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"Formulation And Evaluation Of Polymeric Nanoparticles Of Felodipine"

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Abstract:

Background: Felodipine, a calcium channel blocker, suffers from poor aqueous solubility and limited oral bioavailability, which restricts its therapeutic efficacy. To overcome these limitations, nanoparticle-based delivery systems provide a promising approach for enhancing solubility, stability, and sustained release.

Methods: Felodipine-loaded polymeric nanoparticles were prepared using the nanoprecipitation method with PLGA as the polymer and PVA as the stabilizer. Preformulation studies, including organoleptic evaluation, FTIR, λmax determination, melting point, solubility, partition coefficient, and drug excipient compatibility, were carried out. The formulations (F1–F5) were characterized for physical appearance, particle size, zeta potential, SEM morphology, pH, drug content, entrapment efficiency, in vitro drug release, and stability studies under ICH conditions.

Results: Preformulation confirmed drug identity, purity, and lipophilic character (log P = 4.1). The prepared nanoparticles exhibited uniform, milky dispersions with particle sizes in the range of 234–254 nm. Formulation F4 showed optimal stability with a zeta potential of –13.7 mV, spherical morphology, and high entrapment efficiency (86.4%). In vitro release studies revealed sustained drug release, with F4 showing maximum release (92.9% over 8 hours) following zero-order kinetics. Stability testing confirmed no significant changes in drug content, pH, or release profile after three months at accelerated conditions.

Conclusion: Felodipine-loaded PLGA nanoparticles, particularly formulation F4, demonstrated favorable physicochemical characteristics, enhanced entrapment, controlled release, and stability. This delivery system offers a promising strategy to improve the solubility, bioavailability, and therapeutic efficacy of Felodipine compared to conventional formulations.

Keywords: Felodipine, Polymeric Nanoparticles, PLGA, Nanoprecipitation, Controlled Release, Oral Bioavailability.

1. INTRODUCTION:

1.1. Novel Drug Delivery System

A novel drug delivery system (NDDS) refers to advanced and innovative approaches that are specifically designed to enhance the therapeutic efficacy and safety of drugs by improving their delivery to the target site. Unlike conventional dosage forms such as tablets, capsules, or injections, which often face challenges like poor solubility, low bioavailability, short half-life, and nonspecific distribution, NDDS aims to overcome these limitations by offering more controlled, sustained, and targeted drug release. The primary goal of an NDDS is to deliver the right amount of drug at the right site and at the right time, thereby maximizing therapeutic effects while minimizing side effects. This is achieved through the development of new carriers, technologies, and formulations that can modify the pharmacokinetics and pharmacodynamics of therapeutic agents.[1,3]

Nanoparticle:

Nanoparticles are the fundamental components of nanotechnology. Their size typically ranges from 1 to 100 nm, and they can be composed of metals, metal oxides, organic matter, or carbon [1,2]. Nanoparticles vary in dimensions, shape, and size, with surfaces that may be irregular with variations or uniform. Structurally, some are crystalline or amorphous, consisting of single or multiple crystal solids, either agglomerated or free [3].

Polymeric Nanoparticles

Polymeric nanoparticles are colloidal carriers ranging from 10–1000 nm, made from biodegradable and biocompatible polymers [1,2]. They can deliver small molecules, proteins, peptides, nucleic acids, and vaccines [3]. Natural polymers (chitosan, alginate, gelatin) and synthetic ones (PLA, PGA, PLGA) are commonly used [4,5]. The polymer matrix stabilizes drugs, prevents degradation, and enables controlled release, improving pharmacokinetics [6]. Based on structure, they are classified as nanospheres (drug dispersed in polymer) or nanocapsules (drug enclosed in a polymeric shell) [7,8]. Both enhance solubility, stability, and bioavailability, with nanocapsules being more suitable for lipophilic drugs. Advantages include sustained release, reduced dosing, prolonged circulation, ability to cross barriers like the blood–brain barrier, and preferential accumulation in diseased tissues via the EPR effect [9,10]. Surface modifications with antibodies, peptides, or aptamers allow targeted delivery with fewer side effects [11]. Limitations include challenges in large-scale production, variable size and loading, possible toxicity, burst release, low encapsulation efficiency, and storage instability [12–14]. Current research in polymer chemistry and nanotechnology aims to create safer, more efficient, and targeted nanoparticle systems [15,16].

MATERIALS AND METHODS:

Materials

- The standard raw material active pharmaceutical ingredient (Drug) of Felodipine was procurement from Dhamtech Pharma and Consultant, Navi Mumbai, Maharastra, India.
- The standard raw material polymer, Poly(lactic-co-glycolic acid) (PLGA), was procured from Sigma-Aldrich, Mumbai, Maharashtra, India.
- The airtight collapsible tubes used for storing the Felodipine-loaded polymeric nanoparticle formulations were procured from Aneeta Technopack Pvt. Ltd.

Methods:

A. Preformulation Studies

Preformulation testing is the first step in the rational development of a drug dosage form. It is defined as the systematic investigation of the physicochemical properties of a new drug substance, both alone and in combination with excipients, to generate data useful for designing a safe, stable, potent, bioavailable, and efficacious dosage form [6, 7, 29, 30].

1. Organoleptic Character

Organoleptic evaluation involves assessing the general appearance of the drug, including its physical nature, color, and odor. Observations were performed visually and compared with the standards specified in the pharmacopoeia to ensure proper identification of Felodipine [6, 7].

2. Identification of Drug by FTIR

Felodipine was identified using Fourier Transform Infrared (FTIR) spectroscopy. Solid drug samples were triturated with IR-grade potassium bromide (KBr) in a 1:100 ratio using a mortar and pestle. The prepared sample was then placed in a sample holder and scanned over a wavelength range of 4000–400 cm^{-1}, with 45 scans recorded using a Shimadzu IR Solution 1.50 equipped with a DLATGS detector. For liquid samples, Nujol was used instead of KBr. The obtained spectra were compared with standard reference spectra, and the principal peaks were matched to confirm the identity of Felodipine [6, 7, 29, 30].

3. Determination of λ Max

To prepare the standard stock solution of Felodipine, 10 mg of the drug was accurately weighed and transferred into a 100 ml volumetric flask. A small volume of methanol was added to dissolve the drug completely, aided by gentle shaking or sonication if necessary. The volume was then made up to 100 ml with methanol to obtain a stock solution of 100 µg/ml. For the UV-Visible scanning, 2–3 ml of the stock solution was transferred into a clean quartz cuvette, and methanol was used as a blank in a separate cuvette. The blank was placed in the reference compartment, while the sample was placed in the sample compartment of the spectrophotometer. The solution was scanned from 200 nm to 400 nm to identify the wavelength at which maximum absorbance (λ max) occurred [6, 7, 29, 30].

4. Calibration Curve of Pure Drug

A series of standard solutions of Felodipine was prepared from the previously described stock solution (100 µg/ml) in methanol. Aliquots of 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, and 2.5 ml were transferred into separate 10 ml volumetric flasks and diluted to volume with methanol to obtain concentrations in the range of 0.5–2.5 µg/ml. The absorbance of each solution was measured at the maximum wavelength (λ max = 240 nm) using a UV-Visible spectrophotometer. The calibration curve was constructed by plotting absorbance (y-axis) versus concentration (x-axis) using Microsoft Excel, and linear regression analysis was performed to determine the correlation between concentration and absorbance [6, 7, 29, 30].

5. Melting Point

The melting point of Felodipine was determined using a Thiele tube. The drug sample was filled halfway in a sealed capillary tube, which was attached to a thermometer with a thread. The Thiele tube was heated gradually, and the temperature range at which Felodipine melted was observed and recorded [6, 7].

6. Solubility

Semi-quantitative solubility determination was carried out by adding a suitable solvent to a volumetric flask containing an accurately weighed amount of Felodipine. The flask was sealed, vigorously shaken, and maintained at room temperature for three days. After this period, the solution was visually inspected for any undissolved particles. Solubility was expressed as the ratio of the drug to the solvent [6, 7, 29].

7. Partition Coefficient

The partition coefficient, a critical parameter reflecting the lipophilicity of Felodipine and its potential to permeate biological membranes, was determined using the shake flask method. Briefly, 5 mg of Felodipine was added to a mixture of 25 ml distilled water and 25 ml n-octanol. The mixture was shaken vigorously for 30 minutes, then transferred to a separating funnel and further shaken on a mechanical shaker for 4 hours. After allowing the two phases to separate completely, the concentration of the drug in each phase was measured using UV spectrophotometry. The partition coefficient (P) was calculated as the ratio of the drug concentration in the organic phase (n-octanol) to that in the aqueous phase (water) [6, 7, 29, 30].

8. Drug–Excipient Compatibility

Drug–excipient compatibility studies were conducted to evaluate potential interactions between Felodipine and selected excipients, including polymers such as Ethyl Cellulose and PEG. Fourier Transform Infrared (FTIR) spectroscopy was employed, scanning the samples over the wavenumber range of 400–4000 cm^{-1}. The characteristic functional groups of both the pure drug and the excipients were analyzed to detect any chemical interactions or changes in the spectra, which could indicate incompatibility [6, 7, 29, 30].

B. Formulation of Polymeric Nanoparticles

Felodipine-loaded polymeric nanoparticles were prepared using the nanoprecipitation technique. The drug and polymer (PLGA) were dissolved in 10 mL of acetone to form the organic phase. The aqueous phase was prepared by dissolving 1% w/v polyvinyl alcohol (PVA) in distilled water under constant magnetic stirring at 1000 rpm. The organic phase was added dropwise into the aqueous phase at a rate of 1 mL/min using a syringe while maintaining continuous stirring. Spontaneous precipitation of PLGA occurred due to the diffusion of acetone into the aqueous medium, entrapping Felodipine within the polymeric matrix to form nanoparticles.

The resulting dispersion was stirred for 3 hours at room temperature to ensure complete evaporation of the organic solvent. Probe sonication was performed for 5 minutes at 40% amplitude to reduce particle aggregation and achieve a uniform size distribution. Nanoparticles were collected by centrifugation at 15,000 rpm for 30 minutes at 4°C, washed three times with distilled water to remove residual PVA and free drug, and lyophilized using 5% w/v mannitol as a cryoprotectant. The dried formulations were stored in airtight containers for further physicochemical characterization and drug release studies [29, 30, 31, 32].

C. Characterization of Felodipine-Loaded Polymeric Nanoparticles

1. Physical Appearance

The physical characteristics of Felodipine-loaded polymeric nanoparticles (F1–F5) were examined both in dispersion and after lyophilization. Freshly prepared nanoparticle dispersions were visually assessed against white and black backgrounds to evaluate color, clarity, turbidity, and homogeneity. All formulations appeared milky to opalescent with no visible particulate matter or drug crystals, indicating uniform nanoparticle formation. The dispersions remained physically stable without phase separation or sedimentation for 24 hours at room temperature and could be easily re-dispersed upon gentle shaking. The pH values were within the neutral range, confirming suitability for further studies. Lyophilized powders were off-white with intact, porous cakes, non-sticky in nature, and readily reconstituted in water without aggregation. These observations confirmed that the nanoprecipitation method produced homogeneous, stable nanoparticles with acceptable physical characteristics [29, 30, 31].

2. Particle Size and Zeta Potential

Particle size and zeta potential were measured using dynamic light scattering (DLS) on a Litesizer 500 instrument. Nanoparticle dispersions were appropriately diluted with double-distilled water to prevent multiple scattering effects and analyzed to determine average particle size, polydispersity index (PDI), and size

distribution. Zeta potential was measured to assess surface charge and predict colloidal stability. Particles with zeta potential above ±30 mV generally indicate good stability, while values between ±20 mV and ±30 mV suggest moderate stability; values below ±5 mV are prone to aggregation. Many systems stabilized by non-ionic surfactants such as PVA exhibit zeta potentials between −10 and −20 mV, with steric stabilization maintaining physical stability [29, 30, 36]. The combined evaluation of particle size and zeta potential provides crucial insight into dispersion stability and suitability for drug delivery applications.

3. Scanning Electron Microscopy (SEM)

SEM was employed to examine the surface morphology and structural characteristics of the nanoparticles. Lyophilized samples were mounted on double-sided carbon tape adhered to aluminum stubs, sputter-coated with a thin gold layer under vacuum to prevent charging, and imaged at suitable accelerating voltages. SEM micrographs confirmed the spherical nature, uniform distribution, and smooth surface of the Felodipine-loaded polymeric nanoparticles [29, 30, 36].

4. pH Determination

The pH of nanoparticle dispersions was measured using a calibrated digital pH meter, standardized with pH 4.0 and 7.0 buffers. The electrode was immersed directly into freshly prepared dispersions, and readings were recorded after stabilization. Measurements were performed in triplicate at ambient temperature. Monitoring pH is important because it can influence surface charge, zeta potential, and overall colloidal stability [29, 30].

5. Drug Content and Entrapment Efficiency

Drug content and entrapment efficiency were determined using a UV–Visible spectrophotometer. Approximately 1 g of lyophilized nanoparticles was dissolved in 100 mL methanol and sonicated for 10–15 minutes to extract the drug completely. A 1 mL aliquot of this stock solution was further diluted to 10 mL with methanol, and absorbance was measured at 210 nm against methanol as blank. Drug concentration was calculated using the previously established calibration curve of Felodipine in methanol, allowing determination of actual drug content and encapsulation efficiency [29, 30, 31, 32].

The percentage drug content and entrapment efficiency were calculated using the following equations:

$$\%\,\text{Drug Content (DC)} = \frac{\text{Practical drug content}}{\text{Theoretical drug content}} \times 100$$

$$\%\,\text{Entrapment Efficiency (EE)} = \frac{\text{Entrapped drug}}{\text{Total drug added}} \times 100$$

6. *In-Vitro* Drug Release

The in-vitro drug release profile of Felodipine from polymeric nanoparticles was assessed using a USP Type II (paddle) dissolution apparatus. The study was performed in 900 mL of phosphate buffer (pH 6.8), maintained at 37 ± 0.5 °C to simulate intestinal conditions. The paddle speed was set at 100 rpm to ensure uniform mixing of the medium [29, 30].

Accurately weighed amounts of the nanoparticle formulations, pure Felodipine, and physical mixtures were dispersed in the dissolution medium. Samples of 5 mL were withdrawn at predetermined intervals of 10 minutes over a period of 120 minutes and immediately replaced with fresh buffer to maintain sink conditions. The withdrawn samples were filtered through a 0.45 µm membrane filter, appropriately diluted, and analyzed using a UV–Visible spectrophotometer (Shimadzu UV-1800) at 210 nm [31, 32].

The cumulative percentage of drug released was calculated and plotted against time to obtain release profiles. The data were further fitted into kinetic models, including zero-order, first-order, and Higuchi models, to elucidate the mechanism of drug release from the polymeric nanoparticles [36].

7. Stability Studies

The stability of Felodipine-loaded polymeric nanoparticle formulations was evaluated according to modified ICH guidelines to assess their physical and chemical integrity over time [29, 36]. Selected formulations were stored in airtight, light-protected collapsible tubes under accelerated stability conditions of 40 °C ± 2 °C and 75% ± 5% relative humidity (RH) for a duration of one month.

At predetermined intervals, samples were withdrawn and analyzed for any changes in physical appearance, clarity, and aggregation. Clarity was assessed by visual inspection against white and black backgrounds under ambient light to detect any turbidity, opalescence, or phase separation. Aggregation was evaluated by gently shaking the formulations and observing for sedimentation, flocculation, or formation of visible particles. Additionally, pH, drug content, viscosity, and in-vitro drug release profiles were measured. Observed variations were compared with freshly prepared formulations to determine the extent of stability.

These studies provided critical insight into the robustness of the Felodipine-loaded nanoparticle system, indicating its suitability for long-term storage and potential therapeutic application [31, 32, 36].

RESULTS AND DISCUSSION:

A. Preformulation Studies:

1. Organoleptic Character of Pure Drug:

Organoleptic character of drug substance was carried out the characteristics feature like taste, colour, odour etc were studies. The results are shown in table 1.

Table 1: Organoleptic Character of Felodipine

S. No.	Properties	Result
1.	Description	Crystalline fine powder
2.	Taste	Slightly Bitter
3.	Odour	Odourless
4.	Colour	White Colour

2. Identification of drug by FTIR:

It was found that the peak obtained by performing FTIR pure drug were found to be in between the range of main principle peaks recorded previously as theoretical range, hence this indicate that the drug is pure. These observations were found to be in concurrence with the structure of the drug (Felodipine) molecules.

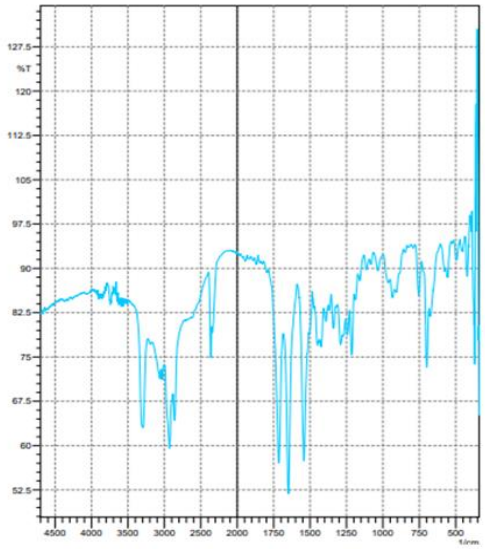

Figure1: FTIR of Felodipine

Table 5.2: Peak table with principles peak of Felodipine

S. No.	Functional Group	Theoretical Peak (Cm^1)	Practical Peak (Cm^1)
1.	N-H Stretch (Amide)	3300–3500(Cm^1)	3349.53 (Cm^1)
2.	C-H Stretch (Aliphatic)	2950–2850(Cm^1)	2880.81 (Cm^1)
3.	C=O Stretch (Carboxyl & Amide)	1750–1680(Cm^1)	1721.04 (Cm^1)
4.	N-H Bend (Amide II)	1600–1550(Cm^1)	1547.28 (Cm^1)
5.	C-H Bending (Alkanes)	1500–1400 (Cm^1)	1481.70 (Cm^1)
6.	C-N Stretch (Amide)	1250–1050 (Cm^1)	1188.20(Cm^1)
7.	C-H Bending (Aromatic)	1000–900 (Cm^1)	963.07 (Cm^1)
8.	C-H Out-of-Plane Bending (Aromatic)	750–700 (Cm^1)	663.07 (Cm^1)

3. Determination of λ max:

The absorption spectrum of the pure drug Felodipine was recorded over a wavelength range of 200 to 800 nanometers using a UV-Visible spectrophotometer. For this analysis, a standard solution of the drug was prepared at a concentration of 10 micrograms per milliliter (10 µg/mL) using ethanol as the solvent. The prepared solution was then subjected to spectrophotometric scanning to determine the characteristic absorption pattern of the drug. The resulting spectrum revealed a distinct maximum absorbance, referred to as λ max, at a wavelength of 270 nanometers. This λ max value represents the wavelength at which Felodipine exhibits its highest absorbance, indicating the optimal point for its quantitative analysis in further spectrophotometric studies.

Table 3: λ Max of Felodipine

S. No.	Drug	λ max	Selected Wavelength
1.	Felodipine	270 nm	270 nm
2.		273 nm	
3.		270 nm	

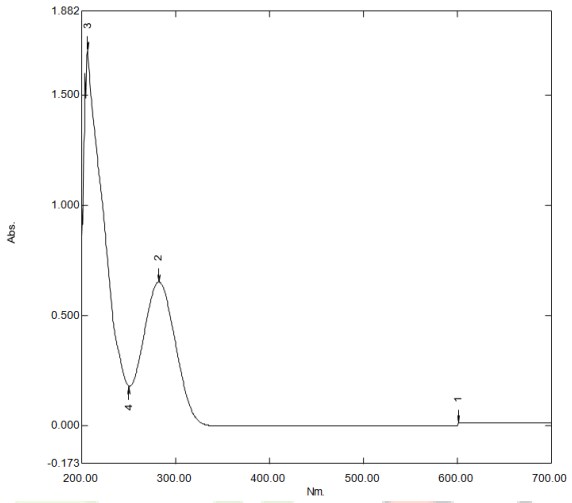

Figure2: λ max of Felodipine

4 Calibration Curve

Standard calibration curve of Felodipine was carried out in ethanol at 270 nm. The absorbance value obtained are shown in table. Using concentration and absorbance data, a beer lumbert's plot was obtained. The plot in the given figure. The R^2 value of Felodipine was found to be 0.998, which is near to1, which signifies linearity.

Table 4: Calibration Curve of Felodipine

S. No.	**Actual Concentration (µg/ml)**	**Absorbance (λ Max= 270)**
1	0.5	0.259
2	1	0.384
3	1.5	0.542
4	2	0.668
5	2.5	0.811

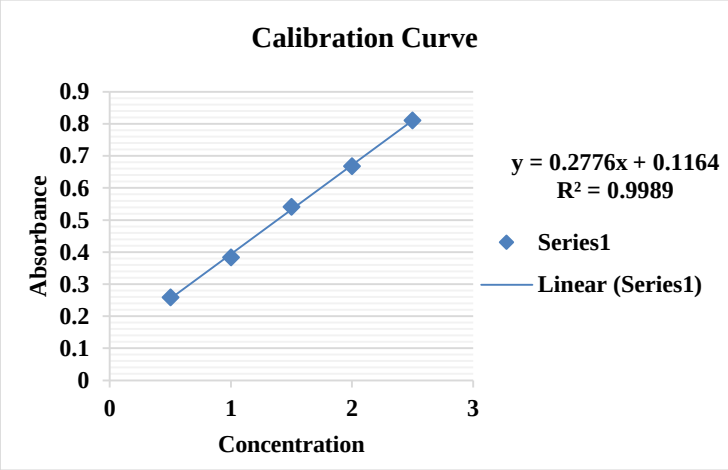

Figure 3: Calibration curve of Felodipine

5. Melting Point

The melting point of Felodipine was obtained to be 142^{0}C, which compiles the indian pharmacopoeia so it was conformed that it is Felodipine drug.

Figure 4: Melting Point determination of Felodipine Drug

Table 5: Determination of Melting Point of Felodipine

S. No.	Melting Point of Nateglinide	Mean Value
1.	141 ºC	142 ºC
2.	143 ºC	
3.	142 ºC	

6. Solubility

The solubility of the pure drug Felodipine was evaluated using a range of solvent media to understand its behavior in different environments. In this study, 1 mg of Felodipine was tested in 10 ml of various solvents, including distilled water, methanol, ethanol, and acetone. The results demonstrated distinct solubility characteristics depending on the solvent used. In distilled water, Felodipine exhibited very limited solubility and was categorized as partially insoluble, indicating a poor affinity for aqueous environments. On the other hand, Felodipine showed high solubility in both methanol and ethanol, where it was classified as freely soluble, suggesting a strong interaction between the drug and these organic solvents. In acetone, the solubility of Felodipine was found to be moderate, and thus it was described as sparingly soluble. These findings highlight the influence of solvent polarity and chemical nature on the solubility profile of Felodipine, which is a critical factor in its formulation and bioavailability.

Table 6: Solubility of pure drug Felodipine

S.No.	Drug (Felodipine)	Solvent Media	Solvent Amount	Solubility Status
1	1 mg	Distilled Water	10 ml	Partially Insoluble
2	1 mg	Methanol	10 ml	Freely Soluble
3	1 mg	Ethanol	10 ml	Freely Soluble
4	1 mg	Acetone	10 ml	Sparingly Soluble
5	1 mg	Isopropyl Alcohol	10 ml	Soluble

7. Partition Coefficient:

The partition coefficient of the drug Felodipine was experimentally determined by measuring its distribution between two immiscible phases: n-octanol, representing the organic (lipophilic) phase, and water, representing the aqueous (hydrophilic) phase. The resulting value, expressed as log P, was found to be 4.1. This indicates that Felodipine exhibits a significantly higher solubility in the organic phase compared to the aqueous phase, suggesting its lipophilic nature and potential for membrane permeability, which is an important factor in its absorption and pharmacokinetic behavior.

Table 5: Partition Coefficient of Felodipine

S. No.	Partition Coefficient of Felodipine (log P)	Mean Value (log P)
1.	4.1	4.1
2.	4.2	
3.	4.1	

8. Drug Excipient Compatibility Studies:

All the peaks observed in the FT-IR of Felodipine were appeared unchanged when used with or in combination with the polymer. The above interpretational data clearly states that there is no interaction between the drug and polymer. Therefore, it can be concluded that the drug and Polymer are compatible as shown in FTIR studies.

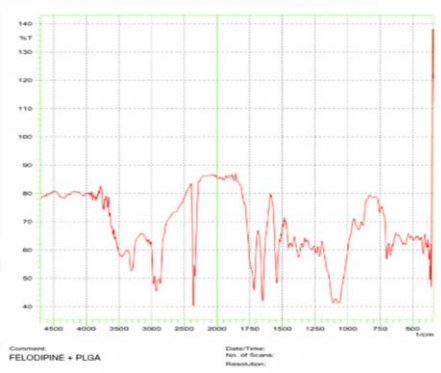

Figure 5: FTIR of Felodipine + PLGA

Table 5: Peak table with principles peak of Felodipine

S. No.	Functional Group	Theoretical Peak (cm^{-1})	Practical Peak (cm^{-1})
1.	N–H Stretch (Amide)	3300–3500	3449.53
2.	C–H Stretch (Aliphatic)	2950–2850	2860.81
3.	C=O Stretch (Carboxyl & Amide)	1750–1680	1721.04
4.	N–H Bend (Amide II)	1600–1550	1547.28
5.	C–H Bending (Alkanes)	1500–1400	1461.70
6.	C–N Stretch (Amide)	1250–1050	1188.20
7.	C–H Bending (Aromatic)	1000–900	963.07
8.	C–H Out-of-Plane Bending (Aromatic)	750–700	743.07

B. Formulation Studies for Polymeric Nanoparticles

Table9: Formulation of Polymeric Nanoparticles

Formulation	Felodipine (mg)	PLGA (mg)	Acetone (mL)	PVA (1% w/v in water, mL)	Cryoprotectant (Mannitol, 5% w/v)
F1	10	50	10	100	5% w/v
F2	10	100	10	100	5% w/v
F3	10	150	10	100	5% w/v
F4	10	200	10	100	5% w/v
F5	10	250	10	100	5% w/v

C. Characterization of Polymeric Nano Particles

1. Physical Appearance

The prepared felodipine-loaded polymeric nanoparticles were visually examined for their physical appearance. The formulations appeared as a uniform, milky white colloidal dispersion without any visible aggregates, clumps, or sedimentation. The suspension was found to be stable with no signs of phase separation throughout the observation period. The nanoparticles showed good dispersibility in aqueous medium, indicating efficient stabilization by the surfactant (PVA). The appearance was smooth and homogeneous, suggesting successful formation of nanoparticles by the nanoprecipitation method. These observations confirmed that the method employed was suitable for producing stable polymeric nanoparticles with acceptable physical properties.

2. Particles size and Zeta Potential of Polymeric Nanoparticle

At a controlled temperature of 25°C, the particle sizes of Polymeric Nanoparticles were measured for all the prepared formulations, labeled F1 through F5. Among these, formulation F4 exhibited the smallest particle size, indicating superior results in terms of nanoscale size optimization. For the particle size analysis, a diluted dispersion of each Polymeric Nanoparticle formulation was prepared and transferred into a clean cuvette. This cuvette was then carefully placed into the instrument's designated cuvette holder for measurement. The particle size was determined using the Litesizer 500, a zeta sizer software known for its precision in nanoparticle characterization.

The particles size results for each formulation are summarized in Table 5.10. Specifically, formulation F1 had a particle size of 240.25 nm, F2 showed 235.31 nm, F3 recorded 244.52 nm, F4 demonstrated the smallest diameter at 254.4 nm, F5 was measured at 234.15 nm. As evidenced by these results, formulation F4 had the smallest average particle diameter, suggesting better stability and potential bioavailability among the tested formulations.

In addition to particle size, the zeta potential of each formulation was analyzed to assess the stability of the nanoparticles. These zeta potential results are presented graphically in Figure 6, providing further insight into the electrostatic stability of the Polymeric Nanoparticles. The zeta potential results of formulation are shown in figure 7.

Table 10: Particle Size and Zeta Potential of Polymeric Nanoparticles

Formulation Code	Particle Size (nm)	Zeta Potential (mV)
F1	240.25	-10.9
F2	235.31	-16.5
F3	244.52	16.2
F4	254.40	-13.7
F5	234.15	-11.8

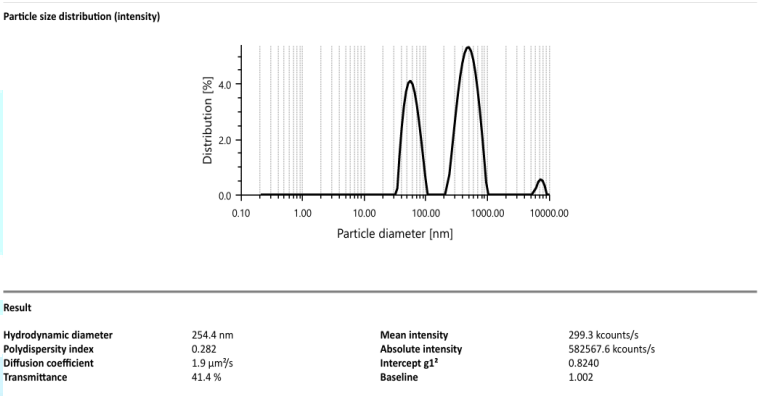

Figure 6: Particles Size of Polymeric Nanoparticles formulation

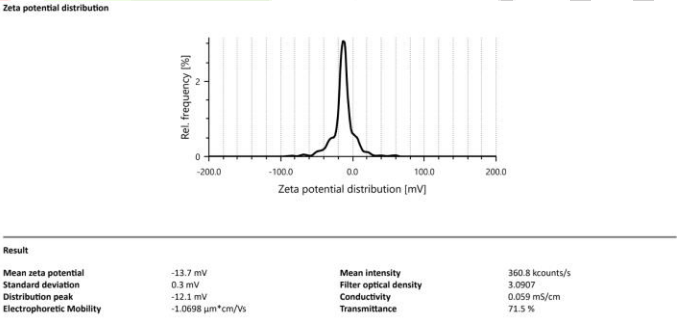

Figure 7: Zeta Potential of Polymeric Nanoparticles formulation

3. Scanning electron microscopy (SEM):

All Polymeric Nanoparticle formulations were thoroughly characterized for their morphological properties using Scanning Electron Microscopy (SEM). Among the various formulations tested, formulation F4 exhibited the most promising results in terms of particle shape and size. The SEM analysis provided clear visual evidence that the particles were uniformly distributed, with minimal aggregation. Notably, the particles of formulation F4 were observed to possess a nearly spherical morphology, which is considered ideal for improved stability and drug delivery performance. Furthermore, the particle size was found to be within the nanometric range,

indicating successful nanoformulation. These findings are visually represented in Figure 8, which showcases the well-defined, spherical nature of the nanoparticles in the F4 formulation.

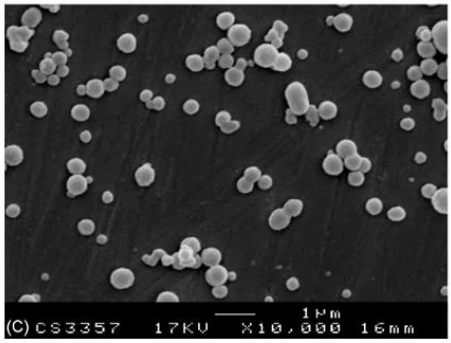

Figure 8: SEM of Polymeric Nanoparticles

4. PH Determination

The pH values of all Polymeric Nanoparticles formulations were measured, and the results are presented in Table 11. It was observed that the pH of each formulation was below 7, indicating that they are mildly acidic and therefore suitable for oral administration.

Table 11: pH determination of Polymeric Nanoparticles formulation

Sl. No.	Formulation	pH
1.	F1	4.6
2.	F2	4.7
3.	F3	4.7
4.	F4	4.6
5.	F5	4.6

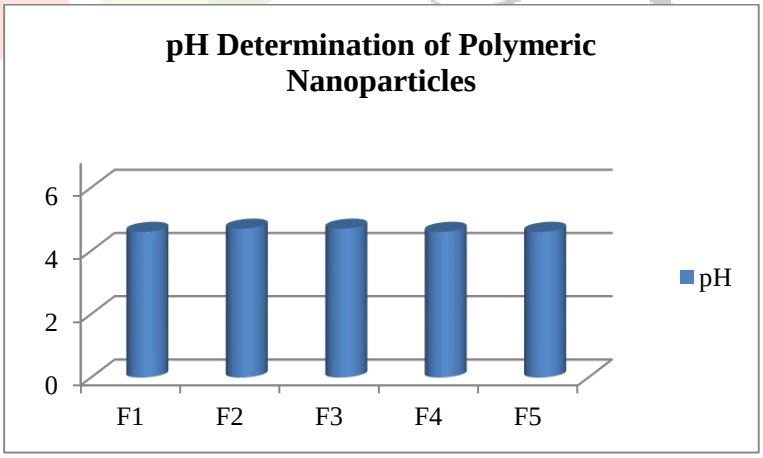

Figure 9: pH of Polymeric Nanoparticles formulations

5. Drug Content and Drug Entrapment Determination

The drug content and drug entrapment efficiency of all the prepared formulations were thoroughly evaluated, and the results indicated that both parameters fell within the range of 72.3% to 85.5%. These findings, which are comprehensively presented in Table 12, suggest that the formulations were capable of incorporating and retaining a substantial amount of the active pharmaceutical ingredient. This range reflects a consistent and satisfactory performance across the various formulations tested, highlighting the effectiveness of the formulation process in achieving desirable drug loading and retention characteristics.

Table 5.12: Drug Content and drug entrapment of Felodipine Polymeric Nanoparticle

S. No.	Formulation Code	Drug Content (%)	Drug Entrapment (%)
1	F1	74.7	72.2
2	F2	72.35	69.78
3	F3	76.6	76.78
4	F4	85.6	86.4
5	F5	79.6	77.8

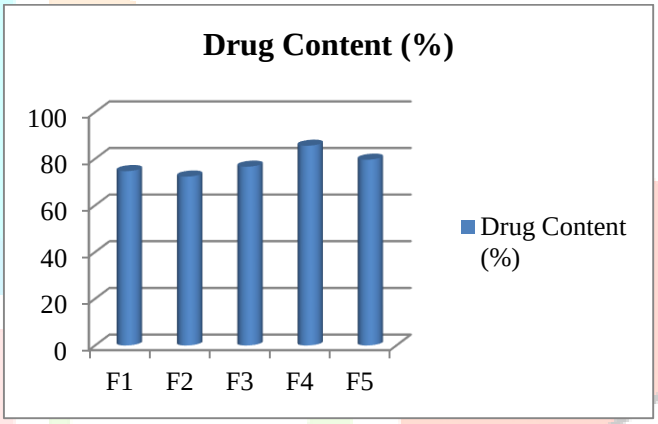

Figure 10: Drug Content of Polymeric Nanoparticle Formulations

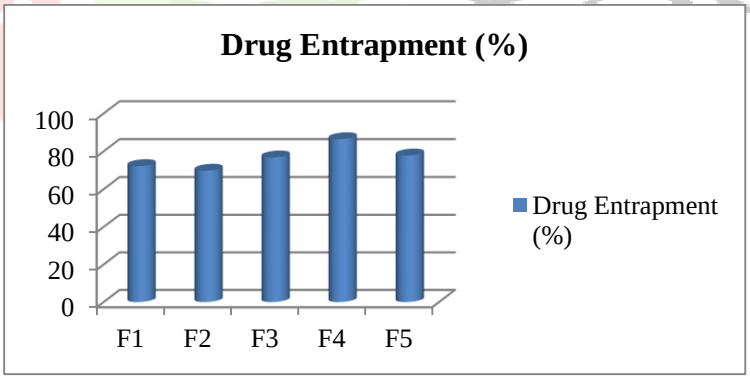

Figure 11: Drug Entrapment Efficacy of Polymeric Nanoparticle Formulations

6. *In-Vitro* Drug Release:

Tables 5.13 are displaying the Felodipine in-vitro release characteristics for each of its several Polymeric Nanoparticle formulations. At the conclusion of the experiment, it was noted that all formulations had inflated as a result of diffusing medium penetrating into the gel matrix, which broke the gel matrix and allowed the drug to be released. Formulations F4 were shown to have a greater drug release. This results in a less packed gel matrix that is more easily broken, which increases the drug's release. At the conclusion of eight hours, the formulations F4 demonstrated cumulative drug release of 92.9%, as seen in Table 14. For every composition, an initial burst release and a control release were noted. Linear plots were produced when zero-order kinetics was used to plot the data. The zero-order values, which ranged from 0.997 to 0.994, had the highest regression coefficient values, indicating that zero-order kinetics was the mechanism of release for all formulations.

Table 5.13: Cumulative Drug Release of Felodipine from Polymeric Nanoparticle Formulations

S. No.	Time (Hr)	F1	F2	F3	F4	F5
1	1	10.7	9.7	10.6	11.8	9.4
2	2	17.3	15.9	21.3	22.6	20.1
3	3	28.9	26.1	33.1	34.3	32.8
4	4	39.1	39.8	44.5	46.4	43.1
5	5	47.8	51.5	54.7	55.7	54.3
6	6	59.2	63.8	67.1	68.3	67.3
7	7	68.2	76.8	77.1	79.2	78.3
8	8	78.1	87.7	89.5	92.9	86.9

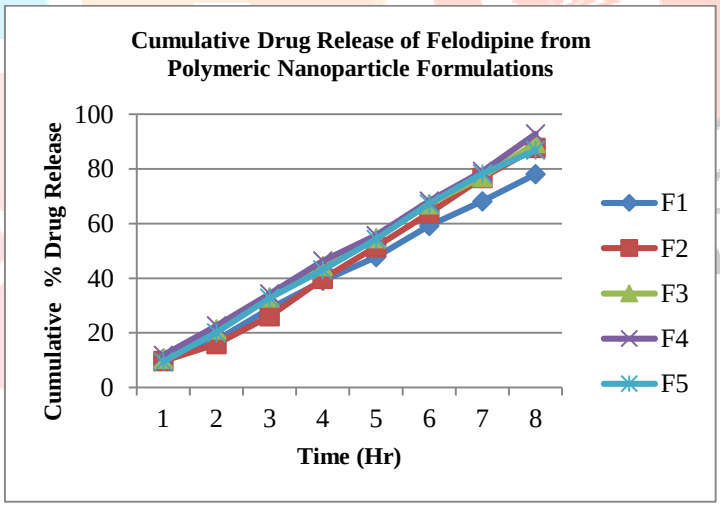

Figure 12: Cumulative Drug Release of Felodipine from Polymeric Nanoparticle Formulations

Table 14: Drug release kinetics of Polymeric Nanoparticle Formulations

Formulation Code	Drug release kinetics, correlation coefficient "R2"			
	Zero Order Model	First Order Model	Higuchi Model	Best Fit Model
	R2	R2	R2	
F1	0.9931	0.8543	0.8356	Zero Order
F2	0.9921	0.8131	0.8468	Zero Order
F3	0.9972	0.8576	0.9135	Zero Order
F4	0.9943	0.9126	0.8545	Zero Order
F5	0.9932	0.9245	0.8957	Zero Order

5.1.3.7. Stability Studies:

A comprehensive three-month accelerated stability study was carried out to assess the short-term stability of the Polymeric Nanoparticle formulation, specifically the F4 formulation. This study was performed under controlled environmental conditions, maintained at a temperature of 40°C and a relative humidity of 75%, which are standard conditions recommended for accelerated stability testing. Throughout the duration of the study, various physicochemical parameters of the formulation were closely monitored and evaluated at predetermined intervals.

The parameters assessed included drug content, physical appearance, pH, and in vitro drug release profile. These tests were conducted to determine whether the formulation maintained its integrity, efficacy, and overall quality over the storage period. After three months of storage under these stress conditions, the PNs (F4) formulation exhibited no significant changes in its physical characteristics it retained a homogenous consistency and its original creamy white color, indicating good physical stability.

Quantitative analysis revealed that the drug content remained at 85.6%, suggesting minimal degradation or loss of the active pharmaceutical ingredient (API) during the testing period. Additionally, the in vitro drug release study showed a drug release percentage of 85.9%, further supporting the formulation's capability to consistently release the drug even after prolonged exposure to accelerated storage conditions.

These findings, summarized in Table 5.15, demonstrate that the F4 formulation of PNs exhibited satisfactory stability characteristics over the three-month period. The formulation maintained its desired physical and chemical properties, thereby indicating its potential suitability for long-term storage and commercial development.

Table 15: Stability Studies of Felodipine Nanoparticle

Formulation	Appearance	% Drug Content	% Drug Release
F4	Whitish Colour	85.6	85.9

- **Discussion**

Preformulation confirmed Felodipine's identity, purity, and physicochemical properties. Poor aqueous solubility (log P 4.1) supported nanoparticle delivery. FTIR showed no drug–excipient interaction with PLGA. Nanoparticles formed uniform dispersions, with particle size 234–254 nm; F4 had smallest size and stable zeta potential (–13.7 mV). SEM confirmed spherical morphology. Formulations were mildly acidic (pH 4.6–4.7), with drug content and entrapment efficiency 72–85%, highest in F4 (85.6%, 86.4%). In vitro release showed sustained zero-order kinetics, with F4 achieving 92.9% release in 8 h. Stability studies confirmed F4's robustness, highlighting PLGA nanoparticles' potential to enhance Felodipine's oral bioavailability.

CONCLUSION:

This study developed and evaluated Felodipine-loaded polymeric nanoparticles using the nanoprecipitation method with PLGA and PVA. Preformulation confirmed drug identity, purity, and compatibility with excipients. The nanoparticles were stable, uniformly spherical, and nanosized (234–254 nm) with acceptable pH (4.6–4.7) and zeta potential. Among the formulations, F4 showed superior performance with highest drug content (85.6%), entrapment efficiency (86.4%), and sustained release (92.9% over 8 h) following zero-order kinetics. Stability studies confirmed robustness under accelerated conditions. Overall, Felodipine-loaded PLGA nanoparticles demonstrated improved solubility, controlled release, and potential for enhanced oral bioavailability, making them a promising alternative to conventional dosage forms.

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