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Solid Lipid Nanoparticles of Naftopidil: Formulation Design & *In Vitro* Evaluation for Improved Oral Absorption

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Abstract

Objective: In response to the low bioavailability of Naftopidil (NAF) attributed to its poor solubility, permeability, and extensive first-pass metabolism, this study aimed to enhance its oral bioavailability by formulating solid lipid nanoparticles (SLNs) of NAF.

Methods: SLNs loaded with NAF were prepared using the solvent emulsification/evaporation method, employing Compritol 888 ATO and Poloxamer 188 as excipients. Among the formulations, F10 exhibited superior entrapment efficiency (EE), prompting its selection for further optimization of particle size, zeta potential, surface morphology, Fourier transform infrared spectroscopy (FTIR), in vitro drug release, and stability assessments.

Results: Successful incorporation of NAF into SLNs was confirmed, with EE ranging from 56% to 88%, drug loading between 17% and 20%, and drug content from 77% to 98%. Formulation F10 demonstrated a particle size of 270.2 nm, zeta potential of 21.7 mV, and FTIR analysis indicated no interactions between the drug and lipid components. In vitro release studies revealed a significant increase in NAF release from SLNs, reaching up to 82.418% in pH 6.8 buffer. The release data were best fit to the Korsmeyer-Peppas model, with a high correlation coefficient (R^2 = 0.916). Stability studies suggested improved formulation stability and potential enhancement of bioavailability.

Conclusion: This study underscores the potential of SLNs as an effective nano platform for enhancing the oral bioavailability of NAF. The successful formulation, characterization, and stability evaluation of NAF-loaded SLNs provide valuable insights for future pharmaceutical development aimed at improving the therapeutic efficacy of NAF formulations.

Keywords: Naftopidil; Solid Lipid Nanoparticles; Oral Bioavailability; Entrapment Efficiency

Abbreviations: BPH: Benign Prostatic Hyperplasia; FTIR: Fourier Transform Infrared Spectroscopy; EE: Entrapment Efficiency; SLNs: Solid Lipid Nanoparticles; BCS: Biopharmaceutical Classification System; GIT:

Gastrointestinal Tract; TEM: Transmission Electron Microscopy; PSD: Particle Size Distribution; ZP: Zeta Potential; NAF: Naftopidil.

Introduction

Naftopidil (NAF) is a potent alpha1-adrenergic receptor antagonist employed in the treatment of benign prostatic obstruction and related lower urinary tract symptoms associated with benign prostatic hyperplasia (BPH). Its pharmacological action involves the blockade of alpha1-adrenergic receptors, leading to vasodilation and consequent antihypertensive effects. Despite its clinical efficacy, NAF faces significant challenges in oral delivery due to its classification as a Biopharmaceutical Classification System (BCS) Class IV drug, characterized by low aqueous solubility (0.11 mg/mL) and poor permeability at intestinal pH (log P 3.77). These factors contribute to its modest oral bioavailability of approximately 20% in humans, primarily limited by the rate of intestinal absorption and extensive first-pass metabolism in the liver. Consequently, the required dosage of NAF is comparatively higher than that of alternative pharmaceutical treatments for BPH, necessitating frequent dosing regimens [1-3]. To address the limitations associated with high dosing frequency and suboptimal oral bioavailability, nanoparticulate drug delivery systems offer a promising solution. Nanoparticles present several advantages, including their nano size, enhanced solubility, mucoadhesive properties, targeted drug delivery, dual-release behaviour, and improved bioavailability. Among these, solid lipid nanoparticles (SLNs) have garnered significant attention in recent decades for their potential in oral drug delivery [4-6].

SLNs represent a novel class of solid nanoscale delivery systems wherein the traditional oil phase is replaced by a solid lipid matrix. These lipid matrices predominantly comprise triglycerides, partial glycerides, fatty acids, steroids, and waxes, chosen for their biocompatibility, biodegradability, and low toxicity [7-9]. Notable characteristics of SLNs include their small particle size, large surface area, and capacity for phase interactions at interfaces, all of which contribute to their effectiveness in drug-delivery applications [10]. SLNs have been explored for various administration routes, including oral delivery, owing to their ability to enhance drug stability, controlled release, and bioavailability [11-13]. Given NAF's lipophilic nature, it presents an ideal candidate for formulation within lipid-based nanoparticle systems [4,14]. Compritol 888 ATO (CMP), an FDA-approved lipid composed of behenic acid esters and glycerol, emerges as a promising lipid carrier for NAF-loaded SLNs. CMP's elongated behenic acid chain facilitates drug entrapment through intermolecular interactions and offers resistance to enzymatic degradation within the gastrointestinal tract (GIT), thus optimizing drug release profiles [15,16].

In pursuit of enhancing NAF's oral absorption, various strategies, including solid dispersion and buccal formulations, have been explored [12,17-19]. This study endeavours to elevate NAF's bioavailability through the development of SLNs. Leveraging CMP as the lipid carrier and Poloxamer 188 as the stabilizer, NAF-loaded SLNs were prepared via the solvent emulsification/evaporation method. Optimization parameters included surfactant concentration and homogenization speed, with subsequent evaluation encompassing particle size, zeta potential, entrapment efficiency (EE), surface morphology, and in vitro release kinetics. Through meticulous formulation and characterization efforts, this study aims to unveil the potential of SLNs as a novel platform for enhancing the oral bioavailability of NAF, thereby advancing its therapeutic efficacy in the management of BPH-related symptoms [20,21].

Methods

Materials

NAF was generously supplied as a gift sample by Intas Pharmaceuticals Pvt. Ltd., located in Gujarat, India. The lipid excipient, Compritol 888 ATO, was procured from Gattefosse, headquartered in Saint-Priest, Cedex, France, while Poloxamer 188 was sourced from BASF Corporation in India. Distilled water was employed in all experimental procedures, ensuring the highest purity standards. Additionally, all chemicals and solvents utilized throughout the study were of analytical grade, guaranteeing the accuracy and reliability of the experimental outcomes [22,23].

Preparation of SLN of NAF

The preparation of NAF-loaded SLNs via the solvent emulsification/evaporation method involved a series of meticulously controlled steps. Initially, 50 mg of NAF was dissolved in 1 mL of chloroform, while varying concentrations of lipid were dissolved in 2 mL of chloroform separately. Subsequently, the NAF and lipid solutions were combined to form a homogeneous mixture. To ensure the complete removal of organic solvent residues, the mixture underwent evaporation at 70°C using a rotary evaporator (Per fit, India) [16,21].

The resulting drug-embedded lipid layer was then carefully introduced into 10 mL of an aqueous surfactant solution maintained at 70°C using a hot plate. Homogenization was carried out for 10 minutes at different speeds employing a high-speed homogenizer to achieve optimal particle size distribution and homogeneity. Following homogenization, the suspension was allowed to cool to room temperature, promoting the formation of stable SLN-NAF formulations.

To further enhance stability and facilitate long-term storage, the SLN-NAF suspensions underwent lyophilization for 36 hours at a temperature of 60°C and a pressure below 15 Pascal using a lyophilizer (SP Scientific Instruments, India). The formulations of NAF-loaded SLNs were varied to explore different compositions, as outlined in Table 1. The optimization process primarily focused on encapsulation efficiency as a critical parameter for formulation selection and refinement [22,23].

Characterization of SLN of NAF

Visual Appearance: Depending on the composition and particle size, SLN can range from translucent to milky.

Determination of EE and Drug Loading: To assess the encapsulation efficiency (EE) and drug loading of NAF in SLNs, an appropriate volume of the dispersion was carefully transferred into a centrifuge tube. The dispersion underwent centrifugation using a centrifuge machine (Remi Scientific Instruments, Mumbai) for 15 minutes at a speed of 15,000 rpm [24]. Following centrifugation, the supernatant was meticulously collected for further analysis. The determination of the percentage of free NAF and subsequent calculation of EE and drug loading was conducted spectrophotometrically, with the absorbance measured at a wavelength of λ-max=232 nm [25]. The calculation of EE and drug loading was based on the following equation [22,26]:

EE%= W (Added Drug)-W (Free Drug) / W (Added Drug) X 100

DL%= W (Added Drug)-W (Free Drug) / W (Total Drug) X 100

Where, W (added drug) is the amount of drug added during the preparation of SLN, W (free drug) is the amount of free drug measured in the lower chamber of the centrifugal tube after centrifugation, and W (total drug) is the amount of both drug and excipients in the whole formulation. These parameters are essential for calculating the encapsulation efficiency (EE) and drug loading of NAF in the SLNs, offering valuable insights into the efficiency of the formulation process and the distribution of the drug within the nanoparticles.

Determination of Drug Content: To determine the drug content of the SLNs, a precisely weighed 50 mg formulation was dissolved in 10 mL of methanol. Subsequently, the resulting solution was appropriately diluted, and the absorbance was measured using a UV-Spectrophotometer (Shimadzu, Japan) at the designated wavelength of λ-max=232 nm [6,27,28]. This spectrophotometric analysis facilitated the quantification of the drug content within the SLNs, providing crucial data on the concentration of the active pharmaceutical ingredient in the formulation.

Particle Size and Zeta Potential Analysis: The particle size diameter and zeta potential of the prepared SLNs were evaluated at ambient temperature employing a Zeta Potential/Particle Sizer analyser (Malvern). A 1 mL aliquot of the sample was appropriately diluted with double-distilled water prior to assessment for the respective parameters [29-31]. This analysis enabled the characterization of the SLNs' particle size distribution and surface charge, offering valuable insights into their stability and colloidal behaviour.

Morphology Studies: The optimized formulation underwent morphological analysis using transmission electron microscopy (TEM) operating at 100 kV. A few drops of the sample were carefully deposited onto a 300-mesh carbon-coated copper grid and left to air-dry at room temperature [32,33]. This preparation method ensured the uniform distribution of SLNs on the grid surface, allowing for high-resolution imaging and detailed examination of their morphology and internal structure.

Fourier Transform Infrared Spectroscopy (FTIR): For structural analysis, Fourier-transform infrared (FT-IR) spectroscopy was employed to investigate potential interactions between the drug and excipients. Spectra were acquired using an FT-IR spectrometer (Bruker Alpha, Berlin, Germany) across the wavelength range of 4000–400 cm^{-1}. Samples of pure NAF, a mixture of the drug with excipients, and the final formulation were loaded into the die cavity of the sample holder, and their respective IR spectra were recorded. This analytical approach facilitated the identification of any molecular interactions or chemical changes occurring between the drug and excipients within the formulation [34,35].

***In Vitro* Drug Release Study:** In this study, the in vitro release kinetics of SLNs was assessed using the dialysis method. Initially, 1.0 mL of SLN suspension or an equivalent drug solution was enclosed within a dialysis bag and submerged in 100 mL of phosphate-buffered saline at pH 6.8, serving as the release medium [5,36,37]. The entire system was maintained at a constant temperature of 37°C ± 0.5°C under continuous magnetic stirring to ensure uniform distribution.

At predetermined time intervals (0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, and 24 hours), 5 mL aliquots of the release medium were withdrawn and replaced with an equal volume of fresh release medium to maintain sink conditions. The collected samples were appropriately diluted and analyzed using a UV-visible spectrophotometer at a wavelength of 232 nm to quantify the amount of drug released. The cumulative percentage release was then calculated based on the measured drug concentrations.

To elucidate the release kinetics, several mathematical models were employed, including zero order (cumulative percentage release vs. time), first order (logarithm of percentage drug remaining vs. time), Higuchi's model (cumulative percentage drug release vs. square root of time), and the Korsmeyer-Peppas model (logarithm of drug release vs. logarithm of time). Regression analysis of the obtained

plots facilitated the calculation of correlation coefficients (r^2) and release rate constants (k), providing insights into the underlying release mechanisms and kinetics of the SLN formulations.

Stability Studies: The stability studies carried out for the best SLN formulation were performed by being stored at 4°C and 27±2°C/65%±5% of relative humidity for time period of 90 days and they were examined at the regular time intervals for changes in the EE of SLN [36].

Results and Discussion

Preparation of SLN-NAF

The solvent emulsification/evaporation method employed for the preparation of NAF SLNs demonstrated robustness, simplicity, and reproducibility. The resulting SLNs exhibited a uniform and homogeneous appearance, devoid of any foreign particles. This method proved to be effective in achieving consistent particle size distribution and encapsulation of NAF within the lipid matrix. The absence of visible impurities underscored the reliability of the formulation process, further validating its potential for pharmaceutical applications.

EE, Drug Loading and Drug Content

EE, drug loading, and drug content are pivotal parameters in characterizing SLNs, reflecting the efficiency of drug encapsulation and formulation homogeneity. The optimization process involved the manipulation of various factors, including lipid type and concentration, surfactant concentration, and homogenization speed, as outlined in Table 1. The results of EE, drug loading, and drug content for all prepared formulations are summarized in Table 2 and depicted in Figure 1.

The EE values ranged from 56.45% to 88.81%, indicating the successful encapsulation of NAF within the SLNs. Similarly, the drug loading ranged from 17.64% to 20.65%, signifying the proportion of the SLN formulation composed of the active pharmaceutical ingredient. Moreover, the drug content of the SLNs fell within the range of 77.274% to 98.784%, affirming the consistency and uniformity of NAF distribution across the formulations.

These findings underscore the effectiveness of the formulation parameters in optimizing the encapsulation efficiency and drug loading of NAF within the SLNs, thereby enhancing their potential for pharmaceutical applications.

Formulation Batch	Naftopidil (mg)	Stearic Acid (mg)	Compritol 888 (mg)	Precirol (mg)	Poloxamer 188 (mg)	Chloroform (mL)	Homogenization Speed (rpm)
F1	50	10	-	-	100	3	6000
F2	50	-	10	-	100	3	6000
F3	50	-	-	10	100	3	6000
F4	50	-	10	-	150	3	6000
F5	50	-	10	-	200	3	6000
F6	50	-	5	-	150	3	6000
F7	50	-	15	-	150	3	8000
F8	50	-	20	-	150	3	6000
F9	50	-	15	-	150	3	6000
F10	50	-	15	-	150	3	10000

Table 1: Composition of NAF-loaded Formulation Using Different Types of Lipids, Homogenization Speed, and Different Concentrations of Lipid and Surfactant.

S. No.	Formulation Code	Entrapment Efficiency (%) (mean ± SD) *	Drug Loading (%) (mean ± SD) *	Drug Content (%) (mean ± SD) *
1	F1	56.459±0.504	17.643±0.157	77.274±0.347
2	F2	71.690±0.417	22.403±0.130	80.748±0.306
3	F3	62.338±0.306	19.480±0.095	85.758±0.417
4	F4	85.886±0.030	20.449±0.007	79.211±0.504
5	F5	75.364±0.504	14.493±0.096	93.039±0.306
6	F6	79.847±0.040	19.475±0.009	87.428±0.504
7	F7	88.217±0.030	20.515±0.007	97.782±0.306

Table 2: Percentage entrapment efficiency, drug loading, and drug content of different SLN formulations containing Naftopidil.

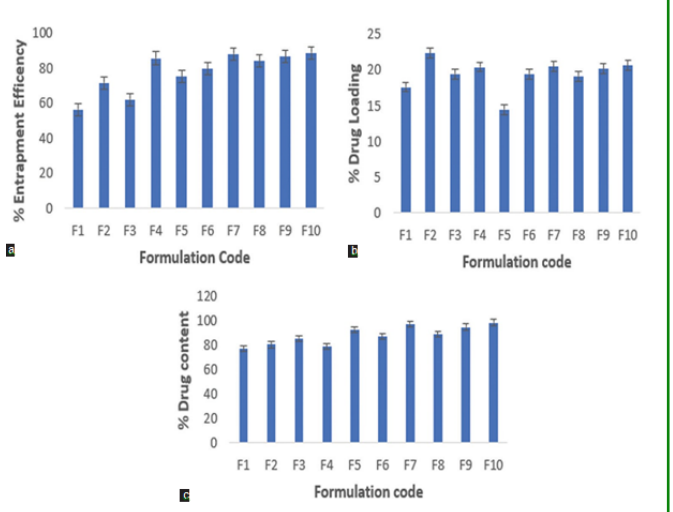

Figure 1: Percentage (a) Entrapment efficiency, (b) Drug loading, and (c) Drug content of SLN formulations containing Naftopidil.

Influence of Different Type of Lipids and Its Concentration on EE

The impact of various lipid types on encapsulation efficiency (EE) was evaluated, encompassing three distinct lipids: stearic acid (F1), compritol 888 ATO (F2), and precirol (F3). Notably, compritol 888 ATO (F2) exhibited superior EE, reaching 71.69%, surpassing the EE achieved with other lipid variants. Subsequently, the influence of lipid concentrations on %EE was explored, focusing on four different concentrations of compritol 888 ATO: 5 mg (F6), 10 mg (F4), 15 mg (F7), and 20 mg (F8). Remarkably, formulation F7 containing 15 mg of compritol 888 ATO demonstrated the highest EE at 88.21%, outperforming other lipid concentrations. Detailed lipid concentrations are outlined in Table 1, while Table 2 presents the corresponding %EE values, elucidating the significant impact of lipid type and concentration on the encapsulation efficiency of NAF-loaded SLNs.

Influence of Surfactant Concentration and Homogenization Speed on EE

The influence of surfactant concentrations on encapsulation efficiency (EE) was investigated across three different concentrations: 100 mg (F2), 150 mg (F4), and 200 mg (F5). Notably, formulation F4 containing 150 mg of surfactant exhibited the highest EE at 85.88%, surpassing the EE observed with other surfactant concentrations. This observation underscores the critical role of surfactant concentration in optimizing EE, as detailed in Table 1 & Table 2.

Furthermore, the impact of homogenization speed on EE was explored, varying across three different speeds: 6000 rpm (F9), 8000 rpm (F7), and 10,000 rpm (F10). The results revealed a notable influence of homogenization speed on EE, with an observed increase in EE as the homogenization speed increased. This phenomenon can be attributed to the enhanced surface coverage of nanoparticles achieved at higher homogenization speeds, thereby mitigating drug leaching from the lipid matrix. Across all three batches of SLN formulations, the concentration of 150 mg surfactant consistently yielded superior EE, emphasizing its role in enhancing formulation stability and drug retention.

Based on the EE findings, formulation F10 was selected for further investigation due to its exceptionally high EE of 88.818±0.041%. This choice reflects its potential for optimized drug encapsulation and underscores its suitability for subsequent research endeavours.

Particle Size Distribution and Zeta Potential Analysis

The particle size distribution (PSD) analysis of the freshly prepared SLN-NAF sample confirmed the production of nanoparticles exhibiting a unimodal and sharply defined distribution, with a median particle size of 270.2 nm, as depicted in Figure 2. The zeta potential (ZP) measurement of +21.7 mV denotes the surface charge of the nanoparticles, serving as an indicator of the degree of repulsion between particles of similar charge. This repulsion mechanism effectively prevents particle aggregation, thereby contributing to the long-term physical stability of the colloidal system. The stabilization of SLNs within the colloidal system, facilitated by poloxamer 188, primarily operates through steric action.

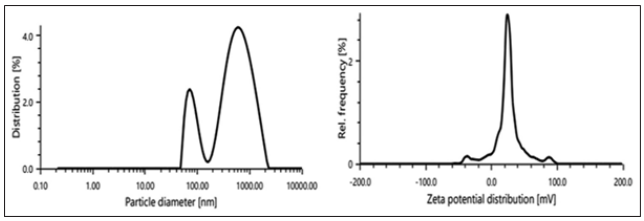

Figure 2: (a) Particle size peak and (b) Zeta potential graph of SLN formulation (F10).

It is noteworthy that a zeta potential exceeding (±) 20 mV is generally considered sufficient for stabilizing nanoparticles when the stabilization mechanism involves a combination of steric and electrostatic effects. Consequently, the PSD of the produced SLNs is anticipated to remain stable over time, ensuring sustained colloidal stability and uniform dispersion characteristics.

Surface Morphology

TEM images were utilized to elucidate the morphology of the SLNs, as illustrated in Figure 3. These TEM micrographs

depicted the colloidal sizes and spherical structure of all dispersions. It is worth noting that the TEM micrographs exhibited relatively lower intensity due to the lower concentration of NAF in the formulation compared to pure NAF.

Moreover, the presence of NAF in the formulation induced discernible changes in the spectrum profile of the SLNs. Additional peaks were observed, notably at 3339.36 cm^{-1}, attributed to primary amines and alcohols present in both Compritol 888 and NAF, along with a distinct stretch of C=O at 1635.12 cm^{-1}. These peak alterations serve as indicators of interactions within the system, corroborating the successful loading of NAF within the lipid matrices of the SLNs.

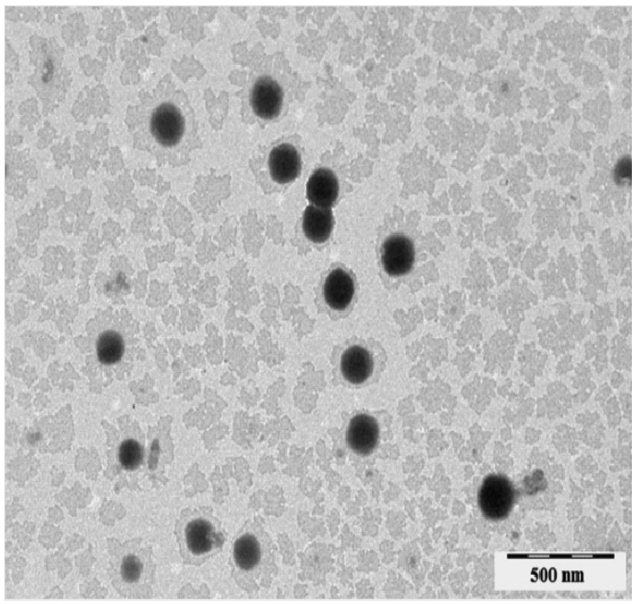

Figure 3: TEM image morphology of the SLNs.

FTIR

FT-IR analysis was conducted to investigate the chemical interactions among NAF, excipients, physical mixtures, and formulations (Figure 4). NAF exhibited prominent peaks at specific wavenumbers, including 2822.59 cm^{-1} (CH stretching), 1575.5 cm^{-1} (C=C stretching), 1266.31 and 1239.10 cm^{-1} (CN and CO stretching), 1332.83 cm^{-1} (CH bending), 1780.44 cm^{-1} (C=O stretching), and 1181.09 cm^{-1} (C–O–C stretching), as observed in its spectra. Similarly, excipients like Compritol 888 ATO displayed characteristic peaks at 2915.13 cm^{-1} (C–H stretching band of long fatty acid chain), 1734.88 cm^{-1} (Carbonyl stretching band in the fatty acid ester), and 1342 cm^{-1} (C–H bending). Poloxamer 188 showed distinctive peaks at 2883.11 cm^{-1} (C–H stretching band of long fatty acid chain), 1341.82 cm^{-1} (O–H bending), and 1101.26 cm−1 (C-O stretching).

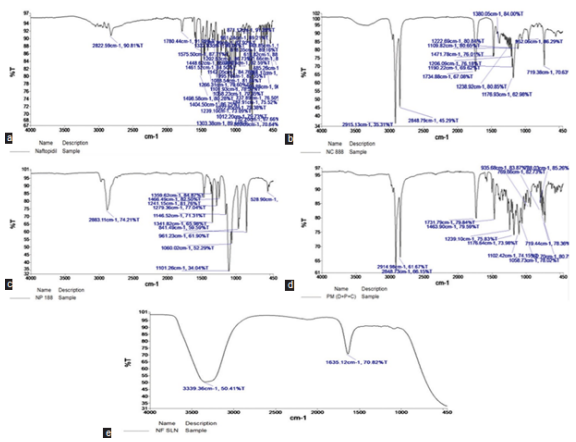

Figure 4: FTIR spectra of (a) Pure drug, (b) Compritol 888, (c) Poloxamer 188, (d) Physical mixture (A+B+C), and (E) SLN-NAF formulation (F10).

Analyzing the spectra of physical mixtures revealed diagnostic bands such as 2914.98 and 2848.73 cm^{-1} (CH stretching), 1239.10 cm^{-1} (CO stretching), 1176.64 cm^{-1} (C–O–C stretching), 1731.79 and 1102.42 cm^{-1} (C=O stretching), as well as 1635.12 cm^{-1} (C=O stretching) in formulation F10. These findings provided evidence of a NAF coating on the surface of solid lipid nanoparticles (SLNs), characterized by a distinctive grey shell. This analysis underscores the successful formulation of F10 and its potential for targeted drug delivery.

In vitro Drug Release Study

In Figure 5, the release profiles of the optimal formulation were compared to those of the pure drug solution. The pure drug solution, containing 5.523% NAF, exhibited a rapid release within 30 minutes, with 27.508% released over 24 hours. In contrast, NAF-loaded solid lipid nanoparticles (NAF-SLNs) displayed a biphasic release pattern. A significant initial release occurred within 2 hours, followed by a sustained release for up to 24 hours.

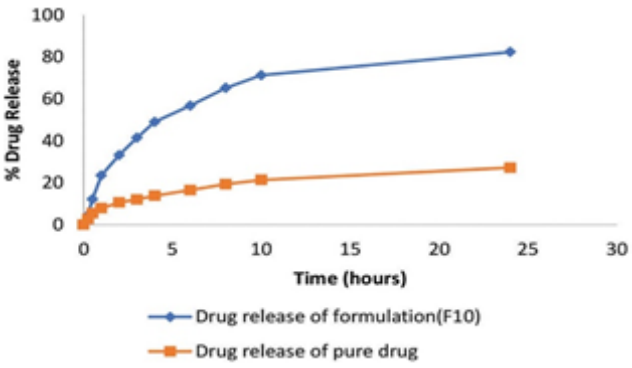

Figure 5: In vitro drug release of F10 formulation and pure drug.

The rapid initial release was attributed to the faster dissolution of NAF adsorbed on the surface of the SLNs. Subsequently, NAF entrapped within the inner lipid matrix of the SLNs was released slowly via diffusion, leading to sustained release beyond 2 hours. This behaviour was indicative of the lipid matrix's role in prolonging drug release, possibly due to the drug's resistance to desorption and diffusion.

Over the 24-hour study period, the release of NAF-SLNs increased notably, reaching a maximum of 4.547–82.418% in a pH 6.8 buffer medium. NAF's poor water solubility limits its dissolution and bioavailability, making it a suitable candidate for nanoparticle delivery systems, which have demonstrated efficacy in improving the solubility and dissolution rates of poorly soluble drugs.

To elucidate the release mechanism, various kinetics models were applied to the release data. Among these models, the Korsmeyer-Peppas model exhibited the highest correlation coefficient (R^2=0.916), suggesting that the release mechanism of NAF from NAF-SLNs was controlled. This finding underscores the potential of NAF-SLNs as a promising controlled-release formulation for enhancing the therapeutic efficacy of NAF.

Stability Studies

The stability assessment of batch F10 involved storage at 4°C and 27°C with 65%±5% relative humidity for a duration of 90 days. After this period, a slight alteration in the encapsulation efficiency (EE) of solid lipid nanoparticles (SLNs) was observed at 27°C compared to 4°C. This change, as depicted in Table 3 and Figure 6, was attributed to heightened drug exposure from lipid matrices at elevated temperatures.

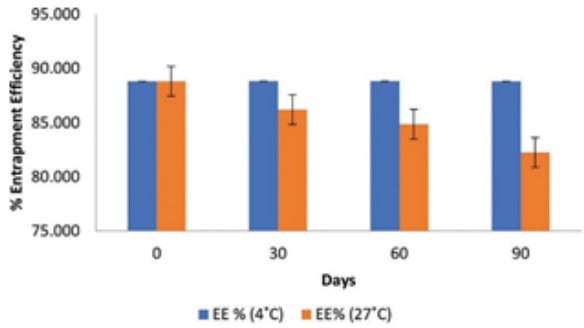

Figure 6: Effect of storage temperature (at 4°C and 27°C) on Entrapment Efficiency of F10.

Sr. No.	Days	Entrapment Efficiency (%) (at 4°C) (mean±SD) *	Entrapment Efficiency (%) (at 27°C) (mean±SD) *
1	0	88.818±0.042	88.818±0.042
2	30	88.839±0.031	86.213±0.031
3	60	88.832±0.046	84.857±0.040
4	90	88.812±0.012	82.239±0.050
*Each value is the average of three independent determinations (n=3)			

Table 3: Effect of Storage Temperature (at 4°C and 27°C) on Entrapment Efficiency of F10.

The findings underscored the long-term stability of the SLN formulation, which could be credited to several factors. Firstly, the presence of poloxamer 188 contributed to enhanced drug solubility within the lipid matrix. Additionally, owing to its nonionic nature, poloxamer 188 reduced electrostatic repulsions between particles, thereby stabilizing the nanoparticles by forming a protective coat around their surfaces.

This stability study highlights the robustness of the SLN formulation, affirming its potential for extended shelf-life and reliable performance, even under varied storage conditions.

Conclusion

The preparation of NAF-loaded solid lipid nanoparticles (SLNs) was accomplished using the solvent emulsification/evaporation method, proving to be a valuable technique for effectively incorporating the poorly water-soluble drug NAF. This method ensured the production of NAF-SLNs with minimal particle size and maximum encapsulation efficiency (EE%). Notably, the optimized NAF-SLNs exhibited sustained physical stability even after 3 months of storage at 4°C.

This robust physical stability suggests a potential enhancement in bioavailability. Consequently, it can be inferred that SLNs of NAF offer a controlled drug release

profile, making them promising drug carriers for lipophilic compounds. By leveraging nanoparticles, these systems hold the capacity to significantly improve the bioavailability of poorly water-soluble drugs, thus serving as an effective drug delivery platform.

In conclusion, the development of NAF-loaded SLNs represents a strategic approach towards enhancing drug delivery efficiency, particularly for compounds with low water solubility. These SLNs not only facilitate controlled release but also hold promise for optimizing therapeutic outcomes through improved drug bioavailability.

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