

RESEARCH ARTICLE

FORMULATION, CHARACTERIZATION AND STABILITY ASSESSMENT OF FENOPROFEN CALCIUM-LOADED EUDRAGIT RL100 POLYMERIC NANOPARTICLES

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ABSTRACT: Objective: The objective of this work was to design, prepare and evaluate the stability of fenopropfen calcium loaded polymeric nanoparticles with Eudragit RL100. **Methods:** Nine formulations (F1 to F9) were made by the solvent displacement method using 100 mg fenopropfen calcium, different quantities of Eudragit RL100 (100–300 mg) and PVA (1–3% w/v). The particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug loading, percentage yield and *in-vitro* drug release were evaluated as the qualities of formulations. Drug–excipient compatibility was evaluated by FTIR spectroscopy, particle morphology by SEM and the stability was determined under refrigerated, room temperature and accelerated conditions for a period of three months. **Results:** Particle size ranged from 168.54 to 265.48 nm, PDI from 0.215 to 0.302, and zeta potential from +18.62 to +30.18 mV. The efficiencies of entrapment were between 68.45% and 88.64% and drug loading ranged from 17.32% to 31.24%. Formulation F6 was selected as the optimized batch, exhibiting a particle size of 198.72 ± 3.15 nm, PDI of 0.215 ± 0.007 , zeta potential of $+25.83 \pm 0.74$ mV, entrapment efficiency of $82.16 \pm 1.26\%$, drug loading of $20.35 \pm 0.43\%$, and percentage yield of $83.28 \pm 1.35\%$. Drug release reached $92.85 \pm 1.35\%$ at 24 hours. FTIR indicated that there were no significant changes in the spectra, and SEM revealed a major amount of spherical particles with some aggregation. Other conditions failed to maintain the physicochemical characteristics as well as refrigerated storage. **Conclusion:** The successful formulation of Eudragit RL100 nanoparticles along with the desirable overall properties and sustained release of F6 was observed. The long-term stability and pharmaceutical performance should be determined in further studies.

Keywords: Fenopropfen calcium, Eudragit RL100, Polymeric nanoparticles, PVA; Drug release, stability.

I. INTRODUCTION

Fenopropfen calcium is a non-steroidal anti-inflammatory drug (NSAID) which belongs to a group of pain relievers that relieve inflammation and pain [1]. It is a member of the propionic acid derivatives and its therapeutic effect is primarily due to the inhibition of enzymes of the cyclooxygenase pathway responsible for prostaglandin synthesis. The drug has beneficial anti-inflammatory activity but its physiochemical properties must be taken into account to develop an appropriate drug delivery system [2]. The present study indicated that fenopropfen calcium was poorly soluble in water, but was soluble in methanol. This was considered when formulating with a solvent system was chosen. Polymeric nano particles can be used to encapsulate the drug in a polymeric matrix and study drug release pattern. Their properties are influenced by the type of polymer, the concentration of stabilizer and the preparation conditions [3]. Therefore, parameters like particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug loading and *in-vitro* drug release should be carefully evaluated in

developing an appropriate nanoparticle formulation. These attributes aid in the comparison of various formulations and in selecting a formulation with the appropriate overall performance [4].

Eudragit RL100 was used as a polymeric carrier for fenopropfen calcium and polyvinyl alcohol (PVA) was used as a stabilizer in this study. The organic solvent system used was acetone/methanol (3:1). The preparation of the nanoparticles was carried out using the solvent displacement method, where the organic phase, which is a mix of drug and polymer, was poured into the aqueous phase containing PVA solution while stirring [5]. The drug concentration was fixed and nine different formulations (F1–F9) were manufactured by changing the amount of Eudragit RL100 and the concentration of PVA. With this approach, the formulations could be compared in the chosen preparation conditions [6]. The obtained nanoparticles were analyzed by various methods in order to find out their physical and pharmaceutical characteristics. The compatibility of fenopropfen calcium with selected excipients was examined by using FTIR spectroscopy.

Particle size, PDI, ζ -potential, EE, drug loading and percentage yield were determined, and in-vitro drug release was investigated to see the different release profile of the formulations. The morphology of the selected formulation was also studied using scanning electron microscopy (SEM) [7]. Stability was also deemed to be an important part of the investigation, in addition to formulation development and characterization [8]. The optimised nanoparticles were kept in various conditions, and the changes in the measured characteristics of these nanoparticles were monitored over the period of the study. This evaluation was used to assess the stability of the formulation during storage with regard to its physicochemical properties [9].

The present study was designed to prepare and test fenopropfen calcium loaded polymeric nanoparticles of eudragit RL100, using PVA as a stabilizer. The primary aim was to evaluate the compatibility of the drug(s) with the excipients, compare the nine formulations, determine the best formulation based on all of its characteristics, study the drug release profile of the optimized formulation and analyse the surface morphology and stability of the optimized formulation under various storage conditions.

2. MATERIALS AND METHODS

2.1 Materials

Fenopropfen calcium salt dihydrate was purchased from Tokyo Chemical Industry Co., Ltd. (TCI), Japan. The polymeric carrier used was Eudragit RL100 which was purchased from Rohm Pharma, Germany. The polyvinyl alcohol (PVA) was purchased as a stabilizer, while the acetone and methanol were purchased as organic solvents all from Sigma-Aldrich, Mumbai, India. Acetone:Methanol was kept at a ratio of 3:1. The drug and excipients were used in the preparation and evaluation of Fenopropfen calcium loaded polymeric nanoparticles in experimental formulation plan.

2.2 Preformulation Studies

The physical and chemical properties of fenopropfen calcium were investigated prior to formulation development (preformulation studies). The physical appearance, identification, water content, assay and related substances were assessed as per the original experimental protocol. Solubility was also studied to select the solvents system for preparation of nanoparticles [10]. A calibration curve of fenopropfen calcium was prepared using solutions with concentrations ranging from 5 to 30 $\mu\text{g/mL}$. Absorbance values were used to construct a plot of drug concentration vs. absorbance to use for quantitative analysis [11].

2.3 Drug–Excipient Compatibility Study

Routine Fourier Transform Infrared (FTIR) analysis was used to determine drug–excipient compatibility. The calcium salt of fenopropfen and the physical mixture of fenopropfen with the other ingredients (Eudragit RL100, PVA) were analysed. The physical mixtures were obtained by mixing the drug with the excipients in the appropriate ratios [12].

To analyze the composition of the samples using FTIR, powdered samples were mixed with potassium bromide (KBr) and pressed to obtain transparent specimens. The spectra were taken in the range 4000 – 400 cm^{-1} .

The characteristic absorption bands of the pure drug were compared with those of the excipients and physical mixtures to detect any shift in the peak position, peak intensity or appearance. This comparison was made to evaluate the spectral changes that can be detected with the components that were selected in the formulation [13].

2.4 Preparation of Fenopropfen Calcium-Loaded Polymeric Nanoparticles

Polymeric nanoparticles of fenopropfen calcium (FPCN) were prepared by the solvent displacement method in which Eudragit RL100 as polymeric carrier and PVA as stabilizer were used.

2.4.1 Preparation of the organic phase

The fenopropfen calcium (100 mg) and the appropriate amount of Eudragit RL100 were accurately weighed and dissolved in 20 mL of the acetone–methanol solution (3:1). The quantity of Eudragit RL100 was adjusted in a formulation plan in order to ensure a uniform organic phase [14].

2.4.2 Preparation of the aqueous phase

The PVA was dissolved in water to 1%, 2% and 3% w/v solutions. For the formation of the nanoparticles, a volume of 40 mL of the respective PVA solution was used as the receiving phase [15].

2.4.3 Nanoparticle formation

The fenopropfen calcium and Eudragit RL100 were added to the aqueous PVA solution at a rate of 1 mL/min using a 0.22 μm orifice in the organic phase. The aqueous phase was stirred at 1000 rpm under magnetic stirring during the addition. The complete addition of the organic phase followed by stirring for 1 h was used to promote the formation of nanoparticles and achieve a uniform distribution [16].

2.4.4 Sonication and solvent removal

The dispersion of nanoparticles was subsequently sonicated for 2 minutes before removing the solvent. Then the dispersion was heated at 58°C under reduced pressure to evaporate the organic solvents. The resulting dispersion of nanoparticles was collected for additional characterization [17].

2.5 Formulation Design

The fenopropfen calcium content was fixed at 100 mg per formulation, while the amount of Eudragit RL100 and concentration of PVA were varied, to create nine formulations (F1–F9). Eudragit RL100 was used at 100, 200 and 300 mg, whereas PVA was used at concentrations of 1%, 2% and 3%

w/v [18]. The volume of the organic phase was kept constant at 20 mL and the aqueous phase volume was kept constant at 40 mL.

The following formulations were designed:

Formulation	Fenopropfen calcium (mg)	Eudragit RL100 (mg)	PVA (%) w/v
F1	100	100	1
F2	100	100	2
F3	100	100	3
F4	100	200	1
F5	100	200	2
F6	100	200	3
F7	100	300	1
F8	100	300	2
F9	100	300	3

The prepared formulations were compared to determine the effect of the quantity of polymer used and the concentration of the stabilizer on the physicochemical and pharmaceutical properties of the formulations.

2.6 Characterization of Polymeric Nanoparticles

2.6.1 Particle size and polydispersity index

A particle size analyser was used to measure the particle size and polydispersity index (PDI). A suitable diluted dispersion of the nanoparticles was pipetted into the measurement cell and analysed under the desired measurement conditions. The mean particle size was measured in nm, and the PDI was used for the evaluation of the particle size distribution [19].

2.6.2 Zeta potential

A zeta potential analyser was used to measure the zeta potential. A proper diluted dispersion of the nanoparticles was poured into the measurement cell and the surface charge was measured in millivolts (mV) [20].

2.6.3 Drug content

The appropriate amount of the nanoparticle formulation, which was accurately weighed, was used to extract the therapeutic agent. The solution obtained was diluted as needed and then analysed with the procedure developed for fenopropfen calcium. Drug content was calculated as percentage value [21].

2.6.4 Entrapment efficiency

The free fenopropfen calcium outside the nanoparticles was measured to calculate the entrapment efficiency [22]. The untrapped amount of the drug was subtracted from the total amount of drug and the percentage entrapment efficiency was calculated by the following:

$$\text{Entrapment efficiency (\%)} = \frac{\text{Total drug} - \text{Untrapped drug}}{\text{Total drug}} \times 100$$

2.6.5 Percentage yield

The percentage yield was selected as one of the parameters used for the formulation evaluation. The yield was used to determine the quantity of formulation produced compared with the quantity of material during the formulation process. The method of calculation should be carried out according to the experimental method described in the original research records [23].

2.6.6 In-vitro drug release study

The dialysis bag diffusion method was used to investigate in-vitro drug release. The amount of fenopropfen calcium loaded nanoparticles required for the drug dose was inserted in a dialysis membrane and dipped in phosphate buffered saline (PBS, pH 7.4). The temperature of the release medium was kept at 37 °C with constant magnetic stirring [24]. Samples were withdrawn at 0.5, 1, 2, 4, 6, 8, 12 and 24 hours. Withdrawals were made and equal amounts of fresh PBS added after each withdrawal to maintain the release conditions. All the collected samples were analyzed spectrophotometrically at 200 nm as specified in the original experimental protocol for fenopropfen calcium. Cumulative percentage drug release was calculated with sample withdrawal correction. The original protocol calls for triplicate measurements, and the results are given as the mean $\pm$ standard deviation (SD) [25].

2.6.7 Surface morphology

Surface morphology of selected nanoparticle formulation was investigated using scanning electron microscopy (SEM). A representative sample was prepared and mounted on the SEM sample holder and was then examined at the appropriate magnification. The micrographs obtained were analyzed for particle shape and surface appearance and morphology [26].

2.7 Selection of the Optimized Formulation

Physicochemical and pharmaceutical properties of formulations were used as parameters to compare the nine formulations. The particle size, PDI, zeta potential, drug content, and in-vitro drug release were taken into account. SEM observations were also taken into account. A formulation with the best overall balance of the properties evaluated was chosen for additional formulation development [27].

2.8 Stability Study

The optimized fenopropfen calcium loaded polymeric nanoparticles formulation was tested under refrigerated conditions (2–8°C), the room-temperature conditions (25 $\pm$ 2°C/60 $\pm$ 5% relative humidity) and accelerated conditions (40 $\pm$ 2°C/75 $\pm$ 5% relative humidity) for three months. Samples were evaluated at regular intervals in respect to particle size, PDI, zeta potential and entrapment efficiency. Changes in these parameters during storage were used to assess the retention of the formulation's physicochemical characteristics [28].

3. RESULTS

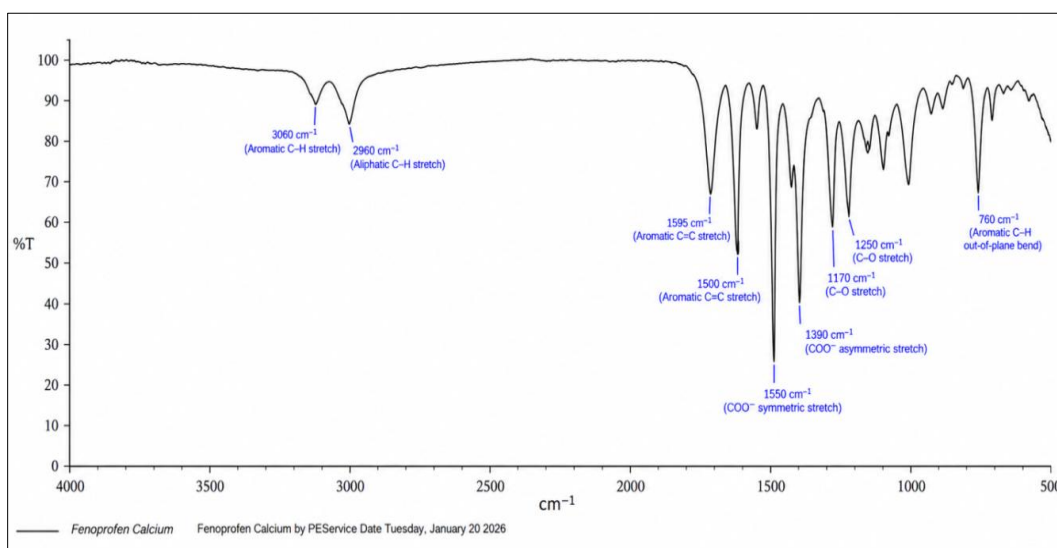
3.1. Drug–Excipient Compatibility Study

FTIR spectroscopy was run to investigate the compatibility of fenoprofen calcium with Eudragit RL100 and polyvinyl alcohol (PVA). The absorption pattern of the pure drug were compared with the pattern of excipients and their physical mixtures. The principal drug-related absorption bands were still easily observed in the physical mixtures as shown in Table 1. Also the characteristic carbonyl absorption band of ester function of Eudragit RL100 was observed at $\sim 1733.89\text{ cm}^{-1}$ and characteristic absorption bands of PVA were also observed in the ternary mixture.

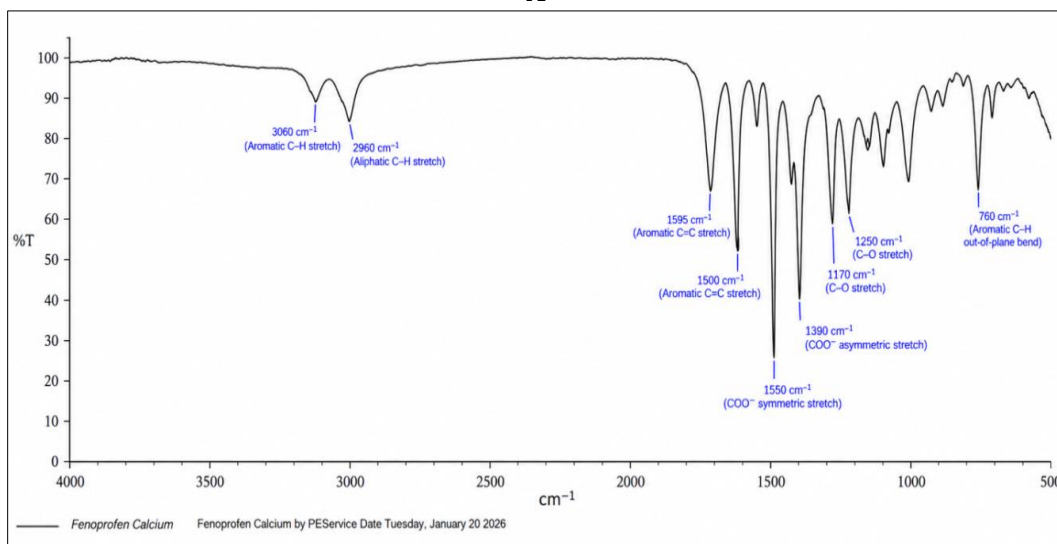
Little differences were noted at some of the peaks. No distinct new absorption band or “total” disappearance of the main absorption bands of the drug were reported. From these observations, it is concluded that there was no significant change in the main peak in the tested mixtures when observed by FTIR. The comparative spectra can be seen in figure 1.

Table 1: Characteristic FTIR absorption bands of fenoprofen calcium and its physical mixtures

Functional group	Pure drug (cm^{-1})	Drug + Eudragit RL100 (cm^{-1})	Drug + PVA (cm^{-1})	Drug + Eudragit RL100 + PVA (cm^{-1})
Aromatic C–H stretching	3060	3060	3060.12	3060.14
Aliphatic C–H stretching	2960	2960	2960.35	2960.42
Ester C=O stretching	—	1734	1709.54	1733.89
Aromatic C=C stretching	1595	1595	1595.27	1595.31
COO ⁻ stretching	1550	1550	1550.12	1550.08
COO ⁻ stretching	1390	1390	1390.65	1389.12
C–O stretching	1250	1255	1250.36	1256.18
C–O–C stretching	1170	1170	—	1170.63
Aromatic C–H out-of-plane bending	760	760	760.29	760.34



A



B

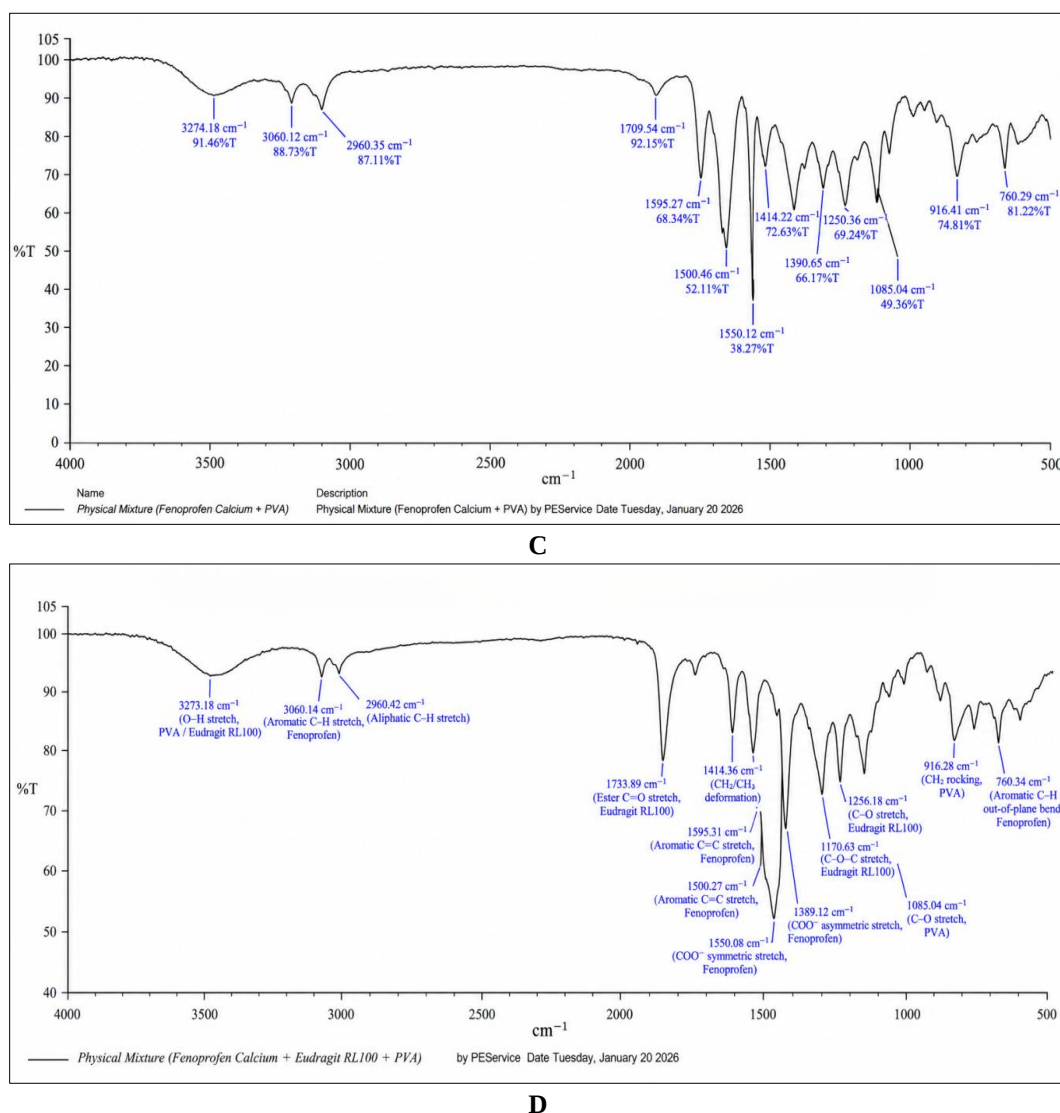


Figure 1: FTIR spectra of (A) pure fenopfen calcium, (B) fenopfen calcium with Eudragit RL100, (C) fenopfen calcium with PVA, and (D) the ternary physical mixture of fenopfen calcium, Eudragit RL100 and PVA

3.2. Physicochemical Characterization of Nanoparticles

All 9 formulations (F1-F9) were analyzed for particle size, PDI, zeta potential, EE and drug loading. The entire results are summarized in Table 2. The particle-size values ranged from 168.54 ± 2.45 to 265.48 ± 5.26 nm. The size of the particles varied as seen in Figure 2; F3 had the smallest particle size while F7 had the largest size.

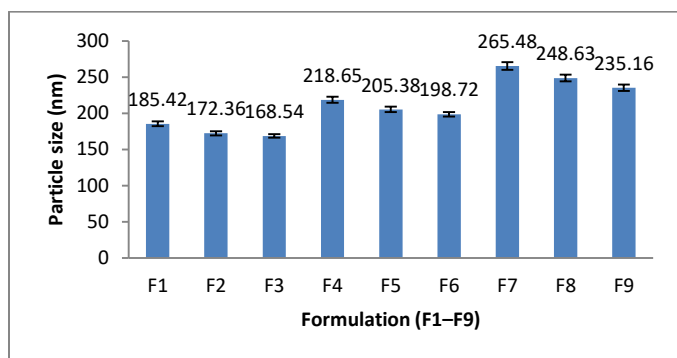
PDI values ranged from 0.215 ± 0.007 to 0.302 ± 0.014 . The narrowest particle size distribution was found for F6. The highest PDI was obtained in F7 when compared to other plant varieties (Figure 3).

All the formulations had positive zeta potential ranging from 18.62 ± 0.85 to 30.18 ± 0.96 mV. The value for F9 was the highest and the lowest value was F1 (Figure 4). It is likely that the cationic nature of Eudragit RL100 is responsible for the positive surface charge; however, it is not possible to separate the effect of Eudragit RL100 from that of PVA since both of these formulation variables were changed.

Table 2: Physicochemical characterization of fenopfen calcium-loaded Eudragit RL100 polymeric nanoparticles (F1–F9)

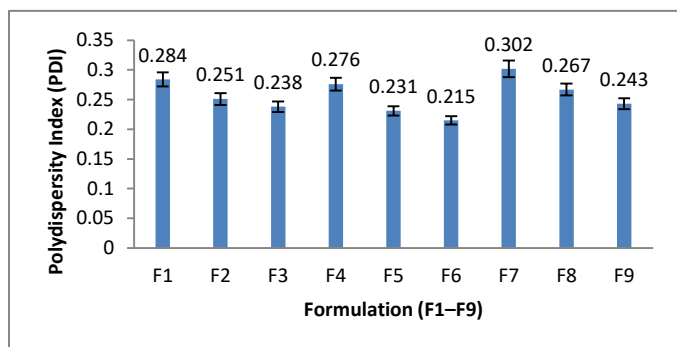
Form.	Particle size (nm)	PDI	Zeta potential I (mV)	Entrapment efficiency (%)	Drug loading (%)
F1	185.42 ± 3.24	0.284 ± 0.012	+18.62 ± 0.85	68.45 ± 1.42	31.24 ± 0.68
F2	172.36 ± 2.86	0.251 ± 0.010	+20.35 ± 0.92	71.28 ± 1.36	27.83 ± 0.54
F3	168.54 ± 2.45	0.238 ± 0.009	+21.47 ± 0.78	73.62 ± 1.25	25.16 ± 0.47
F4	218.65 ± 4.12	0.276 ± 0.011	+22.18 ± 0.96	76.35 ± 1.48	24.68 ± 0.62
F5	205.38 ± 3.68	0.231 ± 0.008	+24.56 ± 0.82	79.42 ± 1.32	21.84 ± 0.51
F6	198.72 ± 3.15	0.215 ± 0.007	+25.83 ± 0.74	82.16 ± 1.26	20.35 ± 0.43
F7	265.48 ± 5.26	0.302 ± 0.014	+26.42 ± 1.05	83.58 ± 1.54	19.62 ± 0.58
F8	248.63 ± 4.72	0.267 ± 0.010	+28.74 ± 0.89	86.25 ± 1.38	18.45 ± 0.49
F9	235.16 ± 4.35	0.243 ± 0.009	+30.18 ± 0.96	88.64 ± 1.45	17.32 ± 0.46

Values are expressed as mean $\pm$ standard deviation (SD), $n = 3$.



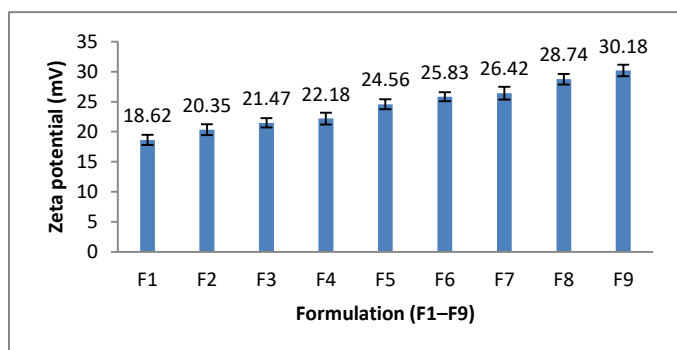
Data are presented as mean $\pm$ SD (n = 3).

Figure 2: Particle size of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)



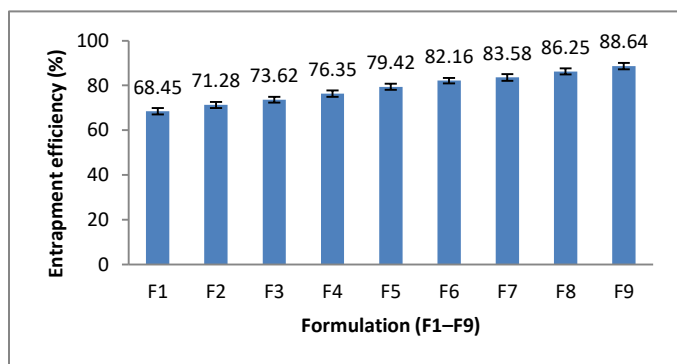
Data are presented as mean $\pm$ SD (n = 3).

Figure 3: Polydispersity index (PDI) of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)



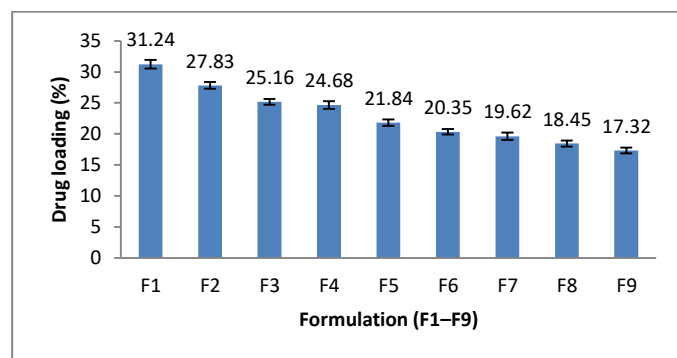
Data are presented as mean $\pm$ SD (n = 3).

Figure 4: Zeta potential of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)



Data are presented as mean $\pm$ SD (n = 3).

Figure 5: Entrapment efficiency of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)



Data are presented as mean $\pm$ SD (n = 3).

Figure 6: Drug loading of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)

The entrapment efficiency of the formulation series ranged from $68.45 \pm 1.42\%$ in F1 to $88.64 \pm 1.45\%$ in F9 (Figure 5). In contrast, drug loading decreased from $31.24 \pm 0.68\%$ in F1 to $17.32 \pm 0.46\%$ in F9 (Figure 6). As the amount of drug remained constant and the amount of polymer varied, the drug loading results should be compared with the composition of the overall formulation.

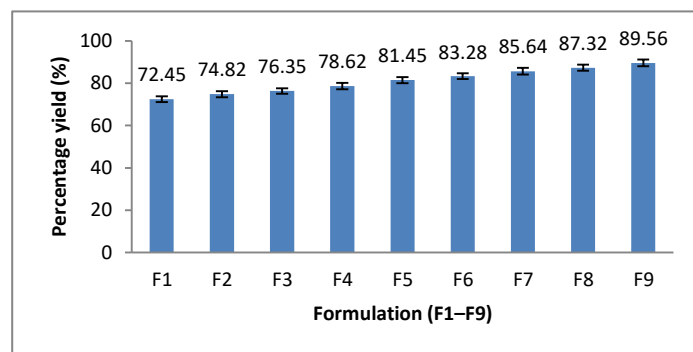
3.3. Percentage Yield

The percentage yield ranged from $72.45 \pm 1.32\%$ to $89.56 \pm 1.55\%$. F1 had the least yield while F9 had the highest yield. The results of the plant yield in the formulation series are presented in Table 3 and Figure 7, with an increase in yield values across the formulation series. F6 had a yield of $83.28 \pm 1.35\%$ which was evaluated together with the other physicochemical parameters.

Table 3: Percentage yield of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)

Formulation	Percentage yield (%)
F1	72.45 ± 1.32
F2	74.82 ± 1.45
F3	76.35 ± 1.28
F4	78.62 ± 1.56
F5	81.45 ± 1.42
F6	83.28 ± 1.35
F7	85.64 ± 1.62
F8	87.32 ± 1.48
F9	89.56 ± 1.55

Values are expressed as mean $\pm$ SD, n = 3.



Data are presented as mean $\pm$ SD (n = 3).

Figure 7: Percentage yield of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9)

The concentrations of both Eudragit RL100 and PVA were altered, therefore it is not possible to determine from the results whether it is a specific effect of one or the other component or whether the effect is the result of their synergistic interaction.

3.4. In-vitro Drug Release

The *in-vitro* drug-release study revealed that the release of the drug was progressive in all nine formulations for 24 hours. At 0.5 hours, cumulative drug release ranged from $8.42 \pm 0.38\%$ to $12.45 \pm 0.62\%$. At 24 hours, it ranged from $88.65 \pm 1.25\%$ to $96.25 \pm 1.45\%$. The release curves are shown in Figure 8, and the results at certain time points are summarized in Table 4.

F1 had the maximum cumulative release at 12 hours and $96.25 \pm 1.45\%$ at 24 hours. F9 showed the lowest 24-hour release, at $88.65 \pm 1.25\%$. For all formulations, the cumulative release was lower at later times when the amount of Eudragit RL100 was high. As Eudragit RL100 and PVA differed in their formulations, the differences that were observed cannot be solely attributed to either of these components.

F6 reached a cumulative drug release of $92.85 \pm 1.35\%$ at 24 hours. This result was taken into consideration with particle size, PDI, EE, and DL and % yield to decide the optimized formulation.

Table 4: Selected cumulative in-vitro drug-release results for fenopropfen calcium-loaded nanoparticles

Parameter	F1	F6	F9
Drug release at 0.5 h (%)	12.45 ± 0.62	9.82 ± 0.45	8.42 ± 0.38
Drug release at 24 h (%)	96.25 ± 1.45	92.85 ± 1.35	88.65 ± 1.25

Values are expressed as mean $\pm$ SD, $n = 3$.

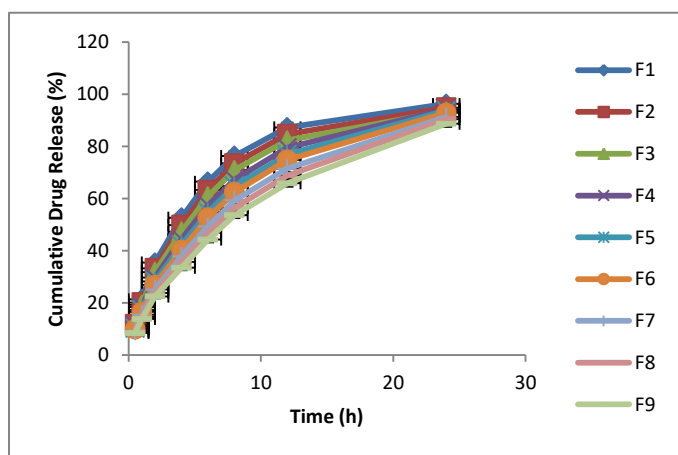


Figure 8: In-vitro cumulative drug-release profiles of fenopropfen calcium-loaded polymeric nanoparticle formulations (F1–F9) over 24 hours

3.5. Selection of the Optimized Formulation

The parameter considered as a whole was used to define the optimum for F6, and not the highest value of any one parameter. As shown in Table 2, F6 had a particle size of 198.72 ± 3.15 nm, PDI of 0.215 ± 0.007 , zeta potential of $+25.83 \pm 0.74$ mV, entrapment efficiency of $82.16 \pm 1.26\%$

and drug loading of $20.35 \pm 0.43\%$. Its percentage yield was $83.28 \pm 1.35\%$ (Table 3), and its cumulative drug release reached $92.85 \pm 1.35\%$ at 24 hours (Table 4).

F6 had the most balanced combination of the measured characteristics among the formulations, but F1 had the highest drug loading and the highest entrapment efficiency and zeta potential of F9. It was selected for further investigation based on its comparatively low PDI and its entrapment efficiency, yield and release profile.

3.6. Scanning Electron Microscopy

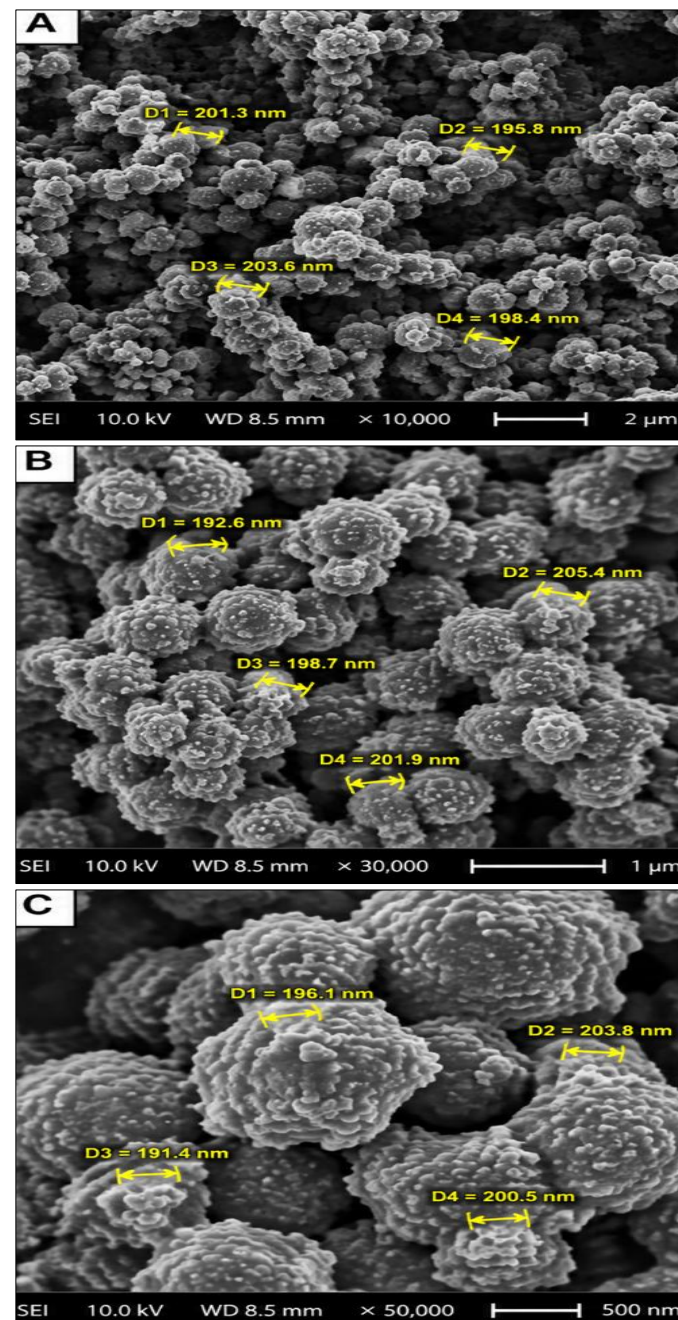


Figure 9: Scanning electron micrographs of the optimized fenopropfen calcium-loaded polymeric nanoparticle formulation (F6) at (A) $\times 10,000$, (B) $\times 30,000$ and (C) $\times 50,000$ magnifications

The surface of F6 was observed by scanning electron microscopy under various magnifications of $\times 10,000$, $\times 30,000$ and $\times 50,000$. The particles were generally found to be spherical in shape with some degree of roughness, irregularities and/or clustering of particles as seen in Figure 9.

The dimension of the particles from the SEM images was approximately 191.4–205.4 nm, which is reasonably close to the particle size obtained by particle-size analysis (198.72 ± 3.15 nm). These measurements are slightly different due to the fact that SEM measures dried particles while particle-size analysis measures particles in a liquid medium.

3.7. Stability Study

F6 was subjected to stability studies for three months at various temperatures, including the refrigerated condition, room temperature and accelerated storage. Changes in particle size, PDI, zeta potential and entrapment efficiency are summarized in Table 5. The formulation exhibited less change when stored at a refrigerated temperature compared to the other conditions.

After three months at $2-8^{\circ}\text{C}$, particle size increased from 198.72 ± 3.15 to 202.48 ± 3.56 nm, while PDI increased from 0.215 ± 0.007 to 0.225 ± 0.009 . The Zeta potential was reduced to $+24.78 \pm 0.82$ mV while the entrapment efficiency was reduced to $80.84 \pm 1.35\%$. The particle size at room temperature was found to be 216.92 ± 4.12 nm and the entrapment efficiency was decreased to $77.86 \pm 1.47\%$. The accelerated condition results in a particle size of 241.35 ± 4.86 nm, PDI of 0.296 ± 0.016 and an entrapment efficiency of $73.95 \pm 1.68\%$.

These results show that the storage conditions affected F6 characteristics measured. Those properties were conserved better in refrigerated storage for the 3 months of the study. These results are not, however, conclusive proof of long term shelf life.

Table 5: Stability of optimized fenopropfen calcium-loaded nanoparticle formulation F6 after three months

Parameter	Initial	Refrigerated ($2-8^{\circ}\text{C}$)	Room temperature ($25 \pm 2^{\circ}\text{C}$)	Accelerated ($40 \pm 2^{\circ}\text{C}$)
Particle size (nm)	198.72 ± 3.15	202.48 ± 3.56	216.92 ± 4.12	241.35 ± 4.86
PDI	0.215 ± 0.007	0.225 ± 0.009	0.258 ± 0.012	0.296 ± 0.016
Zeta potential (mV)	$+25.83 \pm 0.74$	$+24.78 \pm 0.82$	$+22.64 \pm 0.95$	$+19.45 \pm 0.83$
Entrapment efficiency (%)	82.16 ± 1.26	80.84 ± 1.35	77.86 ± 1.47	73.95 ± 1.68

Values are reported as mean $\pm$ SD. Relative humidity conditions were $60 \pm 5\%$ for room-temperature storage and $75 \pm 5\%$ for accelerated storage.

4. DISCUSSION

The results indicate that the formulation composition affected the physicochemical properties and release characteristics of fenopropfen calcium loaded Eudragit RL100 nanoparticles. The improvements in individual parameters were not necessarily

simultaneous as summarized in Tables 2-5 and Figures 2-9. F6 was thus chosen based on an evaluation of particle size, PDI, entrapment efficiency, drug loading, percentage yield, drug release, morphology and stability.

The FTIR spectra of the tested physical mixtures did not exhibit any significant changes in the spectra, and SEM images exhibited mainly spherical particles with a certain degree of surface roughness and aggregation. The stability results also showed that F6 had characteristics that were more stable during refrigerated storage than during room-temperature storage and accelerated storage. Considering the different formulations investigated in this study, F6 was the most appropriate formulation for further pharmaceutical development.

5. CONCLUSION

In the present study, polymeric nanoparticles of fenopropfen calcium were successfully developed and characterized with varying levels of different polymers and PVA. The physicochemical properties and in-vitro drug release of the prepared formulations also differed with regard to particle size, polydispersity index, zeta potential, entrapment efficiency, drug loading, % yield, suggesting that the composition of the formulations has an effect on the physicochemical properties and drug release behaviour of the prepared nanoparticles.

The FTIR spectra indicated that there was a substantial retention of the characteristic peaks of fenopropfen calcium in the drug-polymer mixtures, although some of the peaks showed shifts. The results indicated that there were no significant changes in the characteristic functional groups of the drug in the spectra. The sizes of the particles varied between 168.54 and 265.48 nm and the polydispersity index ranged between 0.215 and 0.302. The formulations also showed positive zeta potential ranging from 68.45% to 88.64% which indicated the formulations were stable. F6 was chosen as the optimized formulation from all the prepared batches due to its overall balance of the physicochemical properties and drug release performance.

The optimized formulation F6 was made up of 100 mg fenopropfen calcium, 200 mg Eudragit RL100 and 3% w/v of PVA. It exhibited a mean particle size of 198.72 ± 3.15 nm, a polydispersity index of 0.215 ± 0.007 , a zeta potential of $+25.83 \pm 0.74$ mV, an entrapment efficiency of $82.16 \pm 1.26\%$, and a drug loading of $20.35 \pm 0.43\%$. Its percentage yield was $83.28 \pm 1.35\%$, and the cumulative drug release reached $92.85 \pm 1.35\%$ at 24 hours. Its particles are mostly spherical, surface has a little bit of roughing, and has a little of aggregation, SEM examination.

The three-month stability evaluation showed that F6 has a more consistent measured characteristic when stored in a refrigerated state than at room temperature or under accelerated storage conditions. The particle size, polydispersity index, zeta potential and entrapment efficiency

parameters were more significant at high temperatures and high humidity, suggesting the need for proper storage conditions to ensure maintenance of formulation quality.

In conclusion, the study results indicated that Eudragit RL100 can be used as a polymeric carrier system for formulation of fenoprofen calcium-loaded nanoparticles (NPs) that exhibited sustained drug release for 24 hours during the study period with nanoscale particle dimensions. The most balanced formulation of the ones tested was F6. Additional relevant studies would need to be conducted to determine the long-term stability, further investigate the drug-release kinetics and evaluate the formulation's performance under other relevant conditions.

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CONFLICT OF INTEREST: Nil

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