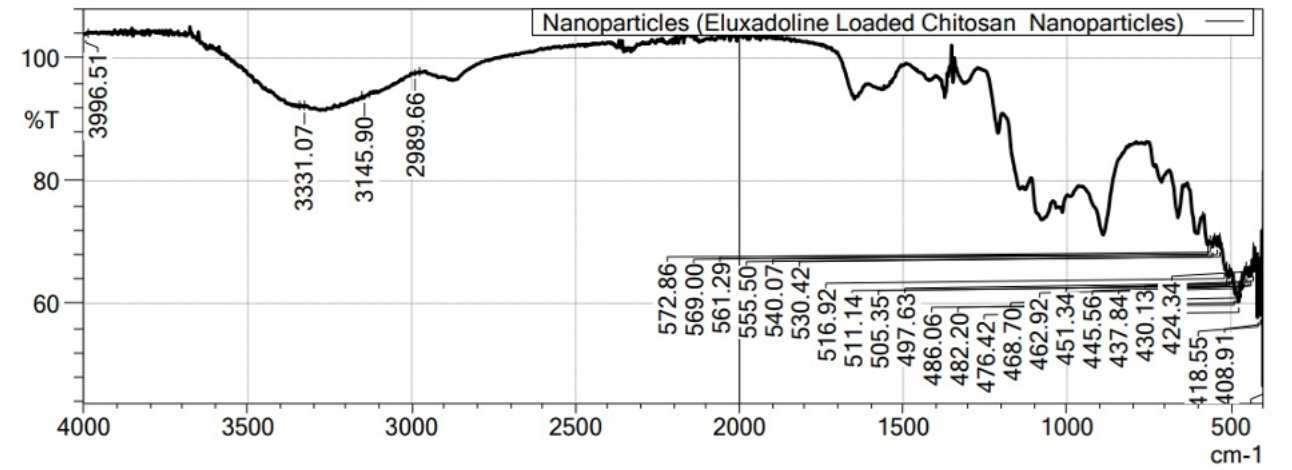


Figure 17: FTIR graph of Chitosan Nanoparticle formulation

levels of sodium tripolyphosphate concentration, and high levels of sodium tripolyphosphate volume. The estimated model can function as a response surface for predicting particle size, PDI, zeta potential, and entrapment efficiency. Figure 8 showcases 3D surface model graphs and contour plots illustrating these relationships.

Particle size, poly dispersibility index and Zeta potential

Particle size, polydispersity index (PDI), and zeta potential are critical factors influencing the interaction and adhesion of nanoparticles during cellular uptake. Smaller particle sizes provide larger surface areas, contributing to reduced toxicity during biodistribution, while the PDI value reflects the uniformity of particle sizes. The optimized Eluxadoline-loaded nanoparticles exhibited a particle size of 300.4 nm

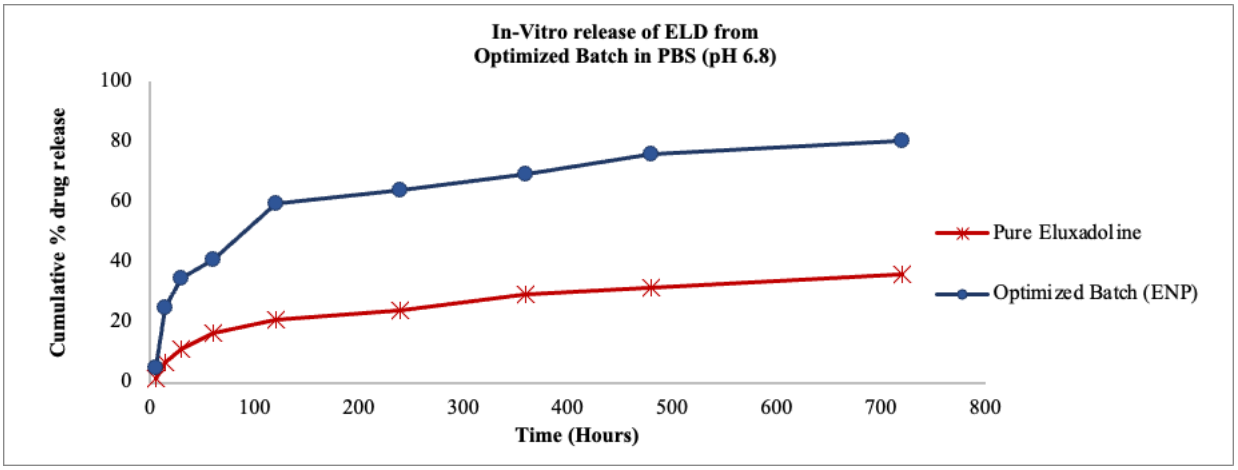


Figure 18: *In Vitro* release of Eluxadoline from Optimized Batch in PBS (pH 6.8)

and a PDI of 0.305, indicating a uniform distribution.

Furthermore, zeta potential serves as an indicator of nanoparticle stability, with the optimized nanoparticles demonstrating a zeta potential of 41.2 mV, confirming their excellent stability. Additionally, the optimized formulation achieved a high encapsulation efficiency of 76.89%, ensuring effective drug loading within the nanoparticles. The graphical representation of particle size and zetapotential of optimized eluxadoline nanoparticles is shown in figure 9 and 10 and observations are recorded in table 6.

Microscopic characteristics of optimized batch of polymeric Eluxadoline nanoparticles

Employing a polarizing microscope (Leica), the morphological features of the optimized nanoparticles were examined, revealing small spherical particles with discernible pores. Furthermore, analysis through FE-SEM exhibited mono-distributed circular structures characteristic of nanoparticles, showcasing particle sizes within the expected range. Microscopic and FE-SEM images of the optimized Eluxadoline-loaded nanoparticles are presented in Figures 11 and 12, respectively.

Drug entrapment and loading of drug

Retaining and incorporating drug molecules within nanoparticles are crucial desirable characteristics. For the final optimized nanoparticles, both the entrapment efficiency and drug loading were found to be 76.89%.

FTIR Studies

A comparative analysis of FTIR spectra was conducted on pure Eluxadoline, Chitosan, Tripolyphosphate, physical mixture and optimized ELD-loaded nanoparticles shown in figure 13 - 17 to ascertain the presence of the encapsulated drug within the nanoparticles. The FTIR spectrum of pure Eluxadoline revealed distinctive peaks corresponding to functional groups at 3117 cm^{-1} (-NH- str), 1696 cm^{-1} (-COOH), 1658 cm^{-1} (-RCONH2-), and 1429 cm^{-1} (-C=C), confirming the purity of the drug. Chitosan spectra exhibited peaks at 3532 cm^{-1} and 3239 cm cm^{-1} (CH aliphatic stretching), characteristic of this polymer. Notably, the characteristic absorption bands of Eluxadoline were diminished or absent in the fingerprint region of the drug, indicating encapsulation within the chitosan polymer. Additionally, the emergence of new peaks in the optimized Chitosan and Tripolyphosphate spectra further validated the encapsulation process

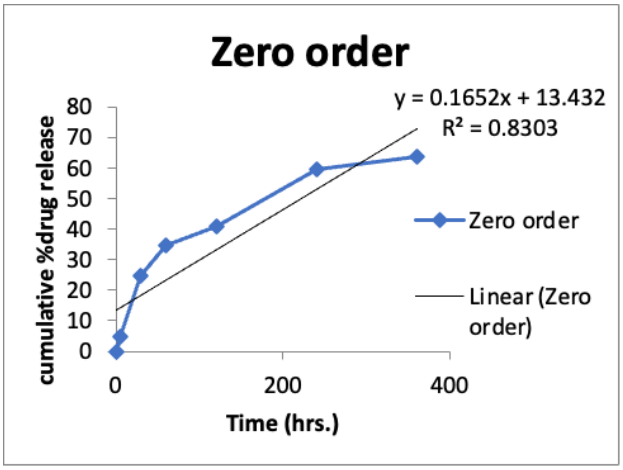
***In-vitro* drug release**

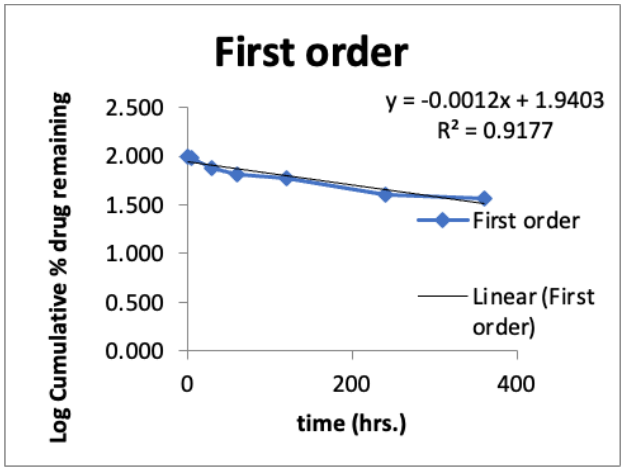
Figure 18 illustrates the absence of drug adsorption onto the surface of the nanoparticles, as indicated by the absence of burst releases of eluxadoline at the beginning of the release profiles at pH 1.2. However, at pH 6.8, a burst release was observed at 2 hours in the studies. The release profile of eluxadoline from nanoparticles at pH 1.2 demonstrated a slower release compared to pure eluxadoline, likely due to chitosan providing protection from the acidic environment. Over a 12-hour period, the release of eluxadoline from nanoparticles in PBS (pH 6.8) was approximately 99%, compared to less than 40% for pure eluxadoline. These findings suggest that eluxadoline was encapsulated within chitosan polymeric nanoparticles and shielded from the highly acidic environment of the stomach. This indicates that the majority of eluxadoline was released once the eluxadoline-loaded nanoparticles reached the small intestine. The enhanced drug release of these nano-sized eluxadoline-loaded nanoparticles was attributed to the greater surface area availability.

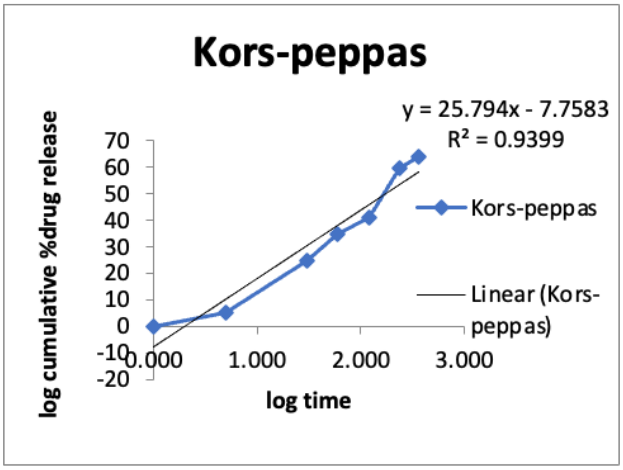
The in-vitro drug release profiles of polymeric microparticles were fitted to zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixon-Crowell model equations. A graph was plotted to analyze the drug release kinetics of the prepared polymeric nanoparticles, as depicted in Figure 19. The regression coefficient ((R2) and release rate constant (k) of the nanoparticles were found to best fit the Higuchi model, with an (R2) value of 0.9718. This model exhibited the highest (R2) value among all release kinetics, indicating an initial burst followed by a continuous release pattern in the formulation.

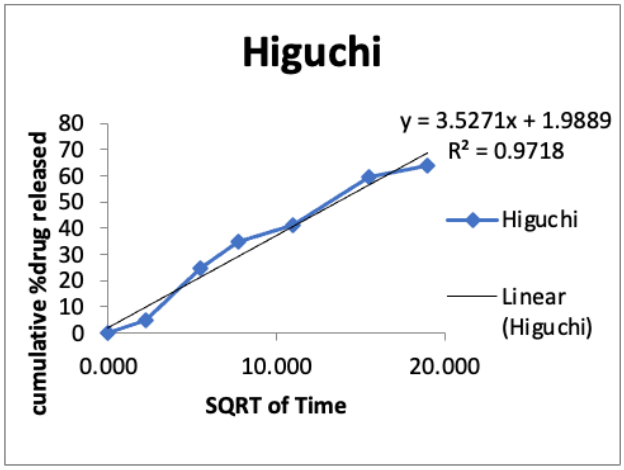
DISCUSSION

In this study, Eluxadoline-loaded nanoparticles (CNP1-CNP17) were prepared using chitosan polymer and sodium tripolyphosphate, and formulations were optimized through Box–Behnken Design software. The optimized nanoparticles exhibited a particle size of 300.4 nm, a PDI of 0.305, a zeta potential of 41.2 mV, and a drug entrapment efficiency of 76.89%. FE-SEM evaluation of the optimized nanoparticles revealed spherical-shaped particles. In vitro









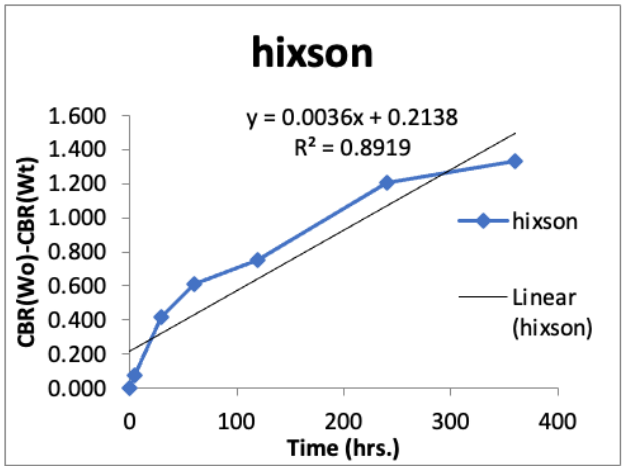


Figure 19: Kinetic modeling of Eluxadoline containing polymeric nanoparticles

release studies indicated that the majority of eluxadoline was released upon reaching the small intestine. ANOVA analysis on encapsulation efficiency was best fitted to a response surface quadratic model, revealing that encapsulation efficiency was highest at a low level of chitosan concentration, a high level of sodium tripolyphosphate concentration, and low levels of sodium tripolyphosphate volume.

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