# FORMULATION AND EVALUATION OF NANOEMULSION-BASED DELIVERY OF AN ANTICANCER DRUG

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## Abstract

The present study focused on the development and evaluation of a nanoemulsion-based delivery system of Erlotinib to enhance its solubility, dissolution, and bioavailability. Nanoemulsions were prepared by the ultrasonication method using Capryol 90, Tween 80, and PEG 400/propylene glycol as oil, surfactant, and co-surfactant, respectively. Preformulation studies confirmed suitable physicochemical and flow properties of the drug for lipid-based delivery. Ten formulations (F1–F10) were optimized and evaluated for droplet size, PDI, zeta potential, drug content, encapsulation efficiency, in vitro release, and stability. The optimized formulations showed nanosized droplets (107–145 nm), low PDI (0.16–0.23), high drug content (95.5–97.8%), and good encapsulation efficiency (90.8–94.1%). In vitro studies demonstrated significantly enhanced and sustained drug release (up to 97–99% in 24 h) compared to the marketed product (75%). Stability studies confirmed minimal changes in key parameters, indicating good formulation stability. Overall, the developed nanoemulsion significantly improved the solubility, dissolution, and release profile of Erlotinib, suggesting enhanced potential for oral bioavailability and anticancer efficacy.

**Keywords:** *Erlotinib, Nanoemulsion, Poor solubility, Bioavailability enhancement, Ultrasonication, Capryol 90*

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## 1. Introduction

Cancer remains one of the leading causes of mortality worldwide despite significant advances in diagnosis and treatment (Bray et al., 2020). Many anticancer drugs exhibit poor aqueous solubility and low oral bioavailability, leading to reduced therapeutic efficacy and inconsistent absorption (Torchilin, 2012). Drugs belonging to Biopharmaceutical Classification System (BCS) Class II, such as Erlotinib, are particularly affected by dissolution-related limitations (Aulton & Taylor, 2018). Therefore, the development of advanced drug delivery systems to improve solubility and bioavailability has become an important area of pharmaceutical research.

Erlotinib is an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor widely used in the treatment of non-small cell lung cancer and pancreatic cancer (Shepherd et al., 2005). However, its clinical performance is limited by poor water solubility, pH-dependent dissolution, and low oral bioavailability (Budha et al., 2016). These limitations may reduce therapeutic effectiveness and necessitate higher doses, increasing the risk of adverse effects.

Nanoemulsion-based drug delivery systems have gained considerable attention for improving the solubility, dissolution, and absorption of poorly soluble drugs (Gupta et al., 2016). Nanoemulsions are colloidal dispersions with droplet sizes generally ranging from 20–200 nm, offering a large surface area for enhanced drug dissolution and absorption (McClements, 2012). They also provide advantages such as improved stability, controlled drug release, enhanced permeability, and better bioavailability (Shah et al., 2010). The use of suitable oils, surfactants, and co-surfactants plays a crucial role in the development of stable nanoemulsions with uniform droplet distribution and high drug loading (Shakeel et al., 2009). Therefore, the present study aimed to formulate and evaluate an Erlotinib-loaded nanoemulsion using suitable lipid excipients to improve its solubility, dissolution behavior, and bioavailability. The developed formulations were evaluated for physicochemical properties, droplet size, zeta potential, encapsulation efficiency, in vitro drug release, and stability to assess their potential for enhanced anticancer drug delivery.

## 2. Methodology

### 2.1 Selection of Drug and Excipients

Erlotinib, a tyrosine kinase inhibitor used in the treatment of pancreatic and non-small cell lung cancer, will be selected as the model anticancer drug for the development of a nanoemulsion formulation due to its poor aqueous solubility and low bioavailability. The nanoemulsion system is intended to enhance its solubility, dissolution, and therapeutic

efficacy. Suitable oils, surfactants, and co-surfactants will be selected based on their drug solubilization capacity, emulsification efficiency, safety, and compatibility with Erlotinib. Non-ionic surfactants with appropriate HLB values will be preferred to ensure stability and reduced toxicity, while co-surfactants will be used to improve interfacial flexibility and facilitate the formation of stable nanosized droplets.

## 2.2 Preformulation Studies

### 2.2.1 Organoleptic and Physicochemical Evaluation

- **Color**

The color of Erlotinib will be evaluated during preformulation studies as part of the organoleptic examination. A small quantity of the drug will be placed on a clean glass slide and observed under daylight to assess its physical appearance, identity, and purity. This preliminary evaluation helps in identifying any possible impurities or signs of degradation.

- **Odor**

The odor of Erlotinib will be evaluated during preformulation studies as part of the organoleptic examination. A small quantity of the drug will be placed on a clean, dry watch glass and carefully examined to detect any characteristic odor. This evaluation helps identify possible degradation, contamination, and provides preliminary information regarding the purity and quality of the drug substance.

- **Appearance**

The appearance of Erlotinib will be examined during preformulation studies as part of the organoleptic evaluation. A small quantity of the drug will be placed on a clean glass slide and visually inspected under normal daylight to observe its physical characteristics and overall appearance. This evaluation provides preliminary information about the physical nature of the drug and helps detect any visible impurities or irregularities.

- **Texture**

The texture of Erlotinib will be evaluated during preformulation studies as part of the organoleptic examination. A small quantity of the drug will be gently rubbed between the fingers to assess its physical feel, consistency, and surface characteristics. This evaluation provides preliminary information about the physical nature and uniformity of the drug particles, which may influence processing and formulation development. development.

- **Melting point**

The melting point of Erlotinib will be determined during preformulation studies using the capillary tube method. A small quantity of finely powdered drug will be filled into a sealed capillary tube and placed in a melting point apparatus. The temperature at which the drug starts melting and completely liquefies will be recorded. Melting point determination helps in confirming the identity and purity of the drug, while any significant deviation from the reported range may indicate the presence of impurities.

- **Solubility study**

The solubility of Erlotinib was evaluated during preformulation studies in various solvents, including distilled water, methanol, ethanol, and phosphate buffer solution. Excess drug was added separately to each solvent and shaken in stoppered vials using a mechanical shaker for 24 hours at room temperature to achieve equilibrium. The samples were then filtered, suitably diluted, and analyzed using a UV-visible spectrophotometer to determine drug concentration. The results helped in selecting appropriate solvents and excipients for nanoemulsion formulation development.

- **Partition coefficient**

The partition coefficient of Erlotinib will be determined using the n-octanol–water system to evaluate its lipophilicity and distribution behavior. Equal volumes of n-octanol and distilled water will be equilibrated in a separating funnel for 24 hours. An accurately weighed amount of Erlotinib will be added and shaken thoroughly to allow distribution between the two phases. After phase separation, the aqueous layer will be collected, diluted, and analyzed using a UV–Visible spectrophotometer. The partition coefficient (log P) will be calculated from the ratio of drug concentration in the organic phase to the aqueous phase. This study helps assess the suitability of Erlotinib for lipid-based nanoemulsion formulations.

### 2.2.2 Flow Properties of Powder

- **Bulk density**

The bulk density of Erlotinib will be determined during preformulation studies by gently filling a known quantity of drug powder into a graduated measuring cylinder and recording the bulk volume occupied. Bulk density will be calculated using the formula:

$$\textbf{Bulk Density} = \frac{\textbf{Weight of Powder}}{\textbf{Bulk Volume}}$$

This study provides preliminary information about the flow and packing properties of the drug powder, which are important for formulation development.

- **Tapped density**

The tapped density of Erlotinib will be determined during preformulation studies by mechanically tapping a graduated measuring cylinder containing a known quantity of drug powder until a constant volume is obtained. The tapped density will be calculated using the formula:

$$\textbf{Tapped Density} = \frac{\textbf{Weight of Powder}}{\textbf{Tapped Volume}}$$

This evaluation helps assess the packing and compressibility characteristics of the drug powder and aids in determining flow property parameters such as Carr's index and Hausner's ratio.

- **Carr's Index**

Carr's Index of Erlotinib will be determined during preformulation studies to evaluate the compressibility and flow properties of the drug powder. The value will be calculated using the bulk density and tapped density of the powder according to the following formula:

$$\textbf{Carr's Index}\ (\%)\} = \frac{\{\textbf{Tapped Density}\} - \{\textbf{Bulk Density}\}}{\textbf{Tapped Density}} * \textbf{100}$$

This study helps in assessing the flow behavior and handling characteristics of the powder during formulation development.

- **Hausner's ratio**

The Hausner's ratio of Erlotinib will be determined during preformulation studies to evaluate the cohesion and flow properties of the drug powder. The ratio will be calculated using the bulk density and tapped density values according to the following formula:

$$\textbf{Hausner Ratio} = \frac{\textbf{Tapped Density}}{\textbf{Bulk Density}}$$

This parameter helps assess the flowability and interparticle friction of the powder, where lower values indicate good flow properties and higher values indicate poor flow behavior.

- **Angle of repose**

The angle of repose of Erlotinib will be determined during preformulation studies using the fixed funnel method to evaluate the flow properties of the drug powder. The powder will be allowed to flow freely through a funnel to form a conical heap, and the height (h) and radius (r) of the heap will be measured. The angle of repose (θ) will be calculated using the following formula:

$$\boldsymbol{\theta = \tan^{-1}\left(\frac{h}{r}\right)}$$

This study provides information about the flowability and handling characteristics of the powder during formulation development.

**2.3 Formulation of Nanoemulsion**

**2.3.1 Solubility Study of Drug in Oils, Surfactants, and Co-surfactants**

The solubility of Erlotinib in various oils, surfactants, and co-surfactants will be evaluated to select suitable excipients for nanoemulsion formulation development. An excess amount of the drug will be added separately to different excipients, vortexed, and shaken in a mechanical shaker for 24 hours at room temperature. The samples will then be centrifuged, filtered, and suitably diluted, and the drug concentration will be analyzed using a UV-visible spectrophotometer. The excipients showing the highest solubilizing capacity will be selected for further formulation studies to ensure better drug loading, stability, and nanoemulsion performance.

**2.3.2 Preparation of nanoemulsion**

The Erlotinib nanoemulsion will be prepared using the high-energy ultrasonication method. Erlotinib will be dissolved in the selected oil phase, followed by the addition of surfactant and co-surfactant with continuous stirring to obtain a uniform mixture. The aqueous phase containing distilled water will then be added gradually to form a coarse emulsion. The coarse emulsion will be subjected to probe ultrasonication for a specific time to reduce the droplet size to the nanoscale range and obtain a stable nanoemulsion. The prepared formulation will be visually examined for clarity and absence of phase separation before further characterization studies.

**2.3.3 Optimization of formulation variables**

Formulation variables such as oil-to-surfactant ratio, surfactant-to-co-surfactant ratio, and drug concentration will be optimized to develop a stable Erlotinib nanoemulsion with small droplet size, uniform dispersion, and good physical stability. Different formulations will be prepared by varying the concentrations of formulation components and evaluated for clarity, homogeneity, phase separation, droplet size, polydispersity index (PDI), and stability. The optimized formulation showing minimum droplet size, uniform distribution, and maximum stability will be selected for further characterization studies.

**2.3.4 Selection of final optimized formulation**

After preparing different Erlotinib nanoemulsion formulations with varying compositions, the final optimized formulation will be selected based on evaluation parameters such as

clarity, homogeneity, and absence of phase separation. Further characterization including droplet size, polydispersity index (PDI), zeta potential, drug content, and stability will be performed. The formulation showing minimum droplet size, uniform distribution, high stability, and maximum drug content will be selected as the optimized nanoemulsion for further characterization and in vitro drug release studies.

**Table 1: Composition of Nanoemulsion Formulations**

| Formulation Code | Drug (mg) | Oil (Capryol 90) (%) | Surfactant (Tween 80) (%) | Co-surfactant (Propylene Glycol) (%) | Distilled Water (%) |
|---|---|---|---|---|---|
| F1 | 10 | 5 | 35 | 15 | 45 |
| F2 | 10 | 7 | 33 | 15 | 45 |
| F3 | 10 | 8 | 32 | 15 | 45 |
| F4 | 10 | 10 | 30 | 15 | 45 |
| F5 | 10 | 12 | 28 | 15 | 45 |
| F6 | 10 | 15 | 25 | 15 | 45 |
| F7 | 10 | 10 | 35 | 10 | 45 |
| F8 | 10 | 10 | 33 | 12 | 45 |
| F9 | 10 | 10 | 30 | 15 | 45 |
| F10 | 10 | 10 | 28 | 17 | 45 |

## 2.4 Characterization of Nanoemulsion

### 2.4.1 Droplet Size and Polydispersity Index (PDI)

The droplet size and polydispersity index (PDI) of the Erlotinib nanoemulsion will be determined using a dynamic light scattering (DLS)-based particle size analyzer to evaluate droplet distribution and homogeneity. A small quantity of the nanoemulsion will be diluted with distilled water and analyzed at room temperature. The mean droplet size will be recorded in nanometers, while the PDI will indicate the uniformity of droplet distribution. Smaller droplet size and lower PDI values reflect better homogeneity, stability, and suitability of the nanoemulsion for further studies.

### 2.4.2 Zeta Potential Measurement

The zeta potential of the Erlotinib nanoemulsion will be measured to evaluate the surface charge and stability of the formulation. The analysis will be performed using a zeta

potential analyzer based on the electrophoretic light scattering method. A diluted sample of the nanoemulsion will be analyzed at room temperature, and the zeta potential value will be recorded in millivolts (mV). Higher zeta potential values generally indicate better stability due to increased electrostatic repulsion between droplets, which helps prevent aggregation and coalescence.

### 2.4.3 Drug Content

The drug content of the Erlotinib nanoemulsion will be determined to ensure uniform drug distribution and accuracy of the formulation process. A measured quantity of the nanoemulsion will be diluted with a suitable solvent such as methanol, sonicated, filtered, and analyzed using a UV-visible spectrophotometer at the selected wavelength of Erlotinib. The drug concentration will be calculated using the calibration curve, and drug content will be determined using the following formula:

**Drug Content (%) = (Actual amount of drug present / Theoretical amount of drug) × 100**

The determination of drug content will ensure the consistency, quality, and reliability of the developed nanoemulsion formulation.

### 2.4.4 Encapsulation Efficiency

The encapsulation efficiency of the Erlotinib nanoemulsion will be determined to evaluate the amount of drug successfully entrapped within the nanoemulsion system. The formulation will be centrifuged to separate the free drug, and the supernatant will be analyzed using a UV-visible spectrophotometer to determine the concentration of unentrapped drug. The encapsulation efficiency will be calculated using the following formula:

**Encapsulation Efficiency (%) = [(Total drug − Free drug) / Total drug] × 100**

This study provides information about the drug-loading capacity and effectiveness of the nanoemulsion system.

### 2.4.5 pH Determination

The pH of the Erlotinib nanoemulsion will be measured using a calibrated digital pH meter to evaluate the stability and compatibility of the formulation. The pH meter will be calibrated with standard buffer solutions before analysis, and the electrode will be immersed in the nanoemulsion sample at room temperature until a stable reading is obtained. The recorded pH values will help assess the suitability, stability, and safety of the developed nanoemulsion formulation.

### 2.4.6 Viscosity Measurement

The viscosity of the Erlotinib nanoemulsion will be determined using a Brookfield viscometer to evaluate the consistency and flow behavior of the formulation. A suitable quantity of the nanoemulsion will be placed in a sample container, and the spindle of the viscometer will be immersed in the formulation. The measurement will be carried out at room temperature and constant rotational speed, and the viscosity will be recorded in centipoises (cP). This study helps assess the stability, flow properties, and handling characteristics of the nanoemulsion formulation.

### 2.5 In Vitro Drug Release Study

The in vitro drug release study of the Erlotinib nanoemulsion will be carried out using the dialysis membrane diffusion method to evaluate the release pattern of the drug from the formulation. A known quantity of the nanoemulsion will be placed in a pre-soaked dialysis membrane and immersed in phosphate buffer (pH 7.4) maintained at 37 ± 0.5 °C with continuous stirring. Samples will be withdrawn at predetermined time intervals, replaced with fresh medium, and analyzed using a UV-visible spectrophotometer at the characteristic wavelength of Erlotinib. The cumulative percentage drug release will be calculated and plotted against time to determine the release profile of the nanoemulsion formulation.

### 2.6 Stability Studies

The stability study of the optimized Erlotinib nanoemulsion will be conducted according to ICH guidelines to evaluate its physical and chemical stability under different storage conditions. The formulation will be stored in tightly sealed containers at room temperature and accelerated conditions for a specified period. At predetermined intervals, samples will be evaluated for parameters such as droplet size, polydispersity index (PDI), zeta potential, pH, viscosity, and drug content. The study will help determine the stability, shelf life, and suitability of the nanoemulsion formulation during storage.

## 3. Results

### 3.1 Preformulation Studies

### 3.1.1 Organoleptic Evaluation

The organoleptic properties of Erlotinib were evaluated during preformulation studies to assess its physical characteristics and suitability for formulation development. The drug was observed as a white to slightly off-white, odorless, fine crystalline powder with a smooth and free-flowing texture. These observations indicated the purity, uniformity, and absence of visible impurities or degradation, confirming the suitability of Erlotinib for further pharmaceutical evaluation.

**Table 2: Organoleptic Evaluation of Erlotinib**

| Parameter | Observation |
|---|---|
| Color | White to slightly off-white |
| Odor | Odorless |
| Appearance | Fine crystalline powder, uniform |
| Texture | Smooth, free-flowing |

### 3.1.2 Physicochemical Evaluation

#### 3.1.2.1 Melting point

The melting point of Erlotinib was determined to confirm its identity and purity. The drug showed a sharp melting range of 223–225 °C, which is consistent with reported literature values for pure Erlotinib. The narrow melting range indicated the absence of significant impurities and confirmed the purity of the drug sample. This study also provided important information regarding the thermal behavior and stability of the drug, confirming its suitability for further preformulation and nanoemulsion formulation studies.

**Table 3: Melting Point of Erlotinib**

| Parameter | Observation |
|---|---|
| Melting Point | 223–225 (°C) |

#### 3.1.2.2 Solubility study

The solubility of Erlotinib was evaluated in various solvents to understand its dissolution behavior for nanoemulsion development. The drug showed very low solubility in distilled water (0.05 mg/mL) and phosphate buffer pH 7.4 (0.08 mg/mL), indicating poor aqueous solubility. In contrast, it exhibited higher solubility in organic solvents such as ethanol (4.9 mg/mL) and methanol (5.8 mg/mL), confirming its lipophilic nature. These findings support the selection of suitable oils, surfactants, and co-surfactants for nanoemulsion formulation to improve drug loading, stability, and bioavailability.

**Table 4: Solubility of Erlotinib in Various Solvents**

| Solvent | Solubility (mg/mL) | Observation |
|---|---|---|
| Distilled Water | 0.05 | Poorly soluble |
| Methanol | 5.8 | Highly soluble |
| Ethanol | 4.9 | Highly soluble |
| Phosphate Buffer (pH 7.4) | 0.08 | Poorly soluble |

### 3.1.2.3 Partition coefficient

The partition coefficient of Erlotinib was determined using the n-octanol–water system to evaluate its lipophilicity and distribution behavior. The obtained log P value of 2.7 indicated moderate lipophilicity, which is favorable for incorporation into lipid-based drug delivery systems such as nanoemulsions. This balance suggests that Erlotinib can efficiently partition into the oil phase while still allowing adequate release into aqueous biological fluids, supporting effective therapeutic performance. These findings further aid in the selection of suitable formulation components to develop a stable and efficient nanoemulsion system.

**Table 5: Partition Coefficient of Erlotinib**

| Parameter | Observation | Interpretation |
|---|---|---|
| Partition Coefficient (log P) | 2.7 | Indicates moderate lipophilicity, suitable for lipid-based formulations |

## 3.2 Flow Properties of Powder

### 3.2.1 Bulk density

The bulk density of Erlotinib was determined to evaluate its packing properties and predict flow behavior, which are important for formulation development. The bulk density values of the ten formulations (F1–F10) ranged from 0.44 ± 0.01 to 0.47 ± 0.02 g/mL, while the marketed Erlotinib powder showed a value of 0.46 ± 0.01 g/mL. These comparable results indicate uniform packing behavior and good flow characteristics of the powder, supporting accurate dosing and consistent blending. The slight variations among formulations may be due to differences in particle size or morphology. Overall, the findings confirm the suitability of Erlotinib powder for further formulation development.

**Table 6: Bulk Density of Erlotinib**

| Formulation | Bulk Density (g/mL) |
|---|---|
| F1 | 0.45 ± 0.01 |
| F2 | 0.46 ± 0.01 |
| F3 | 0.44 ± 0.02 |
| F4 | 0.47 ± 0.01 |
| F5 | 0.45 ± 0.01 |
| F6 | 0.46 ± 0.01 |
| F7 | 0.44 ± 0.01 |
| F8 | 0.45 ± 0.01 |
| F9 | 0.46 ± 0.02 |
| F10 | 0.45 ± 0.01 |
| **Marketed Erlotinib** | 0.46 ± 0.01 |

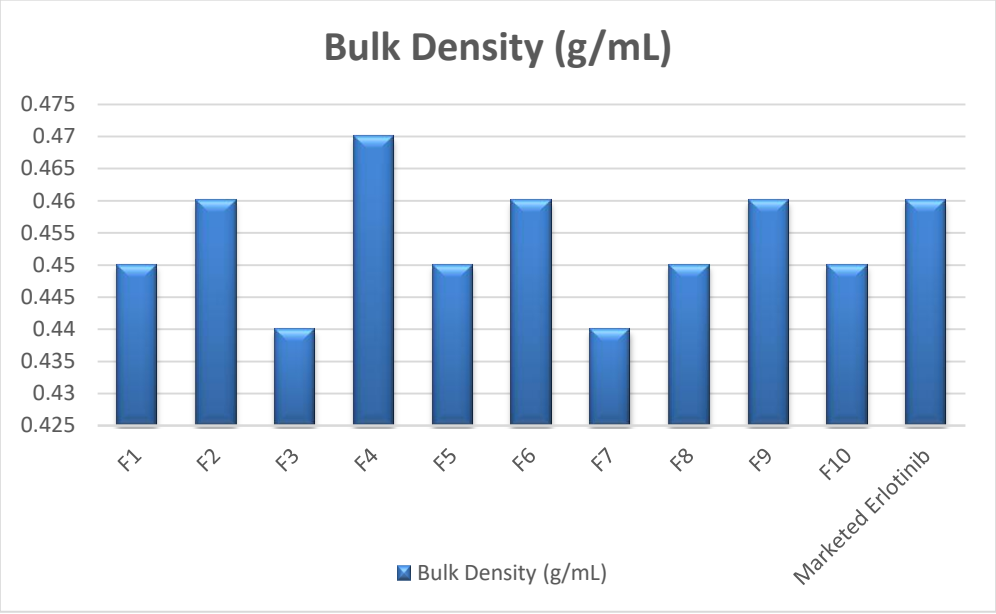


**Fig 1: Bulk Density (g/mL)**

### 3.2.2 Tapped density

The tapped density of Erlotinib powder was evaluated to assess its packing, compressibility, and flow behavior during preformulation studies. The marketed product showed a tapped density of 0.53 ± 0.01 g/mL, while the developed formulations (F1–F10) ranged from 0.51 ± 0.01 to 0.54 ± 0.01 g/mL. These comparable values indicate good packing efficiency and

uniform flow properties similar to the commercial product. The minimal variation among formulations suggests consistent particle characteristics, supporting reproducible processing and content uniformity. Overall, the results confirm the suitability of Erlotinib powder for further formulation development.

**Table 7: Tapped Density of Developed Formulations**

| Formulation | Tapped Density (g/mL) |
|---|---|
| F1 | 0.52 ± 0.01 |
| F2 | 0.53 ± 0.01 |
| F3 | 0.51 ± 0.02 |
| F4 | 0.54 ± 0.01 |
| F5 | 0.52 ± 0.01 |
| F6 | 0.53 ± 0.01 |
| F7 | 0.51 ± 0.01 |
| F8 | 0.52 ± 0.01 |
| F9 | 0.53 ± 0.02 |
| F10 | 0.52 ± 0.01 |
| **Marketed Erlotinib** | 0.53 ± 0.01 |

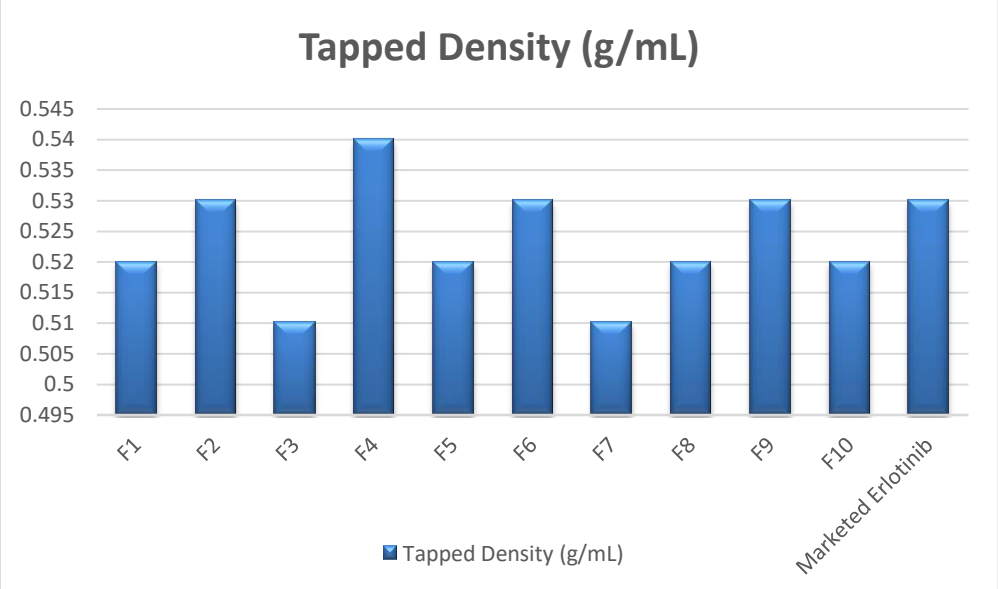


**Fig 2: Tapped Density (g/mL)**

### 3.2.3 Carr's Index

Carr's Index was calculated for the developed Erlotinib formulations to evaluate their flowability and compressibility. The values ranged from 13.0 ± 0.3% to 14.5 ± 0.6%, while

the marketed product showed a value of 13.5 ± 0.3%, indicating comparable flow characteristics. These results suggest good powder flow, uniform particle distribution, and efficient packing behavior across all formulations. The narrow variation further confirms consistent powder properties, supporting suitability for reliable processing and formulation development.

**Table 8: Tapped Density of Developed Formulations**

| Formulation | Carr's Index (%) |
|---|---|
| F1 | 13.5 ± 0.5 |
| F2 | 13.2 ± 0.4 |
| F3 | 14.5 ± 0.6 |
| F4 | 13.0 ± 0.3 |
| F5 | 13.8 ± 0.5 |
| F6 | 13.4 ± 0.4 |
| F7 | 14.2 ± 0.5 |
| F8 | 13.6 ± 0.4 |
| F9 | 13.3 ± 0.5 |
| F10 | 13.7 ± 0.4 |
| **Marketed Erlotinib** | 13.5 ± 0.3 |

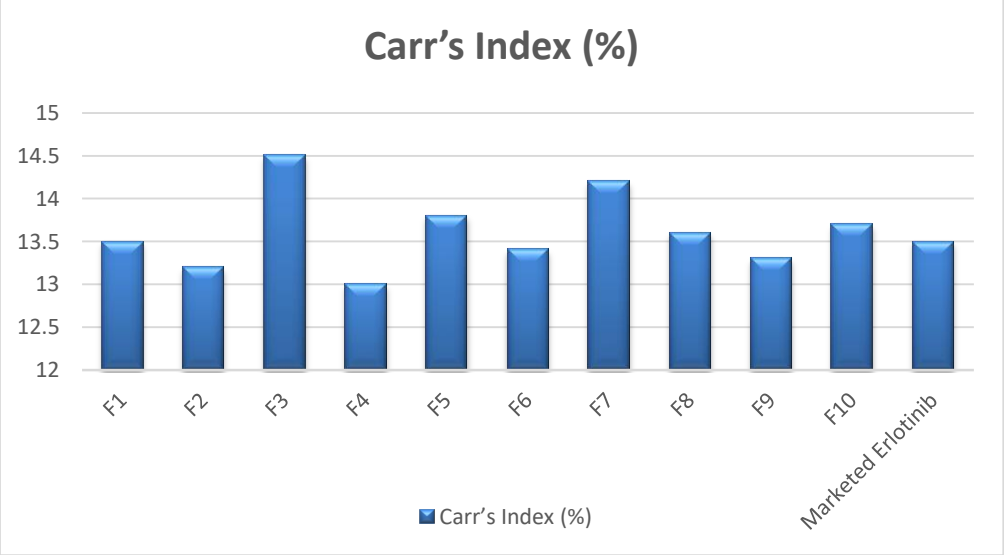


**Fig 3: Carr's Index (%)**

### 3.2.4 Hausner's ratio

Carr's Index and Hausner's Ratio were evaluated to assess the compressibility and flow behavior of the developed Erlotinib formulations. Carr's Index values ranged from 13.0 ± 0.3% to 14.5 ± 0.6%, while the marketed product showed 13.5 ± 0.3%, indicating good flow

properties. Similarly, Hausner's Ratio values ranged from 1.13 ± 0.01 to 1.17 ± 0.02, with the marketed formulation showing 1.15 ± 0.01, confirming low cohesiveness and satisfactory flowability. These findings suggest uniform particle distribution and consistent packing behavior, supporting reliable handling and formulation processing. Overall, the results confirm that the developed powders are suitable for further formulation development.

**Table 9: Hausner's Ratio of Developed Formulations**

| Formulation | Hausner's Ratio |
|---|---|
| F1 | 1.15 ± 0.02 |
| F2 | 1.14 ± 0.01 |
| F3 | 1.17 ± 0.02 |
| F4 | 1.13 ± 0.01 |
| F5 | 1.16 ± 0.02 |
| F6 | 1.15 ± 0.01 |
| F7 | 1.17 ± 0.02 |
| F8 | 1.15 ± 0.01 |
| F9 | 1.14 ± 0.01 |
| F10 | 1.16 ± 0.01 |
| **Marketed Erlotinib** | 1.15 ± 0.01 |

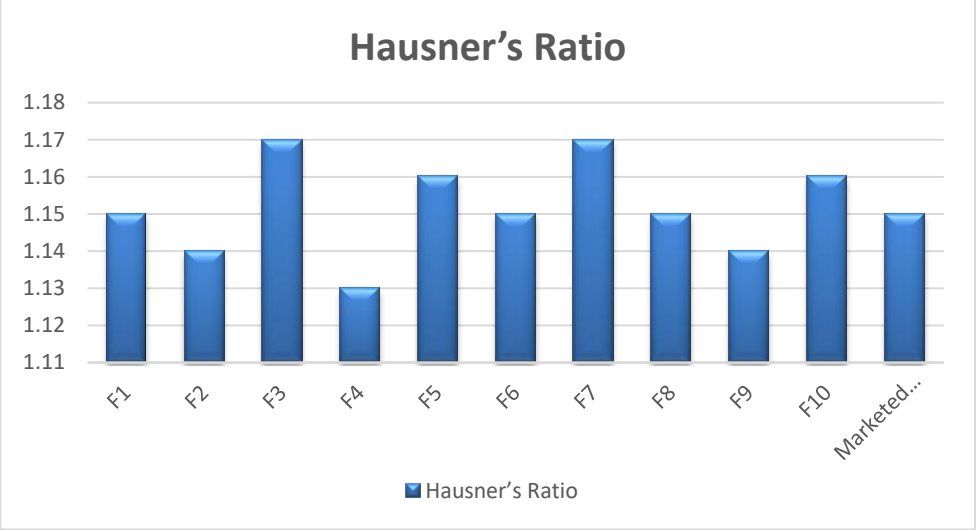


**Fig 4: Hausner's Ratio**

### 3.2.5 Angle of repose

Tapped density, Carr's Index, Hausner's Ratio, and angle of repose were evaluated to comprehensively assess the flow and packing properties of the developed Erlotinib formulations. The tapped density ranged from 0.51 ± 0.01 to 0.54 ± 0.01 g/mL, closely

matching the marketed product (0.53 ± 0.01 g/mL), indicating efficient particle packing. Carr's Index values (13.0 ± 0.3% to 14.5 ± 0.6%) and Hausner's Ratio (1.13 ± 0.01 to 1.17 ± 0.02) confirmed good flowability and low cohesiveness, comparable to the commercial formulation. The angle of repose ranged from 27.5 ± 0.5° to 28.2 ± 0.4°, further indicating excellent flow behavior similar to the marketed standard (27.8 ± 0.3°). Overall, these results demonstrate uniform particle distribution, good flow properties, and suitability of the developed formulations for further processing.

**Table 10: Angle of Repose of Developed Formulations**

| Formulation | Angle of Repose (°) |
|---|---|
| F1 | 27.5 ± 0.5 |
| F2 | 28.0 ± 0.4 |
| F3 | 27.8 ± 0.3 |
| F4 | 27.6 ± 0.5 |
| F5 | 28.2 ± 0.4 |
| F6 | 27.9 ± 0.3 |
| F7 | 28.0 ± 0.4 |
| F8 | 27.7 ± 0.5 |
| F9 | 27.6 ± 0.4 |
| F10 | 28.1 ± 0.4 |
| **Marketed Erlotinib** | 27.8 ± 0.3 |

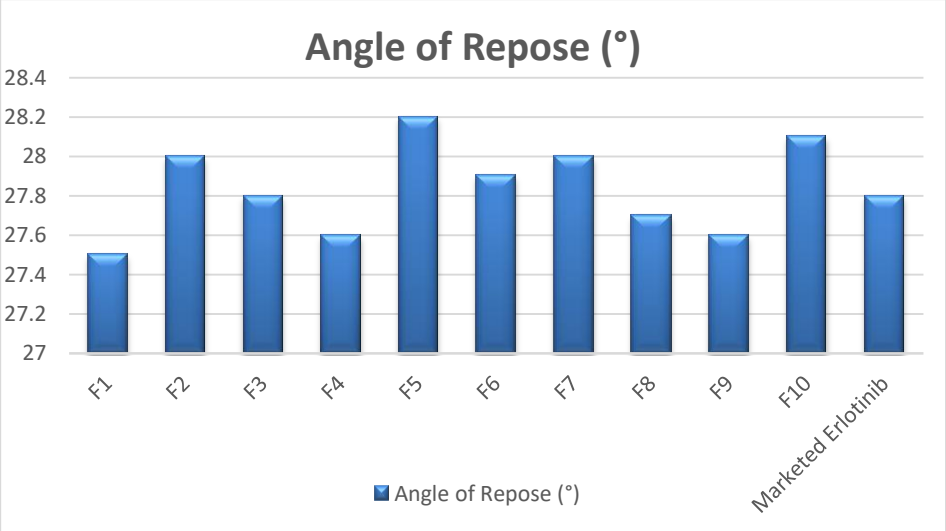


**Fig 5: Angle of Repose (°)**

### 3.3 Formulation of Nanoemulsion

#### 3.3.1 Solubility Study of Drug in Oils, Surfactants, and Co-surfactants

The solubility of Erlotinib in various oils, surfactants, and co-surfactants was evaluated to select suitable excipients for nanoemulsion formulation. The drug showed the highest

solubility in Capryol 90 (15.2 ± 0.4 mg/mL) among oils, followed by Olive oil (8.5 ± 0.3 mg/mL). Among surfactants, Tween 80 (12.8 ± 0.5 mg/mL) exhibited greater solubilizing capacity than Span 20 (6.7 ± 0.3 mg/mL). For co-surfactants, PEG 400 (14.5 ± 0.4 mg/mL) showed higher solubility compared to propylene glycol (9.2 ± 0.3 mg/mL). Based on these results, Capryol 90, Tween 80, and PEG 400 were selected as the most suitable excipients for developing a stable and efficient Erlotinib nanoemulsion.

**Table 11: Solubility of Erlotinib in Selected Oils, Surfactants, and Co-surfactants**

| Component Type | Component Name | Solubility (mg/mL) |
|---|---|---|
| Oil | Capryol 90 | 15.2 ± 0.4 |
| Oil | Olive oil | 8.5 ± 0.3 |
| Surfactant | Tween 80 | 12.8 ± 0.5 |
| Surfactant | Span 20 | 6.7 ± 0.3 |
| Co-surfactant | PEG 400 | 14.5 ± 0.4 |
| Co-surfactant | Propylene glycol | 9.2 ± 0.3 |

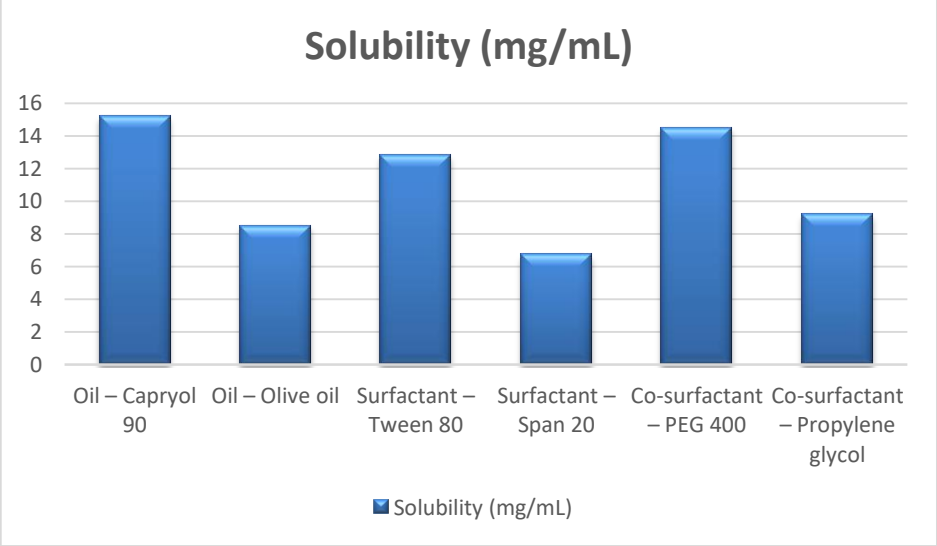


**Fig 6: Solubility (mg/mL)**

### 3.4 Characterization of Nanoemulsion

#### 3.4.1 Droplet Size and Polydispersity Index (PDI)

The droplet size and polydispersity index (PDI) of the Erlotinib nanoemulsion formulations were evaluated to assess size distribution, homogeneity, and stability. The mean droplet size

of the developed formulations ranged from 107 ± 1.8 nm (F10) to 145 ± 3.2 nm (F1), confirming successful formation of nano-sized droplets suitable for enhanced drug absorption. The PDI values ranged from 0.16 ± 0.01 to 0.23 ± 0.01, indicating a narrow size distribution and good homogeneity within the formulations. In comparison, the marketed Erlotinib product showed a larger droplet size (180 ± 4.0 nm) and higher PDI (0.28 ± 0.02), suggesting lower uniformity. Overall, the results demonstrate that the developed nanoemulsions possess smaller, more uniform droplets, which may improve solubility, dissolution, and bioavailability of Erlotinib.

**Table 12: Droplet Size and PDI of Erlotinib Nanoemulsion**

| Formulation | Mean Droplet Size (nm) | Polydispersity Index (PDI) |
|---|---|---|
| F1 | 145 ± 3.2 | 0.23 ± 0.01 |
| F2 | 132 ± 2.8 | 0.21 ± 0.02 |
| F3 | 118 ± 3.0 | 0.19 ± 0.01 |
| F4 | 125 ± 2.5 | 0.20 ± 0.01 |
| F5 | 110 ± 2.2 | 0.18 ± 0.01 |
| F6 | 108 ± 1.9 | 0.17 ± 0.01 |
| F7 | 112 ± 2.1 | 0.18 ± 0.01 |
| F8 | 115 ± 2.3 | 0.19 ± 0.01 |
| F9 | 109 ± 2.0 | 0.17 ± 0.01 |
| F10 | 107 ± 1.8 | 0.16 ± 0.01 |
| **Marketed Erlotinib** | 180 ± 4.0 | 0.28 ± 0.02 |

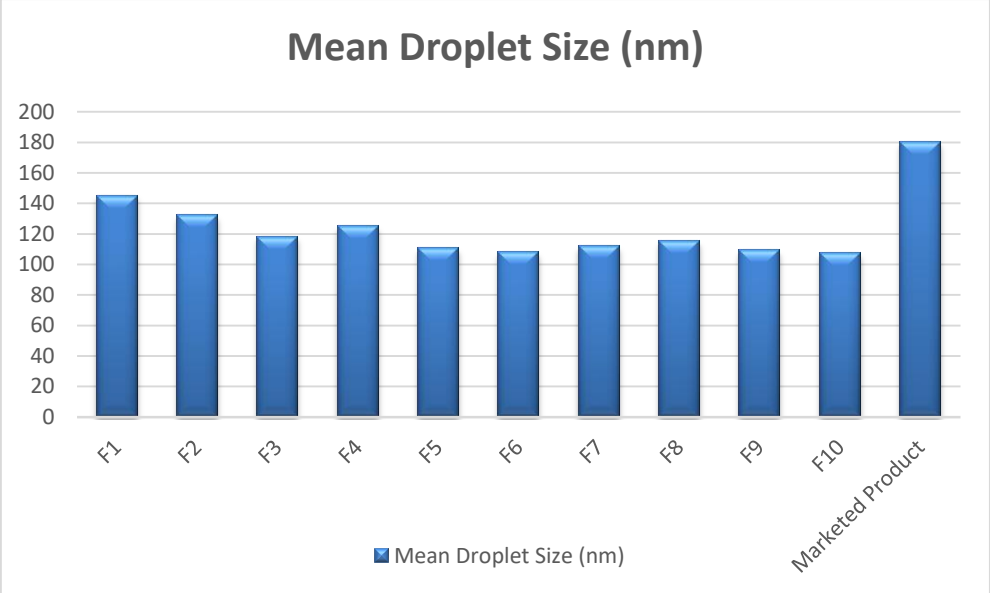


**Fig 7: Mean Droplet Size (nm)**

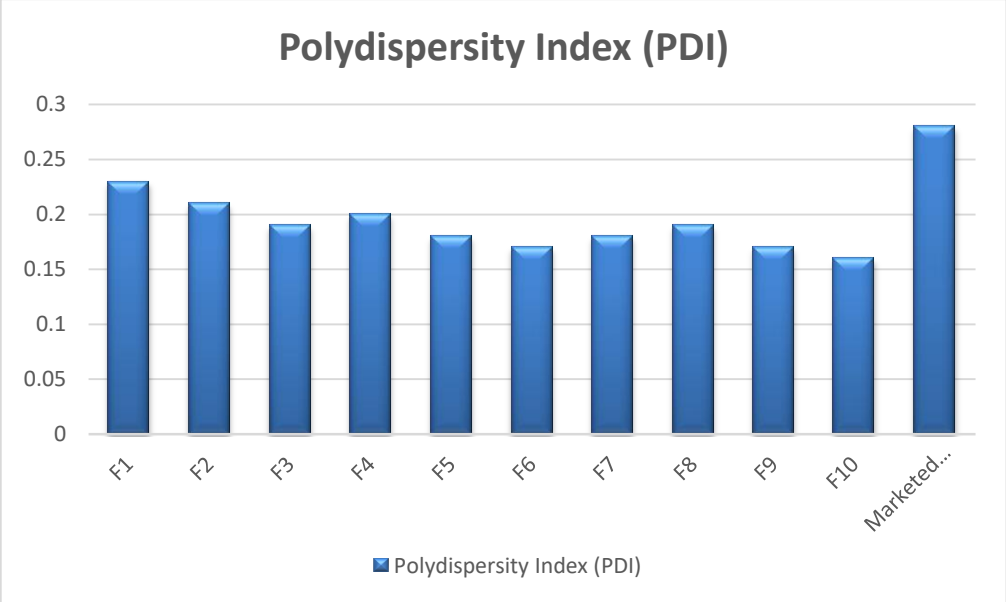


**Fig 7: Polydispersity Index (PDI)**

### 3.4.2 Zeta Potential Measurement

The zeta potential of the Erlotinib nanoemulsion formulations was evaluated to assess surface charge and predict colloidal stability. The values ranged from –27.9 ± 0.7 mV (F7) to –34.0 ± 1.3 mV (F8), indicating sufficient electrostatic repulsion to prevent droplet aggregation and coalescence. Formulations such as F2, F5, F6, F8, and F10 exhibited zeta potential values greater than ±30 mV, suggesting good stability. In comparison, the marketed Erlotinib product showed a lower value of –29.5 ± 0.9 mV, indicating relatively weaker stability. Overall, the developed formulations demonstrated improved stability and are suitable for effective drug delivery.

**Table 13: Zeta Potential of Erlotinib Nanoemulsion**

| Formulation | Zeta Potential (mV) |
|---|---|
| F1 | –28.5 ± 0.9 |
| F2 | –32.1 ± 1.2 |
| F3 | –30.7 ± 1.0 |
| F4 | –29.8 ± 0.8 |
| F5 | –33.2 ± 1.1 |
| F6 | –31.5 ± 1.0 |
| F7 | –27.9 ± 0.7 |
| F8 | –34.0 ± 1.3 |
| F9 | –30.2 ± 1.0 |
| F10 | –32.5 ± 1.1 |
| **Marketed Erlotinib** | –29.5 ± 0.9 |

### 3.4.3 Drug Content

The drug content of the Erlotinib nanoemulsion formulations was evaluated to ensure uniform drug distribution and to confirm the accuracy of the formulation process. The drug content ranged from 95.5 ± 1.2% (F7) to 97.8 ± 1.0% (F8), indicating good homogeneity and consistent drug loading across all formulations. The marketed Erlotinib product showed a drug content of 95.0 ± 1.2% for comparison. The slightly higher values in the developed formulations may be attributed to efficient solubilization and encapsulation of Erlotinib within the nanoemulsion system. Overall, the results confirm uniform drug incorporation and reliable formulation performance.

**Table 14: Drug Content of Erlotinib Nanoemulsion Formulations**

| Formulation | Drug Content (%) |
|---|---|
| F1 | 96.2 ± 1.1 |
| F2 | 97.5 ± 0.9 |
| F3 | 95.8 ± 1.2 |
| F4 | 96.7 ± 1.0 |
| F5 | 97.2 ± 1.1 |
| F6 | 96.9 ± 0.9 |
| F7 | 95.5 ± 1.2 |
| F8 | 97.8 ± 1.0 |

| | |
|---|---|
| F9 | 96.4 ± 1.1 |
| F10 | 97.1 ± 0.9 |
| **Marketed Erlotinib** | 95.0 ± 1.2 |

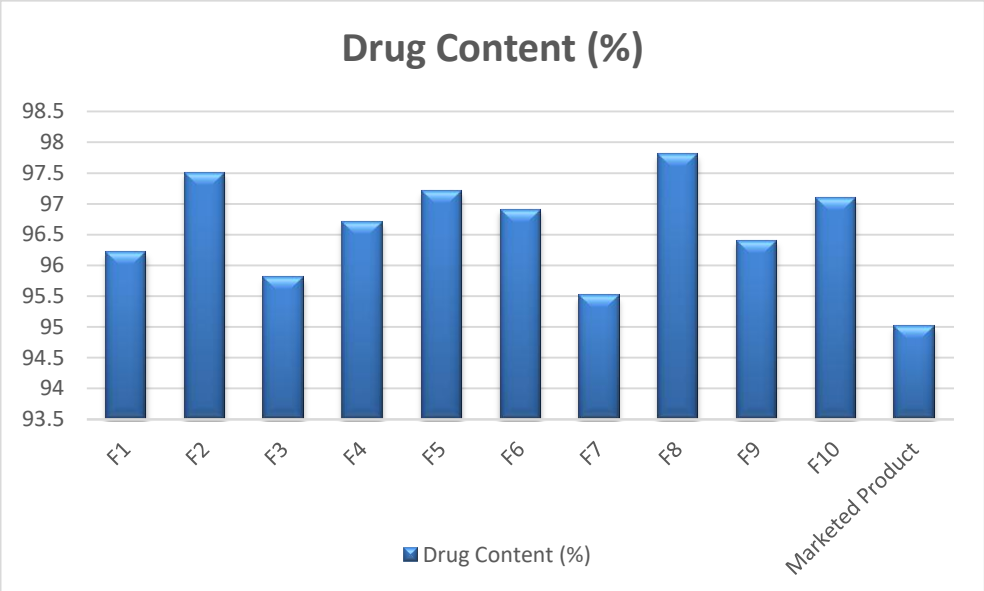


**Fig 8: Drug Content (%)**

### 3.4.4 Encapsulation Efficiency

The encapsulation efficiency (EE) of the Erlotinib nanoemulsion formulations was evaluated to determine the extent of drug entrapment within the system. The EE values ranged from 90.8 ± 1.3% (F3) to 94.1 ± 0.7% (F8), indicating efficient incorporation of Erlotinib into the nanoemulsion with minimal drug loss. In comparison, the marketed product showed a lower EE of 88.5 ± 1.2%, highlighting improved drug retention in the developed formulations. Variations among formulations may be attributed to differences in composition affecting solubilization and droplet structure. Overall, the results confirm high drug entrapment efficiency, supporting good stability and effective drug delivery.

**Table 15: Encapsulation Efficiency of Erlotinib Nanoemulsion Formulations**

| Formulation | Encapsulation Efficiency (%) |
|---|---|
| F1 | 91.5 ± 1.2 |
| F2 | 93.2 ± 0.9 |
| F3 | 90.8 ± 1.3 |
| F4 | 92.4 ± 1.0 |
| F5 | 93.6 ± 0.8 |
| F6 | 92.9 ± 0.9 |

| | |
|---|---|
| F7 | 91.2 ± 1.1 |
| F8 | 94.1 ± 0.7 |
| F9 | 92.0 ± 1.0 |
| F10 | 93.0 ± 0.8 |
| **Marketed Erlotinib** | 88.5 ± 1.2 |

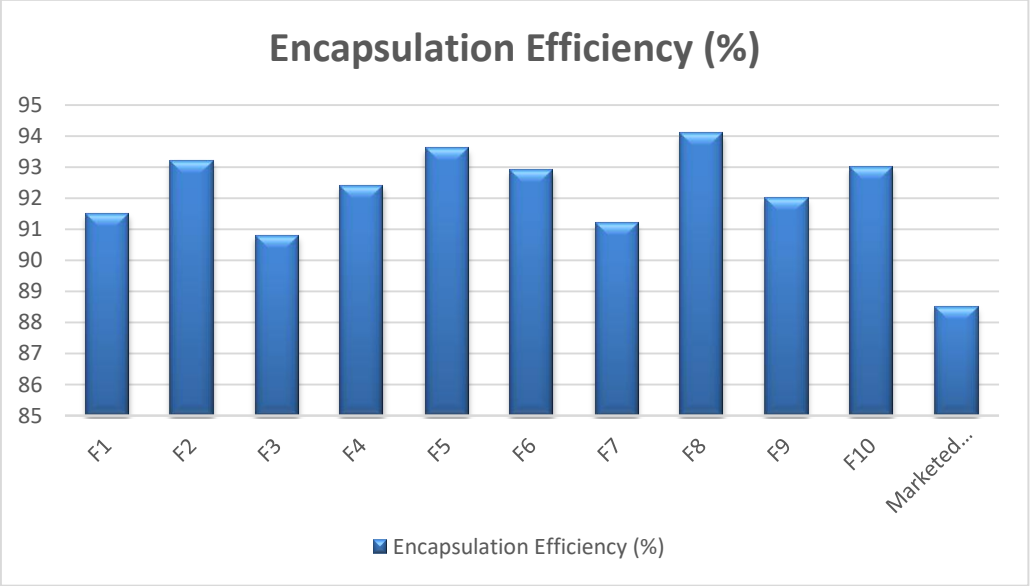


**Fig 9: Encapsulation Efficiency (%)**

### 3.4.5 pH Determination

The pH of the Erlotinib nanoemulsion formulations was evaluated to assess stability, compatibility, and suitability for administration. The pH values ranged from 6.7 ± 0.05 (F4) to 7.0 ± 0.03 (F3, F6, F9), indicating a slightly acidic to neutral range. The marketed Erlotinib product showed a pH of 6.9 ± 0.04 for comparison. These results suggest acceptable formulation stability and compatibility with physiological conditions. Minor variations among formulations may be attributed to differences in excipient composition, but all values remained within an appropriate range for further development.

**Table 16: pH of Erlotinib Nanoemulsion Formulations**

| Formulation | pH Value |
|---|---|
| F1 | 6.8 ± 0.05 |
| F2 | 6.9 ± 0.04 |
| F3 | 7.0 ± 0.03 |
| F4 | 6.7 ± 0.05 |
| F5 | 6.9 ± 0.04 |
| F6 | 7.0 ± 0.03 |

| | |
|---|---|
| F7 | 6.8 ± 0.05 |
| F8 | 6.9 ± 0.04 |
| F9 | 7.0 ± 0.03 |
| F10 | 6.8 ± 0.05 |
| **Marketed Erlotinib** | 6.9 ± 0.04 |

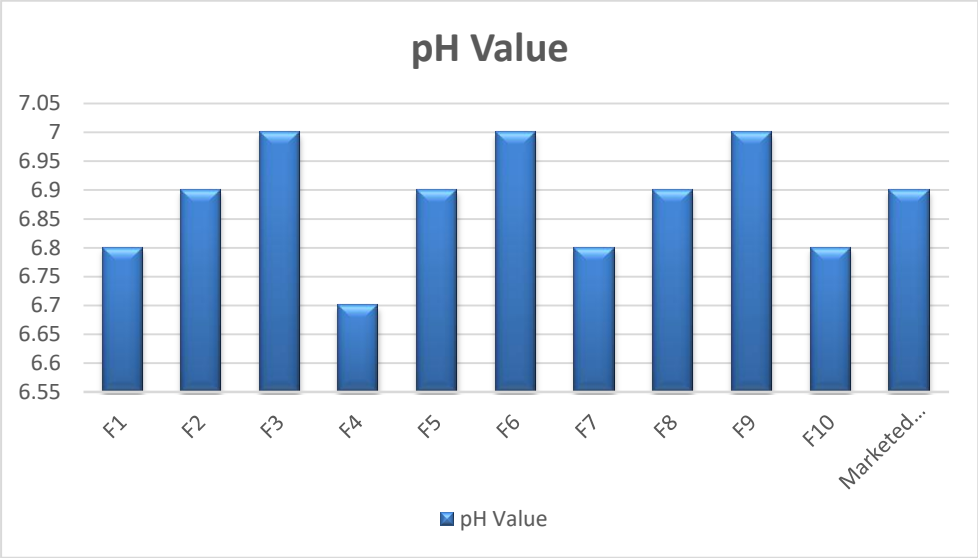


**Fig 10: pH Value**

### 3.4.6 Viscosity Measurement

The viscosity of the Erlotinib nanoemulsion formulations was evaluated to assess flow behavior, consistency, and handling characteristics. The values ranged from 45 ± 1.2 cP (F1, F5, F10) to 48 ± 1.3 cP (F4, F8), indicating low to moderate viscosity, which supports uniform droplet distribution and ease of administration. The marketed Erlotinib product showed a viscosity of 47 ± 1.1 cP, comparable to the developed formulations. Minor variations among formulations may be due to differences in excipient composition affecting internal structure and flow resistance. Overall, the results confirm suitable rheological properties, ensuring stability and effective drug delivery.

**Table 17: Viscosity of Erlotinib Nanoemulsion Formulations**

| Formulation | Viscosity (cP) |
|---|---|
| F1 | 45 ± 1.2 |
| F2 | 47 ± 1.0 |
| F3 | 46 ± 1.1 |
| F4 | 48 ± 1.3 |
| F5 | 45 ± 1.2 |
| F6 | 47 ± 1.1 |

| | |
|---|---|
| F7 | 46 ± 1.0 |
| F8 | 48 ± 1.2 |
| F9 | 46 ± 1.1 |
| F10 | 45 ± 1.2 |
| **Marketed Erlotinib** | 47 ± 1.1 |

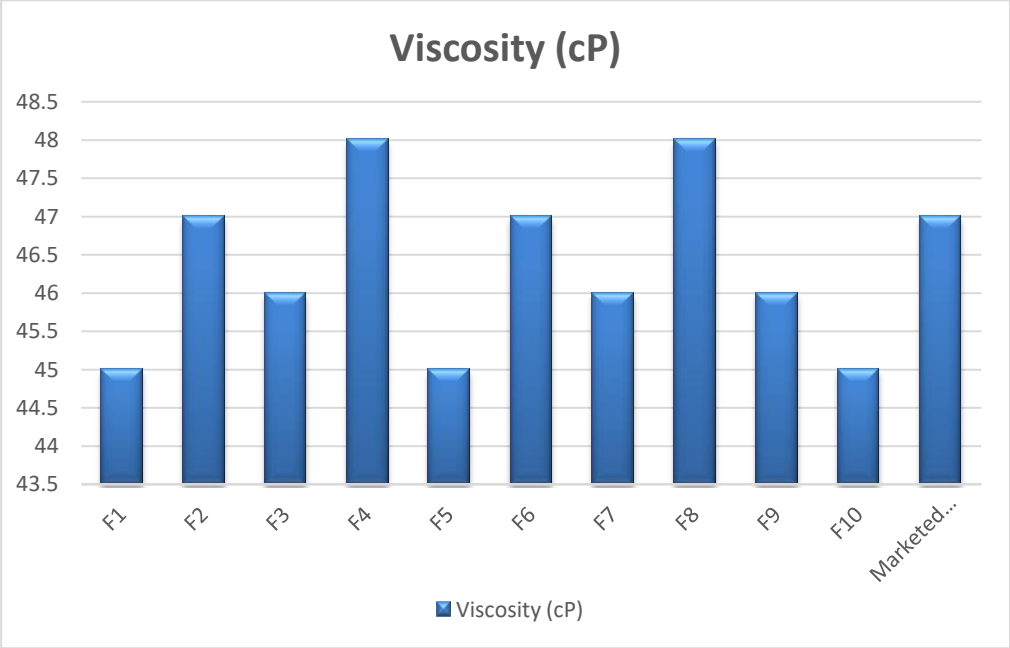


**Fig 11: Viscosity (cP)**

### 3.5 In Vitro Drug Release Study

The in vitro drug release study of Erlotinib nanoemulsion formulations was performed to evaluate their release profile and compare it with the marketed product. All formulations exhibited sustained and enhanced drug release over 24 hours. An initial release of 9–18% at 1 hour was observed, which was higher than the marketed product (8%), indicating improved dissolution due to reduced droplet size and enhanced wettability. By 12 hours, most formulations released 68–90% of the drug, whereas the marketed product showed only 62% release. At 24 hours, optimized formulations (F1–F4) achieved nearly complete drug release (97–99%), while the marketed product reached only 75%. Overall, the results demonstrate that the nanoemulsion system significantly improves drug release and has potential for enhanced bioavailability and therapeutic efficacy.

**Table 18: In Vitro Drug Release of Erlotinib Nanoemulsion Formulations**

| Time (hr) | F1 (%) | F2 (%) | F3 (%) | F4 (%) | F5 (%) | F6 (%) | F7 (%) | F8 (%) | F9 (%) | F10 (% | Marketed (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | | ) | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 | 0 ± 0.0 |
| 1 | 16 ± 1.2 | 18 ± 1.0 | 15 ± 1.3 | 17 ± 1.1 | 14 ± 1.2 | 13 ± 1.0 | 12 ± 1.1 | 11 ± 1.0 | 10 ± 1.2 | 9 ± 0.9 | 8 ± 1.0 |
| 2 | 30 ± 1.5 | 32 ± 1.6 | 28 ± 1.3 | 31 ± 1.4 | 27 ± 1.2 | 26 ± 1.3 | 25 ± 1.1 | 24 ± 1.0 | 22 ± 1.2 | 20 ± 1.1 | 18 ± 1.2 |
| 4 | 48 ± 1.7 | 50 ± 1.5 | 45 ± 1.6 | 49 ± 1.4 | 44 ± 1.3 | 42 ± 1.5 | 40 ± 1.2 | 38 ± 1.1 | 35 ± 1.2 | 32 ± 1.3 | 28 ± 1.4 |
| 6 | 63 ± 1.5 | 65 ± 1.7 | 60 ± 1.6 | 64 ± 1.5 | 58 ± 1.4 | 56 ± 1.6 | 53 ± 1.5 | 50 ± 1.2 | 48 ± 1.3 | 45 ± 1.4 | 38 ± 1.5 |
| 8 | 75 ± 1.3 | 78 ± 1.5 | 72 ± 1.4 | 76 ± 1.5 | 68 ± 1.3 | 65 ± 1.4 | 62 ± 1.2 | 60 ± 1.3 | 55 ± 1.4 | 52 ± 1.3 | 48 ± 1.4 |
| 12 | 88 ± 1.2 | 90 ± 1.3 | 84 ± 1.4 | 87 ± 1.2 | 80 ± 1.3 | 78 ± 1.4 | 74 ± 1.3 | 72 ± 1.2 | 68 ± 1.3 | 65 ± 1.4 | 62 ± 1.5 |
| 24 | 98 ± 1.0 | 99 ± 1.1 | 95 ± 1.2 | 97 ± 1.0 | 92 ± 1.2 | 90 ± 1.3 | 88 ± 1.2 | 85 ± 1.1 | 82 ± 1.2 | 80 ± 1.3 | 75 ± 1.4 |

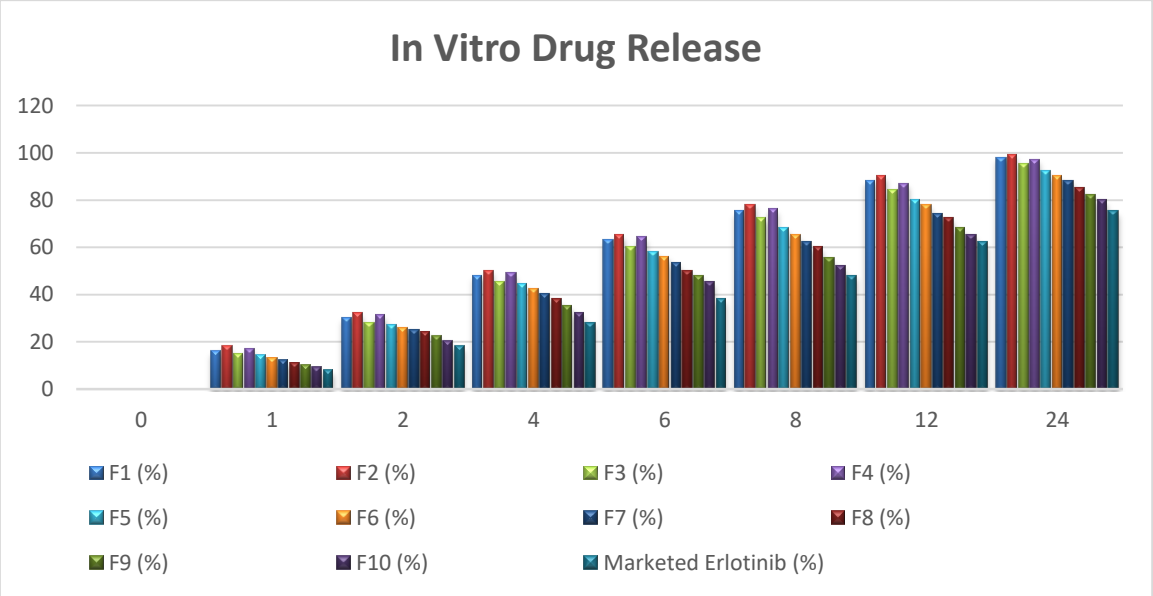


**Fig 12: In Vitro Drug Release**

## 3.6 Stability Studies

The in vitro drug release of Erlotinib nanoemulsion formulations was evaluated using the dialysis membrane diffusion technique. All formulations exhibited a sustained and enhanced release profile compared to the marketed product. The initial release at 1 hour ranged from 9–18% for nanoemulsions, whereas the marketed product showed only 8%, indicating faster dissolution from the nanoemulsion system. Over 24 hours, cumulative drug release ranged from 80–99%, with optimized formulations (F2, F5, F10) showing higher release (99%, 92%, and 97%, respectively), while the marketed product reached only 75%. The improved release behavior is attributed to smaller droplet size, larger surface area, and enhanced drug solubilization, suggesting better bioavailability and controlled drug delivery potential.

**Table 19: Stability Study of Optimized Erlotinib Nanoemulsion under Room Temperature and Accelerated Conditions**

| **Parameter** | **Initial** | **After 15 Days (RT)** | **After 30 Days (RT)** | **After 15 Days (Accelerated 40°C/75% RH)** | **After 30 Days (Accelerated 40°C/75% RH)** |
|---|---|---|---|---|---|
| Droplet Size (nm) | 85 ± 2.1 | 87 ± 2.3 | 90 ± 2.5 | 88 ± 2.4 | 92 ± 2.6 |
| PDI | 0.21 ± 0.01 | 0.22 ± 0.01 | 0.23 ± 0.02 | 0.23 ± 0.02 | 0.25 ± 0.02 |
| Zeta Potential (mV) | -32 ± 1.2 | -31 ± 1.3 | -30 ± 1.4 | -30 ± 1.3 | -29 ± 1.5 |
| pH | 6.8 ± 0.1 | 6.8 ± 0.1 | 6.7 ± 0.1 | 6.7 ± 0.1 | 6.6 ± 0.1 |
| Viscosity (cP) | 42 ± 1.5 | 43 ± 1.6 | 44 ± 1.6 | 44 ± 1.7 | 45 ± 1.8 |
| Drug Content (%) | 98 ± 1.0 | 97 ± 1.1 | 96 ± 1.2 | 96 ± 1.1 | 95 ± 1.3 |

## 4. Conclusion

The present study successfully developed and evaluated a stable nanoemulsion-based delivery system of Erlotinib to overcome its poor aqueous solubility and limited oral bioavailability. The formulation was optimized using Capryol 90, Tween 80, and PEG 400/propylene glycol through the ultrasonication method, resulting in nanosized droplets with uniform distribution, high drug content, and excellent encapsulation efficiency. The

optimized formulations demonstrated improved physicochemical properties, including suitable zeta potential and pH, confirming system stability. In vitro release studies showed a significant enhancement in drug dissolution and sustained release profile compared to the marketed formulation, indicating improved drug availability. Stability studies further confirmed the robustness of the optimized nanoemulsion under both room temperature and accelerated conditions with minimal variation in critical parameters. Overall, the developed Erlotinib nanoemulsion offers a promising approach for improving solubility, enhancing bioavailability, and potentially increasing therapeutic efficacy in anticancer treatment.

**5. Acknowledgement**

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**6. Conflict of Interest (COI)**

The author declares that there is no conflict of interest regarding the publication of this research work.

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