Journal of Applied Pharmaceutical Research
Volume 13 Issue 4, Year of Publication 2025, Page 102 – 111
DOI: https://doi.org/10.69857/joapr.v13i4.969

Check for updates

Research Article

JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | JOAPR
www.japtronline.com ***ISSN: 2348 – 0335***

FORMULATION DEVELOPMENT AND EVALUATION OF OIL-BASED PLGA NANOCARRIERS OF FLUTICASONE PROPIONATE

Aniruddha Shejwal*, Ganesh B. Shevalkar, Laxmikant B. Borse

Article Information
Received: 17th April 2025
Revised: 8th July 2025
Accepted: 10th August 2025
Published: 31st August 2025

Keywords
Corticosteroid formulation, Fluticasone propionate, Nanocarriers, Oil-based formulation, Topical formulation.

ABSTRACT

Background: Fluticasone Propionate (FP), a potent corticosteroid, suffers from poor aqueous solubility and limited skin permeability, which reduces its clinical efficacy in topical applications. This work aims to overcome these limitations; oil-based poly(lactic-co-glycolic acid) (PLGA) nanocarriers were developed to enhance the solubility, stability, and sustained release of FP. **Methodology:** A 3^2 factorial design was employed to formulate nine batches of PLGA nanocarriers loaded with FP using varying concentrations of PLGA and Capmul MCM. The formulations were evaluated for particle size, zeta potential, drug content, and in vitro drug release. The optimized batch was further characterized using Scanning Electron Microscopy (SEM), Differential Scanning Calorimetry (DSC), and X-Ray Diffraction (XRD). Stability studies were conducted over 30 days under accelerated conditions. **Results and Discussion:** Among all batches, formulation F1 exhibited optimal characteristics, with a particle size of 197.5 nm, a zeta potential of -27.4 mV, and a drug content of 99.85%. The in vitro drug release profile showed a sustained release of 97% over 12 hours. SEM confirmed a spherical morphology with uniform distribution, while DSC and XRD analyses indicated the amorphous dispersion of the drug within the PLGA matrix. The formulation remained physically and chemically stable during the 30-day accelerated stability testing. **Conclusion:** The study demonstrates that oil-based PLGA nanocarriers effectively enhance the solubility and controlled delivery of Fluticasone Propionate. Although *in vivo* validation is pending, the system offers promising potential for improving topical corticosteroid therapy in clinical settings. The novelty of this formulation lies in the strategic combination of Isopropyl Myristate and PLGA to create an oil-based nanocarrier platform, which has not been previously reported for Fluticasone Propionate. This approach enables superior drug encapsulation, enhanced skin permeability, and controlled drug delivery.

INTRODUCTION

Fluticasone propionate (FP), which is a potent anti-inflammatory, immunosuppressive, and antiproliferative medication, is a synthetic trifluorinated topical corticosteroid and is used for the therapy of skin disorders such as atopic dermatitis and psoriasis [1]. The compound known as

*Sandip Foundation's, Sandip Institute of Pharmaceutical Sciences, Mahiravani, Nashik, Maharashtra, India 422213

***For Correspondence:** **aniruddha.shejwal@gmail.com**

fluticasone propionate (Figure 1) is a trifluorinated corticosteroid [2]. It is composed of 6alpha,9-difluoro-11beta,17 alpha-dihydroxy-17 beta-{[(fluoromethyl) sulfanyl] carbonyl}-16-methyl-3-oxoandrosta-1,4-diene with a propionyl substituent at position 17 [3]. It possesses anti-inflammatory, anti-asthmatic, and anti-allergic properties. An anti-allergic agent, an anti-asthmatic drug, an anti-inflammatory agent, a dermatological agent, a bronchodilator, and an adrenergic agent are some of the roles it plays in terms of its medication [4]. A corticosteroid, a steroid ester, an 11-beta-hydroxy steroid, a propanoate ester, a fluorinated steroid, a thioester, and a 3-oxo-Delta(1), Delta(4)-steroid are all the many types of steroids that comprise this substance [5,6]. There is a functional connection between it and fluticasone. The hydride of an androstane is the source of this compound [7]. Fluticasone topical is applied to the skin to alleviate the discomfort caused by skin disorders, such as atopic dermatitis, which may include redness, itching, swelling, and other symptoms. It is a corticosteroid, often referred to as a cortisone-like medicine or steroid [8].

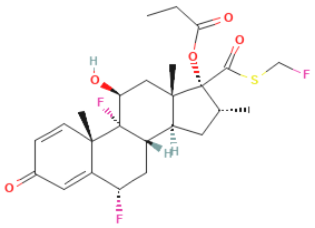

Figure 1: Structure of Fluticasone Propionate

Due to the fact that fluticasone is a medicine that is not very water-soluble, it is possible that the active ingredients will not penetrate the skin very well [9]. To enhance skin penetration and mitigate the undesirable effects of active substances, PLGA oil-based nanocarriers were developed to achieve site-specific drug targeting in the skin, provide sustained and/or regulated drug release, and improve the chemical stability of molecules [10].

Poly (lactic-co-glycolic acid) (PLGA) is a biodegradable polymer that is utilized for the purpose of improving the solubility of drugs that are not suitable for use in water. The PLGA-oil-based nanocarrier is a type of nanoparticle in which the drug is entrapped in the oil base, and the particles are coated with PLGA to enhance the solubility of the drug, potentially leading to an increase in the drug's bioavailability [11]. Unlike in past studies, which mostly used polymeric or water-based nanocarriers for Fluticasone Propionate (FP), the current study suggests a PLGA nanocarrier formulated with oil to tackle the problem of FP's water insolubility and low skin absorption. Since Isopropyl Myristate has a great ability to dissolve many ingredients, including FP, it serves to improve drug absorption and loading efficiency. The IPM-based oil core, encapsulated within a PLGA layer, enables prolonged residence on the skin. Owing to the specific functions of each layer, the FP nanocarriers are more effective for treatment than earlier oil- or water-free versions.

MATERIALS AND METHODS

Materials

Fluticasone propionate was procured from Glenmark Pharmaceuticals Ltd., Sinnar, India. Ethanol, methanol, chloroform, and benzene were purchased from Thermo Fisher Scientific India Pvt. Ltd. Oleic acid, Capmul MCM, Captex 200, Captex 355, and Poloxamer 188 were purchased from Researchlab Fine Chem Industries India. Isopropyl Myristate (IPM) was purchased from Avra Synthesis Pvt. Ltd., and Acetone, Potassium Dihydrogen Phosphate, and Sodium Hydroxide were purchased from Thomas Baker (Chemicals) Pvt. Ltd. All weighing was performed on NABL-calibrated analytical balances. All preparations used Class A glassware.

Methods

Calibration curve of Fluticasone Propionate in methanol and phosphate buffer

A UV-Visible spectrophotometric method was used to create the calibration curve of Fluticasone Propionate (FP) in methanol and phosphate buffer at pH 7.4. A standard stock solution was prepared by dissolving 10 mg of FP in 100 mL of methanol or phosphate buffer, pH 7.4, ensuring complete solubility. From this stock solution, working standard solutions were prepared by diluting 0.4, 0.8, 1.2, 1.6, and 2.0 mL aliquots to 10 mL with the respective solvent, yielding a concentration range of 4-20 µg/mL. The absorbance of these solutions was measured at 240 nm using a UV-Visible spectrophotometer, with methanol or phosphate buffer pH 7.4 as the blank [12,13].

Saturation solubility of Fluticasone propionate in different oils

Saturation solubility of Fluticasone Propionate was determined using different oils (oleic acid, Capmul MCM, Captex 200, Captex 355, isopropyl myristate). The Calibration curve of FP in methanol was used to calculate the concentration of FP in different oil samples from the slope. The analysis was performed in triplicate [14].

Excipient compatibility study

The Excipient compatibility study was performed by preparing a physical mixture of the FP with excipients such as PLGA, Isopropyl myristate, and poloxamer 188, and storing it at 50℃ for 30 days. Then, the samples were analyzed on a UV-Visible spectrophotometer, and the % assay was calculated [15].

Table 1: Excipient Compatibility Study

Ingredients	EC-01	EC-02	EC-03	EC-04
Fluticasone Propionate (mg)	70	70	70	70
Poly(lactic-co-glycolic acid) (mg)	100	-	100	100
Isopropyl Myristate (mg)	100	100	-	100
Poloxamer 188 (mg)	100	100	100	-

Experimental design

A full factorial 3^2 design was employed to investigate the influence of Poly(lactic-co-glycolic acid) (PLGA) (A) and Isopropyl Myristate (IPM) (B) on Particle Size (R1) and Zeta Potential (R2). The independent variables, PLGA & IPM, were examined at three levels each: 160, 200, and 240 mg per batch. Design Expert software (Stat-Ease, version 13.0) was used to conduct the experiment, resulting in nine distinct batches. The results are presented in Tables 2, 3, and 4 [16, 17].

Table 2: 3^2 Factorial Design showing independent factors and Levels.

Independent variables				
Label	Factors	Level (mg)		
		Low (-)	Medium	High (+)
A	Poly(lactic-co-glycolic acid)	160	200	240
B	Isopropyl Myristate	160	200	240
Dependent variables				
Y_1	Particle Size (nm)			
Y_2	Zeta potential (mV)			

Table 3: Factors, levels, and responses taken in 32 complete factorial designs for oil-based PLGA Nanocarriers.

F. Code	(A)	(B)
F1	-1	-1
F2	0	-1
F3	+1	-1
F4	-1	0
F5	0	0
F6	+1	0
F7	-1	+1
F8	0	+1
F9	+1	+1

"-" indicates lower concentration, and "+" indicates higher concentration.

Formulation of FP-PLGA-loaded oil-based Nanocarrier

The PLGA-loaded oil-based nanocarrier was prepared by the standard emulsification-solvent evaporation method [13]. An initial trial was carried out based on a literature review; an organic phase was prepared by dissolving FP, IPM, and PLGA in acetone, and in the main phase, poloxamer 188 was dissolved in water. The water phase was then homogenized at 10,000 rpm, and the acetone phase was slowly added to the water phase, forming an emulsion. The formulation was allowed to mix for 1 hour, and subsequently, it was mixed overnight using an overhead stirrer to ensure that the acetone evaporated completely. Placebo was formulated using a similar methodology. The formulation of the nanocarrier was placed in a freeze dryer (Lyodel, India) to enhance its stability and storage life. The mixture was initially frozen at –40 °C for 12 hours. A vacuum of 0.02 mbar was applied at –20 °C for 24 hours during primary drying. For secondary drying, the material was placed in a drying oven set to 25 °C for an additional 8 hours. After formation, the dry powder was placed in a desiccator until further analysis was required [18].

Table 4: Composition of oil-based PLGA Nanocarriers batches using 3^2 factorial designs.

Ingredients	AF1	AF2	AF3	AF4	AF5	AF6	AF7	AF8	AF9
Fluticasone Propionate (mg)	50	50	50	50	50	50	50	50	50
Poly(lactic-co-glycolic acid) (mg)	160	200	240	160	200	240	160	200	240
Isopropyl Myristate(mg)	160	160	160	200	200	200	240	240	240
Poloxamer 188 (mg)	100	100	100	100	100	100	100	100	100
Acetone (ml)	10	10	10	10	10	10	10	10	10
Water (ml)	100	100	100	100	100	100	100	100	100

Characterization of FP-PLGA-loaded oil-based Nanocarrier

Particle size

The Horiba SZ-100 (Horiba Scientific) was used to measure particle size at 25 °C, with duplicate sets of sizing cuvettes having a constant refractive index, viscosity, and dielectric constant. A dynamic light scattering (DLS) is performed to analyze the particle size. The samples were appropriately diluted in deionized water and then scanned by the instrument [19].

Zeta Potential

At 25℃, the measuring conditions of the refractive index, viscosity, and dielectric constant, and the viscosity constant are as constant as possible, and the Zeta potential was obtained by the Horiba SZ-100 (Horiba Scientific). The samples of the nanocarrier were diluted adequately in deionized water and scanned by the instrument [20].

Drug Content Analysis

Using Methanol as a solvent, the drug content of nanocarriers was determined using a UV-Visible spectrophotometer (Labman Instrument). After that, 100 mL of methanol was dissolved with 5 mg of FP, and the resulting solution was further diluted with 1 mL of the full FP solution to 10 mL. Similarly, the placebo (formulation without the drug) was prepared similarly, and its absorbance was measured at 240 nm using a UV-visible spectrophotometer with methanol as the blank. By using the calibration curve, the concentration of FP was calculated by subtracting the absorbance of the sample solution from the absorbance of the placebo solution [21].

***Ex vivo* drug permeation studies**

The release profile of Fluticasone Propionate (FP) and FP-PLGA nanocarriers was evaluated using the Franz diffusion cell apparatus with ex vivo goat skin to simulate topical application. Freshly excised abdominal goat skin was cleaned, dermal fat removed, and equilibrated in phosphate buffer (pH 7.4) before use. The skin was mounted between the donor and receptor compartments with the stratum corneum facing the donor side. One milliliter of the formulation, containing nanocarriers equivalent to 1 mg of FP, was applied to the skin surface in the donor chamber. The receptor chamber was filled with 20 mL of phosphate buffer (pH 7.4), maintained at 37 °C ± 2 °C, and stirred continuously at 100 rpm to ensure sink conditions. At predetermined time intervals, 1 mL aliquots were withdrawn from the receptor medium and replaced with fresh buffer to maintain constant volume. The samples were centrifuged at 5000 rpm for 10 minutes, and the supernatant was then diluted with methanol to the appropriate concentration. The drug content was quantified using UV-Visible spectrophotometry at the specific λ*max* of FP [22].

Surface morphology by SEM

SEM was used to study the outer shape of three optimal nanocarrier systems. A Quanta Inspect F50 (Hillsboro, OR, USA) with its 1.2 nm resolution FEG performed the SEM analysis. Analysis using a field emission gun operated at 30 kV revealed the morphology of the samples, which had been sputter-coated with a thin gold layer [23].

Differential Scanning Calorimetry (DSC)

The drug within the optimal nanocarriers was analyzed using differential scanning calorimetry tests (DSC, Mettler-Toledo, Switzerland). A DSC analyzer was used to obtain thermograms of nanocarrier systems. A small amount of approximately 1 mg of sample was placed in an aluminum pan followed by a ten-minute temperature adjustment at twenty-five degrees Celsius. Heat scanning was performed between 25 °C and 300°C under a nitrogen gas flow of 20 milliliters per minute. Analysis from the DSC thermometers yielded results in the form of an heat-flow (mW) versus temperature plot [24].

X-ray Diffraction

X-ray diffraction (Rigaku Ultima IV) was performed on the optimized formulation. The sample was mounted in the holder and scanned using the instrument's standard powder parameters. The method enabled researchers to study how the powder exhibited physical properties related to its phase structure and crystalline patterns [25].

Stability study

We studied the stability of the optimized nanocarrier batch under 50℃ heat conditions for one month. The research team tested the formulation for particle size, zeta potential, and drug content after spending one month under analysis [26].

RESULTS & DISCUSSION

Calibration curve of fluticasone propionate in methanol and phosphate buffer

The calibration curve for Fluticasone Propionate (FP) in methanol and phosphate buffer (pH 7.4) exhibited a linear relationship between concentration and absorbance over a range of 4-20 µg/mL. The correlation coefficient (R^2) obtained was close to 1, indicating high accuracy and precision of the UV-Visible spectrophotometric method used. This confirms the reliability of the analytical method for quantifying drugs in subsequent studies, such as determining drug content and in vitro release.

Saturation solubility of Fluticasone propionate in diff. oils

The solubility study revealed significant differences in FP solubility across different oils. Isopropyl Myristate (IPM) demonstrated the highest solubility of FP at 55.28 ± 1.26 mg/mL, followed by Oleic Acid (33.25 ± 0.44 mg/mL), Capmul MCM (26.78 ± 0.27 mg/mL), Captex 355 (19.45 ± 0.64 mg/mL), and Captex 200 (14.18 ± 0.79 mg/mL). The superior solubility in IPM indicates its potential as an effective carrier in the formulation, ensuring better drug loading and efficient delivery. This suggests that using IPM in the nanocarrier system could enhance the solubility of the poorly water-soluble FP.

Excipient compatibility study

To ensure no adverse interactions between FP and the excipients, a stability study was conducted at 50°C for 30 days. The assay values for drug content in different excipient combinations were 101.27% (EC-01), 99.26% (EC-02), 98.37% (EC-03), and 99.19% (EC-04). The minimal variations in drug content indicate no significant degradation or interaction between FP and the excipients, confirming the formulation's stability. This supports the suitability of PLGA, Isopropyl Myristate, and Poloxamer 188 for the nanocarrier formulation.

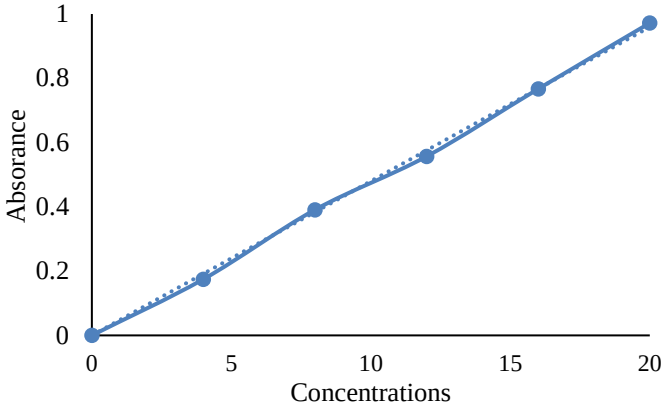

Figure 2: Calibration curve of FP in methanol

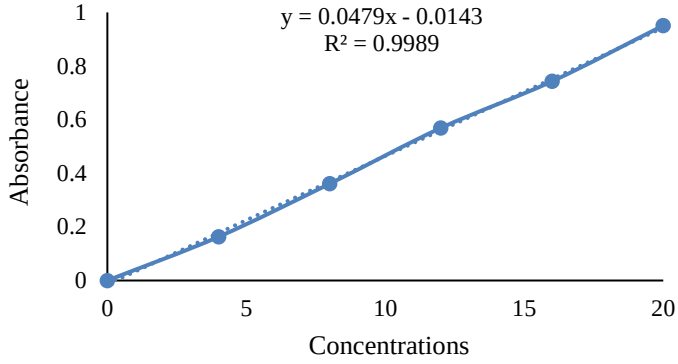

Figure 3. Calibration curve of FP in Phosphate buffer

Table 5: Results of the Solubility of FP in different oils

Oils	Solubility (mg/ml)	± SD
Oleic acid	33.25	0.44
Capmul MCM	26.78	0.27
Captex 200	14.18	0.79
Captex 355	19.45	0.64
Isopropyl Myristate	55.28	1.26

Table 6: Results of Excipient Compatibility

EC Batch	% Assay
EC-01	101.27
EC-02	99.26
EC-03	98.37
EC-04	99.19

Results of particle size, zeta potential, and drug content

The nanocarriers were characterized for their particle size, zeta potential, and drug content across different batches. The results revealed that Batch F1 exhibited the smallest particle size of 197.5 nm and a zeta potential of -27.4 mV, indicating optimal stability and uniform particle distribution. Other batches

displayed particle sizes ranging from 234.7 nm to 527.4 nm, with higher polymer concentration leading to smaller particle sizes. The drug content was consistently high across all batches, ranging from 98.49% to 101.25%, with Batch F1 achieving the highest drug encapsulation of 99.85%. The negative zeta potential across all batches signifies good repulsion between particles, preventing aggregation and enhancing stability.

Table 7: Results of Particle Size, Zeta potential & Drug content

Batch No.	Particle Size (nm)	Zeta Potential (mV)	Drug content (%)
AF1	197.5	-27.4	99.85
AF2	421.7	-15.4	99.46
AF3	365.2	-17.2	98.58
AF4	234.7	-23.2	101.25
AF5	327.8	-20.1	100.13
AF6	337.1	-18.3	98.49
AF7	274.3	-21.5	99.37
AF8	419.4	-16.2	101.22
AF9	527.4	-13.8	99.52

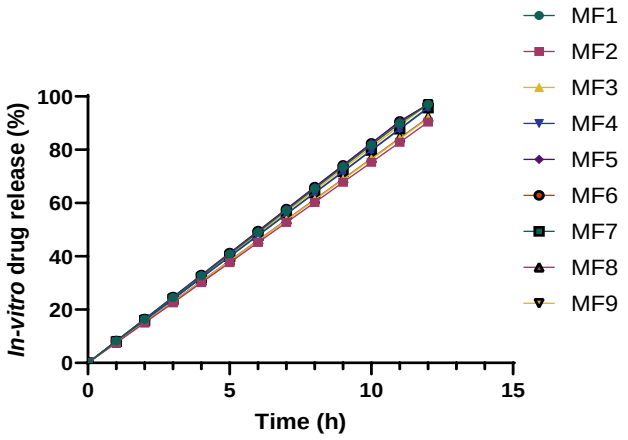

Figure 4: Ex vivo skin permeation profile of FP from PLGA nanocarriers (MF1–MF9)

***Ex vivo* skin permeation study**

The *ex vivo* drug release study is shown in Figure 4. The in-vitro drug release data demonstrated a nearly linear release pattern over 12 hours for all formulations (MF1–MF9), characteristic of zero-order kinetics. Among the tested models, the zero-order model exhibited the best fit ($R^2 > 0.98$), indicating a consistent release rate independent of drug concentration. This sustained-release behavior is desirable for topical corticosteroid therapy, as it helps maintain therapeutic levels over extended periods while minimizing the need for frequent dosing and local irritation. The release mechanism is likely governed by polymer matrix erosion and diffusion, where the PLGA shell gradually degrades, allowing controlled drug diffusion from the oil-based core. The optimized formulation (MF1) achieved a cumulative release of 97% at 12 hours, confirming its potential as an effective sustained-release topical delivery system for Fluticasone Propionate.

Drug release kinetics

Zero-order, first-order, Higuchi, and Korsmeyer–Peppas models were used to check the release pattern of MF1 in vitro. Among all the models, the zero-order model yielded the best correlation (R^2 = 0.9999), as indicated by the regression equation y = 8.1221x + 0.1612, which is illustrated in Figure 5. This verifies that the drug was released at a constant rate for 12 hours, regardless of the concentration. For topical corticosteroid use, this controlled-release formulation suits patients well because it helps the drug act longer, requires less frequent application, and is less irritating to the skin. The release of fluticasone propionate from PLGA nanocarriers can be best explained as a process involving anomalous transport, which combines both molecular diffusion and polymer breakdown. Initially, the drug travels from the oil phase through the PLGA shell, and as time passes, the polymer slowly breaks down, facilitating additional release. Using these dual mechanisms results in the drug being available for a longer period, which could help in developing lasting topical medicines.

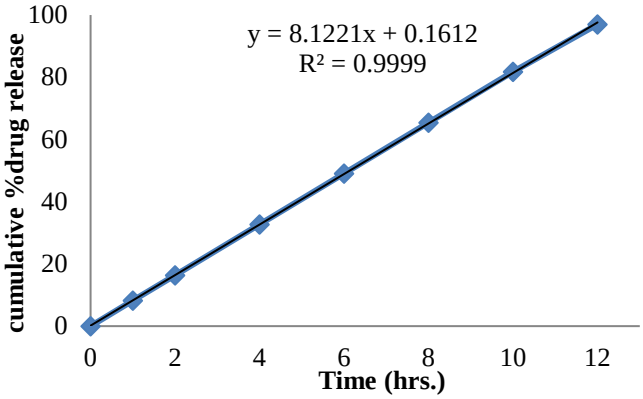

Figure 5: Drug release kinetics best fit model (Zero order)

Prototype F1 was analyzed using SEM, which confirmed smooth, spherical particles with uniform size distribution. Scanning Electron Microscopy (SEM) analysis of Batch F1 revealed smooth, spherical particles with a uniform size distribution, confirming the successful formulation of nanocarriers. The well-defined particle structure supports

efficient encapsulation and controlled drug release. The absence of irregular shapes or large agglomerates further emphasizes the stability and homogeneity of the nanocarrier system (Figure 6).

DSC study

The DSC Thermogram for FP Nanocarrier is given in Figure 7. Differential Scanning Calorimetry (DSC) analysis was conducted to assess the physical state of FP within the nanocarrier system. The absence of sharp endothermic peaks in the thermogram confirmed the amorphous nature of FP in the formulation. This suggests that the drug is molecularly dispersed within the PLGA matrix, which enhances its solubility and bioavailability. The amorphous state is desirable for improved drug dissolution and sustained release properties.

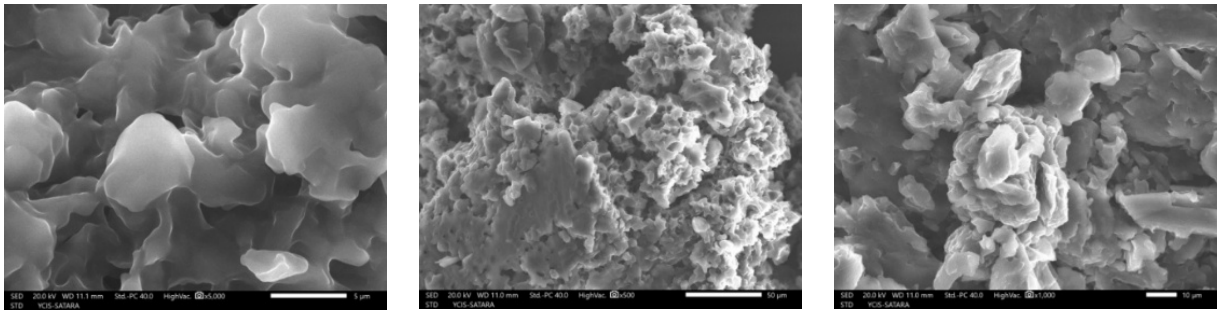

Figure 6: SEM images of Batch F1

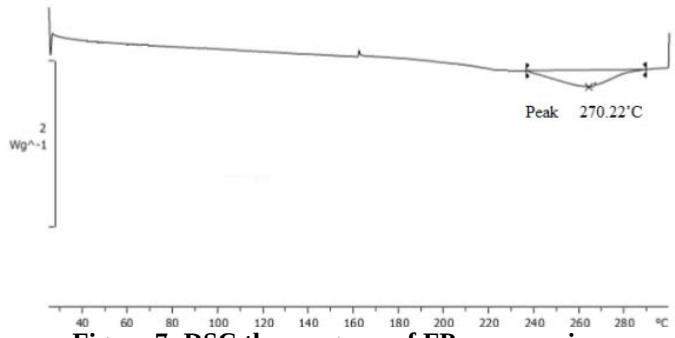

Figure 7: DSC thermogram of FP nanocarrier

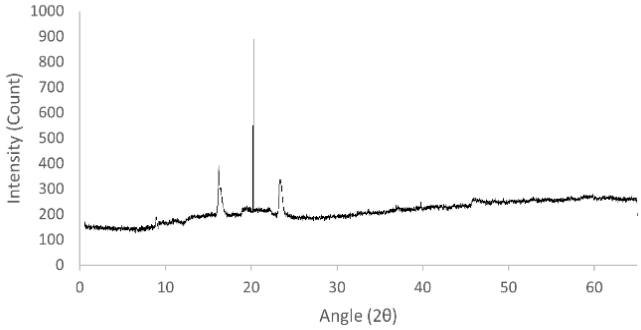

Figure 8: XRD pattern of FP nanocarrier

XRD study

XRD was performed to analyze the produced nanocarriers. The XRD patterns showed no sharp diffraction peaks, suggesting the amorphous nature of FP. X-ray Diffraction (XRD) studies further confirmed the amorphous nature of FP in the optimized nanocarrier system (Figure 8). The lack of sharp diffraction peaks in the XRD spectrum indicates the successful encapsulation of FP within the PLGA polymer, preventing recrystallization. The amorphous nature contributes to enhanced solubility and improved skin penetration, which is crucial for an effective topical formulation.

Stability studies

Stability studies were performed at 50°C for 30 days to evaluate the long-term integrity of the nanocarriers. The particle size increased minimally from 197.5nm to 201.7nm, while the zeta potential remained stable at -26.7 mV. The DC decreased slightly from 99.85% to 99.18% but remained within an acceptable limit. These findings confirm that the formulation maintains its stability under accelerated conditions, making it a viable candidate for pharmaceutical development.

Table 8: Results of the stability study

Parameter	At day 0	After 30 days at 50°C
Particle size (nm)	197.5	201.7
Zeta Potential (mV)	-27.4	-26.7
Drug Content (%)	99.85	99.18

Optimization of the Concentrations of Poly(lactic-co-glycolic acid) and isopropyl myristate using 3^2 Factorial design.

The statistical analysis using ANOVA demonstrated that both PLGA & IPM concentration significantly influenced particle size & zeta potential. The regression models obtained for particle size (Y1) and zeta potential (Y2) had R^2 values of 0.9986 and 0.9478, respectively, indicating strong predictive power of the models (Figure 9). The predicted values closely matched the experimental values, validating the effectiveness of the 3^2 factorial design in optimizing the formulation parameters. This optimization approach ensures reproducibility and enhances the formulation's scalability for further development.

Table 9: ANOVA for the quadratic model for particle size (Y_1)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	84252.95	5	16850.59	413.76	0.0002	significant
A-Polymer Conc	32252.00	1	32252.00	791.94	< 0.0001	
B-Oil Conc	50784.00	1	50784.00	1247.00	< 0.0001	
AB	254.40	1	254.40	6.25	0.0878	
A^2	960.68	1	960.68	23.59	0.0167	
B^2	1.87	1	1.87	0.0459	0.8441	
Residual	122.18	3	40.73			
Cor Total	84375.13	8				

The regression equation obtained for Particle Size is as follows:

$$\boldsymbol{Particle\ size} = \mathbf{329.756} + \mathbf{-73.3167} * \boldsymbol{A} + \mathbf{92} * \boldsymbol{B} + \mathbf{-7.975} * \boldsymbol{AB} + \mathbf{21.9167} * \boldsymbol{A^2} + \mathbf{0.966667} * \boldsymbol{B^2}$$

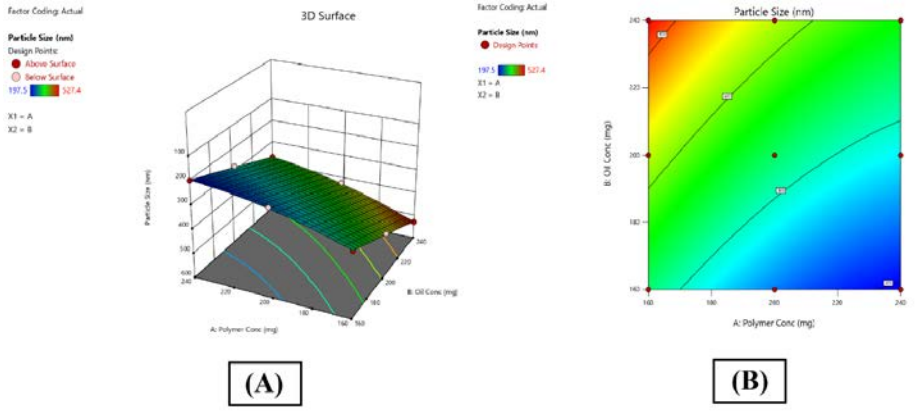

Figure 9: 3D surface plate (A) and Contour plot (B) for the effect of Poly(lactic-co-glycolic acid) and isopropyl myristate on Particle size (Y_1) of oil based PLGA Nanocarriers.

Table 10: ANOVA for Quadratic model for Zeta potential (Y_2)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	139.08	2	69.54	54.48	0.0001	significant
A-Polymer Conc	47.04	1	47.04	36.85	0.0009	
B-Oil Conc	92.04	1	92.04	72.11	0.0001	
Residual	7.66	6	1.28			
Cor Total	146.74	8				

The regression equation obtained for Zeta Potential is as follows: $\boldsymbol{Zeta\ potential} = \mathbf{-19.23} - \mathbf{2.80} \times \boldsymbol{A} + \mathbf{3.92} \times \boldsymbol{B}$

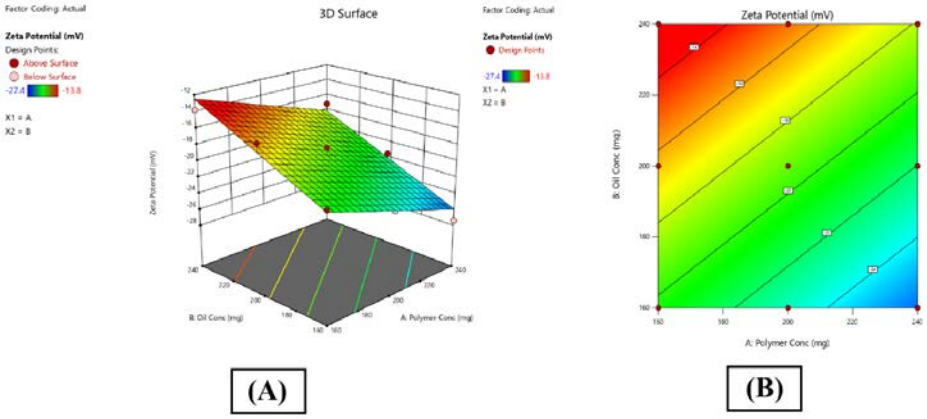

Figure 10: 3D surface plate (A) and Contour plot (B) for the effect of Poly(lactic-co-glycolic acid) and isopropyl myristate on Zeta potential (Y_2) of oil based PLGA Nanocarriers.

Table 11: Summary of the quadratic model results for regression analysis of responses R1 and R2.

Quadratic Model	R^2	Adjusted R^2	Predicted R^2	SD	% CV
Response (Y_1)	0.9986	0.9961	0.9892	6.38	1.85
Response (Y_2)	0.9478	0.9304	0.8619	1.13	5.87

Table 12: The predicted and experimental values of response variables and relative error.

F. Code	Composition	Actual (mg)	Response	Predicted value	Experimental value	Relative Error (%)
AF1	Poly(lactic-co-glycolic acid)	240	Particle size (nm)	196.850	197.5	0.33
	isopropyl myristate	160				
AF1	Poly(lactic-co-glycolic acid)	240	Zeta potential (mV)	-25.950	-27.04	4.20
	Isopropyl myristate	160				

CONCLUSION

The present research work aimed to formulate and evaluate oil-based PLGA nanocarriers loaded with Fluticasone Propionate using a 3^2 factorial design. Among the prepared formulations, F1 exhibited the most promising characteristics in terms of particle size (197.5 nm), zeta potential (-27.4 mV), and drug content (99.85%). The optimized formulation demonstrated sustained in vitro drug release of 97% over a 12-hour period. Surface morphology analysis via SEM confirmed that the nanocarriers were spherical and uniformly distributed. Additionally, DSC and XRD studies indicated that the drug was dispersed in an amorphous form within the polymeric matrix. Stability studies showed that the optimized nanocarrier formulation remained stable for 30 days under accelerated conditions. However, a limitation of the study is the absence of in vivo evaluation to substantiate therapeutic efficacy and skin compatibility. In the current context, where enhancing topical bioavailability and achieving sustained corticosteroid delivery is crucial, the developed PLGA nanocarrier system offers a promising strategy for improving the clinical performance of Fluticasone Propionate.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

Aniruddha Shejwal was responsible for conceptualization, methodology, investigation, and writing the original draft. Ganesh Shevalkar contributed to conceptualization, data curation, formal analysis, validation, writing, review, and editing. Laxmikant Borse provided supervision, resources, and project administration. All authors read and approved the final manuscript & agree to be accountable for all aspects of the work.

REFERENCES

[1] Amasya G, Şengel Türk CT, Badilli U, Tarimci N. Development and Statistical Optimization of Solid Lipid Nanoparticle Formulations of Fluticasone Propionate. *Turkish J. Pharm. Sci.*, **17**, 359–66 (2020) https://doi.org/10.4274/tjps.galenos.2019.27136.

[2] Syed YY. Fluticasone Furoate/Vilanterol: a Review of Its Use in Patients with Asthma. *Drugs*, **75**, 407–18 (2015) https://doi.org/10.1007/s40265-015-0354-5.

[3] Yadav S, Jain V, Magar H, Kumar MV, Warde S, Singh RM. A Novel RP-HPLC Method for Simultaneous Estimation of Vilanterol Trifenatate, Umeclidinium Bromide and Fluticasone Furoate in Inhalation Dry Powder Formulation. *J. Chromatogr. Sci.*, **62**, 761–6 (2024) https://doi.org/10.1093/chromsci/bmad075.

[4] Johnson M. Development of fluticasone propionate and comparison with other inhaled corticosteroids. *J. Allergy Clin. Immunol.*, **101**, S434–9 (1998) https://doi.org/10.1016/S0091-6749(98)70155-1.

[5] Giavina-Bianchi P. Fluticasone furoate nasal spray in the treatment of allergic rhinitis. *Ther. Clin. Risk Manag.*, **4**, 465–72 (2008) https://doi.org/10.2147/TCRM.S1984.

[6] Elsisi R, Helal D, Mekhail G, Abou Hussein D, Osama A. Advancements in Skin Aging Treatment: Exploring Antioxidants and Nanoparticles for Enhanced Skin Permeation. *Arch. Pharm. Sci. Ain Shams Univ.*, **7**, 376–401 (2023) https://doi.org/10.21608/aps.2023.250333.1146.

[7] Tavares Luiz M, Santos Rosa Viegas J, Palma Abriata J, Viegas F, Testa Moura de Carvalho Vicentini F, Lopes Badra Bentley MV, Chorilli M, Maldonado Marchetti J, Tapia-Blácido DR. Design of experiments (DoE) to develop and to optimize nanoparticles as drug delivery systems. *Eur. J. Pharm. Biopharm.*, **165**, 127–48 (2021) https://doi.org/10.1016/j.ejpb.2021.05.011.

[8] Tang C, Niu X, Shi L, Zhu H, Lin G, Xu R. In vivo Pharmacokinetic Drug-Drug Interaction Studies Between Fedratinib and Antifungal Agents Based on a Newly Developed and Validated UPLC/MS-MS Method. *Front. Pharmacol.*, **11**, (2021) https://doi.org/10.3389/fphar.2020.626897.

[9] Ansari MJ, Alnakhli M, Al-Otaibi T, Meanazel O Al, Anwer MK, Ahmed MM, et al. Formulation and evaluation of self-nanoemulsifying drug delivery system of brigatinib: Improvement of solubility, in vitro release, ex-vivo permeation and anticancer activity. *J. Drug Deliv. Sci. Technol.*, **61**, 102204 (2021) https://doi.org/10.1016/j.jddst.2020.102204.

[10] Rane BR, Jain AS, Mane NP, Patil V, Patil MS, Bavaskar KR. Fabrication and Evaluation of Carbocisteine-Loaded Solid Lipid Nanoparticles To Treat Pulmonary Infections. *J. Appl. Pharm. Res.*, **12**, 122–36 (2024) https://doi.org/10.69857/joapr.v12i6.661.

[11] Jojo GM, Kuppusamy G, De A, Karri VVSNR. Formulation and optimization of intranasal nanolipid carriers of pioglitazone for the repurposing in Alzheimer's disease using Box-Behnken design. *Drug Dev. Ind. Pharm.*, **45**, 1061–72 (2019) https://doi.org/10.1080/03639045.2019.1593439.

[12] Pawar SK, Vavia PR. Rice germ oil as multifunctional excipient in preparation of self-microemulsifying drug delivery system (SMEDDS) of tacrolimus. *AAPS PharmSciTech*, **13**, 254–61 (2012) https://doi.org/10.1208/s12249-011-9748-1.

[13] Elmowafy M, Al-Sanea MM. Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. *Saudi Pharm. J.*, **29**, 999–1012 (2021) https://doi.org/10.1016/j.jsps.2021.07.015.

[14] Tamjidi F, Shahedi M, Varshosaz J, Nasirpour A. Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. *Innov. Food Sci. Emerg. Technol.*, **19**, 29–43 (2013) https://doi.org/10.1016/j.ifset.2013.03.002.

[15] Leng D, Thanki K, Fattal E, Foged C, Yang M. Engineering of budesonide-loaded lipid-polymer hybrid nanoparticles using a quality-by-design approach. *Int. J. Pharm.*, **548**, 740–6 (2018) https://doi.org/10.1016/j.ijpharm.2017.08.094.

[16] Hemnani N, Suresh PK. Fabrication and study of release kinetics of moxifloxacin and dexamethasone loaded nanostructured lipid carrier system for ocular drug delivery. *J. Appl. Pharm. Res.*, **13**, 141–53 (2025) https://doi.org/10.69857/joapr.v13i3.1162.

[17] Yin J, Hou Y, Song X, Wang P, Li Y. Cholate-modified polymer-lipid hybrid nanoparticles for oral delivery of quercetin to potentiate the antileukemic effect. *Int. J. Nanomedicine*, **14**, 4045–57 (2019) https://doi.org/10.2147/IJN.S210057.

[18] Pawar MA, Shevalkar GB, Vavia PR. Design and Development of Gastro-retentive Drug Delivery System for Trazodone Hydrochloride: a Promising Alternative to Innovator's Controlled-Release Tablet. *AAPS PharmSciTech*, **23**, 251 (2022) https://doi.org/10.1208/s12249-022-02404-8.

[19] Shevalkar G, Pawar M, Vavia P. Nanostructured Lipid Carriers (NLCs) of Lumefantrine with Enhanced Permeation. *J. Pharm. Innov.*, **17**, 1221–34 (2022) https://doi.org/10.1007/s12247-021-09590-1.

[20] Thete R, Shevalkar G, Borse L. Development of Nanostructured Lipid Carriers for Donepezil Hydrochloride Effective Nose to Brain Delivery. *Biosci. Biotechnol. Res. Asia*, **21**, 1145–56 (2024) https://doi.org/10.13005/bbra/3293.

[21] Darandale SS, Shevalkar GB, Vavia PR. Effect of Lipid Composition in Propofol Formulations: Decisive Component in Reducing the Free Propofol Content and Improving Pharmacodynamic Profiles. *AAPS PharmSciTech*, **18**, 441–50 (2017) https://doi.org/10.1208/s12249-016-0524-0.

[22] Shevalkar G, Vavia P. Solidified nanostructured lipid carrier (S-NLC) for enhancing the oral bioavailability of ezetimibe. *J. Drug Deliv. Sci. Technol.*, **53**, 101211 (2019) https://doi.org/10.1016/j.jddst.2019.101211.

[23] Das S, Chaudhury A. Recent Advances in Lipid Nanoparticle Formulations with Solid Matrix for Oral Drug Delivery. *AAPS PharmSciTech*, **12**, 62–76 (2011) https://doi.org/10.1208/s12249-010-9563-0.

[24] Nunse D, Shevalkar GB, Borse L. Innovative Polymeric Micelles with In-Situ Gelation for Enhanced Ocular Delivery of Ketoconazole. *J. Pharm. Innov.*, **20**, 1–12 (2025) https://doi.org/10.1007/s12247-024-09915-w.

[25] Shevalkar G, Borse L. Self-microemulsifying drug delivery system (SMEDDS) for oral delivery of zafirlukast: Design, formulation, and pharmacokinetic evaluation. *J. Drug Deliv. Sci. Technol.*, **101**, 106298 (2024) https://doi.org/10.1016/j.jddst.2024.106298.

[26] Shevalkar G, Pai R, Vavia P. Nanostructured Lipid Carrier of Propofol: a Promising Alternative to Marketed Soybean Oil–Based Nanoemulsion. *AAPS PharmSciTech*, **20**, 201 (2019) https://doi.org/10.1208/s12249-019-1408-x.