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Optimization and Characterization of Naproxen Loaded Emulsomes

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KEYWORDS

Naproxen, Emulsomes, Lipid-based nanocarriers, Drug delivery, Bioavailability, Sustained release

ABSTRACT:

The present study focuses on the development and evaluation of naproxen-loaded emulsomes to enhance the solubility, bioavailability, and sustained release of the drug. Naproxen, a widely used non-steroidal anti-inflammatory drug (NSAID), suffers from poor aqueous solubility and gastrointestinal side effects, limiting its therapeutic effectiveness. To address these issues, a lipid-based nanocarrier system—emulsomes—was formulated using the thin-film hydration technique followed by sonication. Key excipients included lecithin, cholesterol, tristearin, and stearylamine, selected for their biocompatibility and drug-loading efficiency. Compatibility of naproxen with excipients was confirmed through FTIR analysis, and successful entrapment was validated via Sephadex G-50 column chromatography, yielding an entrapment efficiency of 77.8%. The optimized emulsomal formulation displayed spherical morphology under transmission electron microscopy (TEM), with an average particle size of 545.1 ± 43.3 nm and a zeta potential of 47.2 ± 1.8 mV, indicating excellent colloidal stability. In vitro release studies using a pre-treated dialysis membrane revealed a sustained drug release profile, achieving 96.69% release over 16 hours. Stability studies over six months demonstrated minimal changes in drug content and particle size when stored at 4 ± 1°C, affirming the formulation's robustness. Overall, the emulsomal system significantly improved the dissolution and release profile of naproxen, offering a promising approach for addressing solubility-related challenges in poorly water-soluble drugs.

1. Introduction

Nanotechnology refers to the science and application of materials at the nanometer scale—typically ranging from 1 to 100 nanometers—where unique physical, chemical, and biological behaviors emerge [1]. Interestingly, the cellular machinery within living organisms also functions at this nanoscale level [2]. The field focuses on the design, synthesis, and analysis of nano-sized particles, which act as individual units with specific physical and chemical properties [3]. Particles in the nanometer range exhibit characteristics distinct from their larger counterparts; for example, ultrafine particles are generally smaller than 100 nm, while fine particles fall between 100 and 2500 nm in size [4]. These nano-structures have gained considerable attention in pharmaceutical research due to their ability to improve the therapeutic efficiency and pharmacological profile of drugs [5]. Their large surface area facilitates the attachment of functional molecules, which can target diseased cells—such as tumor cells—more effectively [6].

From a scientific standpoint, nanotechnology encompasses the development of materials and devices whose properties are manipulated at the molecular or atomic level. These materials often exhibit novel and enhanced mechanical, optical, chemical, and biological functions [7]. Among the various areas of application, drug delivery stands out as one of the most transformative. Nanocarriers such as liposomes, nanocrystals, magnetic nanoparticles, protein-nanoparticle conjugates, nanogels, niosomes, ethosomes, and emulsomes have shown promising results in improving drug delivery mechanisms [8].

Emulsomes, in particular, are advanced lipid-based nanocarriers that merge the functional attributes of both liposomes and emulsions. Structurally, emulsomes feature a solid or semi-solid lipid core surrounded by

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one or more layers of phospholipid bilayers [9]. This configuration allows them to encapsulate lipophilic drugs efficiently within the core, while the outer lipid layer enhances physical stability and protects the drug from premature degradation [10]. Their design offers several advantages, including enhanced drug loading capacity, controlled release, improved bioavailability, and reduced dosing frequency [11]. Due to their nano-size, emulsomes facilitate better tissue absorption, cellular uptake, and targeted delivery, making them particularly useful for drugs with poor water solubility [12–14].

Naproxen, a widely used non-steroidal anti-inflammatory drug (NSAID) employed to treat pain, inflammation, and fever associated with conditions like arthritis, tendinitis, gout, and menstrual cramps [15]. Naproxen functions by non-selectively inhibiting cyclooxygenase enzymes (COX-1 and COX-2), which are responsible for the synthesis of prostaglandins—chemical mediators involved in inflammation and pain [16]. Despite its therapeutic efficacy, naproxen presents formulation challenges due to its classification as a Biopharmaceutical Classification System (BCS) Class II drug. This means it has poor aqueous solubility but high permeability, resulting in limited oral bioavailability and gastrointestinal irritation upon administration [17,18]. These drawbacks underscore the need for alternative drug delivery systems that can enhance solubility, minimize side effects, and boost overall efficacy [19,20].

2. Objectives

The present study addresses these issues by formulating and optimizing naproxen-loaded emulsomes. The main objective is to improve the drug's solubility and bioavailability, while offering sustained release to reduce dosing frequency and side effects. The phospholipid bilayer of emulsomes not only aids in drug dispersion in aqueous environments but also facilitates interaction with biological membranes, potentially improving lymphatic absorption. This prolonged-release system helps maintain therapeutic drug levels over extended periods and may reduce the risk of gastrointestinal complications by limiting direct contact between naproxen and the stomach lining. Hence, developing naproxen-loaded emulsomes represents a promising strategy for overcoming the limitations of conventional formulations. This nano-based delivery platform not only addresses solubility and bioavailability challenges but also paves the way for improved therapeutic outcomes in other poorly water-soluble drugs.

3. Methods

Material Naproxen was procured from Dr Reddy, Baddi, Himachal Pradesh, tristearin, and lecithin were procured from HiMedia, cholesterol was procured from LOBA chemie Mumbai, sephadex G-50 was procured from Sigma aldrich USA, stearylamine was procured from Ottokemi, Mumbai

3.1 UV-Visible Spectroscopy

UV-visible spectroscopy serves as a fundamental analytical technique in pharmaceutical sciences for assessing drug concentration and purity. It works on the principle that compounds absorb light in the ultraviolet and visible regions due to electronic transitions between molecular orbitals. Each substance displays a distinct absorption pattern, which aids in its qualitative identification and quantitative analysis. This method is particularly effective for establishing calibration curves to determine drug concentrations and for identifying degradation products or impurities based on alterations in absorbance spectra. Additionally, it is useful for tracking the progress of reactions over time by monitoring changes in absorbance values [21,22].

3.1.1 Determination of λmax:

The UV spectrophotometric analysis involved scanning the sample solutions over the 230–350 nm range, using a mixture of naproxen and methanol as the blank. The wavelength at which maximum absorbance occurred (λmax) was then recorded for further analytical use [23].

3.1.2 Melting Point Determination

Melting point measurement is a routine and essential method for evaluating the purity and physical integrity of a compound. Pure substances exhibit sharp melting ranges, whereas impurities typically broaden the temperature interval. Naproxen demonstrates a melting point in the range of approximately 154–158°C. For determination, a small amount of the drug was loaded into a capillary tube and subjected to gradual heating

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using a calibrated melting point apparatus. The temperature at which the drug transitions from solid to liquid was recorded and compared to standard values to confirm its identity and assess purity [24–26].

3.2. Solubility Analysis

Understanding the solubility of a drug is vital for optimizing its dissolution profile and enhancing its bioavailability. This test involves determining the equilibrium solubility of the compound in various solvents at controlled temperatures. Naproxen, categorized under BCS Class II drugs, is known for its poor water solubility, which hampers its absorption. Studies have shown improved solubility when naproxen is dissolved in solvent systems such as polyethylene glycol 200 (PEG 200) mixed with water, or in ethanol-water blends. In PEG 200-water systems, solubility increases significantly with higher PEG concentration and elevated temperatures, aligning well with predictions by the Jouyban-Acree model. Ethanol also exhibits a notable cosolvency effect by improving naproxen's solubility compared to water, supporting the formulation of more effective drug delivery systems [27–29].

3.3. Partition Coefficient

The partition coefficient (Kp), often expressed as log P, reflects the ratio of a compound's distribution between two immiscible phases—usually water and n-octanol. It provides valuable insights into a drug's lipophilicity and potential for passive membrane permeability. A higher log P denotes lipophilic characteristics, which are typically associated with improved membrane transport. Conversely, a lower log P value suggests hydrophilicity. For naproxen, a moderately high log P value suggests good membrane permeability, supporting its use in lipid-based drug delivery systems such as emulsomes. This property also plays a role in optimizing chromatographic separation techniques and estimating pharmacokinetic behavior in vivo [30–32].

$$\log P = \log \frac{concentration of drug in n-octanol}{concentration of drug\ in\ water}$$

3.4. Formulation Development

3.4.1. Selection of Drug and Excipients

A comprehensive review of scientific literature was carried out to identify a suitable drug and excipients compatible with a lipid-based Emulsome delivery system. The selection was guided by key pharmaceutical parameters, including compatibility with lipid carriers and therapeutic benefits. [33] The ideal drug candidate needed to fulfill several criteria:

1. Exhibit high lipophilicity to ensure effective incorporation into the lipid matrix.
2. Belong to BCS Class II, characterized by low aqueous solubility but high permeability.
3. Be known to cause gastrointestinal side effects (e.g., gastric irritation), supporting the need for targeted delivery.
4. Be chemically and physically compatible with lipid excipients to ensure formulation stability.

Based on these considerations, Naproxen was chosen. It is a poorly water-soluble, lipophilic drug with known gastric side effects, making it a prime candidate for Emulsome encapsulation. Key excipients such as lecithin, tristearin, cholesterol, and stearylamine were selected due to their roles in enhancing vesicle integrity, drug loading, and biological compatibility in lipid-based systems. [34]

3.4.2. Compatibility Studies

To ensure the chemical compatibility between naproxen and the chosen excipients, Fourier Transform Infrared Spectroscopy (FTIR) was employed. Naproxen was mixed in equal ratios (1:1) with each excipient—lecithin, tristearin, and stearylamine—as well as in a combined mixture containing all ingredients.[35] These physical mixtures were stored in airtight glass containers at room temperature for stability. FTIR spectra were recorded in the 2000–600 cm^{-1} range and examined for peak shifts, disappearance, or the emergence of new peaks that would indicate interactions. The analysis revealed no significant alterations in the characteristic peaks of naproxen, confirming its compatibility with the selected excipients.[36]

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3.4.3. Method of Preparation

Emulsomes were formulated using the thin-film hydration technique, a well-established method for encapsulating lipophilic drugs. The process followed a modified version of the method introduced by Amselem and Friedman. [37]

To begin, naproxen was dissolved in methanol, and the lipid phase containing soya lecithin, tristearin, and cholesterol was dissolved in chloroform. Both solutions were added to a 500 mL round-bottom flask. Solvent removal was performed using a rotary evaporator under reduced pressure, resulting in a thin, uniform lipid film deposited on the inner wall of the flask. The dried film was then hydrated with phosphate-buffered saline (PBS, pH 7.4). The dispersion was sonicated using an ultrasonic processor (Lark, India) at 40% amplitude for 12 minutes to reduce particle size and achieve a nanoscale Emulsome suspension. The unencapsulated drug was separated by passing the sample through a Sephadex G-50 column as shown in fig 1, yielding purified naproxen-loaded Emulsomes. [38]

3.5. Characterization of Optimized Naproxen-Loaded Emulsomes

Morphology:
The structural features of the optimized formulation were studied using Transmission Electron Microscopy (TEM). A drop of the Emulsome dispersion was placed on a carbon-coated copper grid and stained with 1% phosphotungstic acid to improve contrast. TEM images confirmed the formation of spherical, well-defined vesicles with dense lipid cores and intact phospholipid bilayers, indicating successful formulation. [39]

Particle Size Analysis:

Dynamic Light Scattering (DLS) was employed to measure average particle size, polydispersity index (PDI), and distribution. Conducted at 25 ± 0.5 °C using a Zetasizer 4000, the analysis showed a narrow PDI (below 0.3), reflecting uniform size distribution and good colloidal stability—both of which are essential for consistent drug release and systemic availability. [40]

Zeta Potential:

The surface charge of the Emulsomes was determined through laser Doppler electrophoresis using a Zetasizer 2000. The calculated zeta potential revealed a sufficiently high charge magnitude, promoting electrostatic repulsion between particles. This charge stability helps to prevent aggregation and ensures prolonged suspension stability, which is beneficial for biological distribution. [41]

Entrapment Efficiency:

Entrapment efficiency was evaluated using Sephadex G-50 column chromatography (fig 1). After separating the unentrapped drug, vesicles were lysed using 0.5% Triton X-100, and the encapsulated naproxen content was quantified by UV spectrophotometry. The results demonstrated high drug loading efficiency, highlighting the compatibility of naproxen with the lipid components and validating the formulation strategy.

Values were recorded as mean ± SD for three replicates. High entrapment efficiency indicates good compatibility of naproxen with the lipidic core and bilayer structure of emulsomes. [42,43]

Fig 1: Image of Sephadex Column used for filtration of Emulsomes.

2.3 In Vitro Drug Release Study

2.3.1 Preparation of Dialysis Membrane

Before conducting the drug release study, the dialysis membrane (with a molecular weight cut-off ~12,000 Da) was carefully pre-treated to ensure the removal of any residual chemicals or preservatives that could interfere with the analysis. Initially, the membrane was thoroughly rinsed under running tap water for approximately 12 hours to eliminate glycerin-based

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preservatives. Following this, it was soaked in a 0.3% w/v solution of sodium sulphite at 70 °C for 20 minutes to remove sulfur-containing residues. To further purify the membrane, it was treated with 0.2% v/v sulfuric acid for 5 minutes. The membrane was then extensively washed with hot distilled water and finally stored in ethanol until needed. This pre-treatment process ensured that the membrane was clean, chemically stable, and suitable for accurate in vitro drug release testing. [44,45]

2.3.2 Drug Release Study

The release profile of naproxen from the optimized emulsomal formulation was assessed using the dialysis bag diffusion method, a commonly employed technique to simulate drug release under controlled conditions. One milliliter of the emulsomal dispersion—free from any unentrapped drug—was carefully loaded into the pre-treated dialysis membrane. This was then immersed in 100 mL of phosphate-buffered saline (PBS, pH 7.4) to mimic physiological pH. The entire setup was maintained at a temperature of 37 ± 1 °C using a magnetic stirrer to replicate in vivo conditions. [46]

At regular time intervals ranging from 0.5 to 16 hours, small samples were collected from the external PBS medium and immediately replaced with fresh buffer to maintain sink conditions. The amount of naproxen released at each time point was quantified using a high-performance liquid chromatography (HPLC) method. All measurements were performed in triplicate, and the results were presented as mean ± standard deviation (SD). These values were used to plot the cumulative drug release profile of the emulsomal formulation, providing insights into its release kinetics and performance. [47]

4. Results

1. UV spectra

On scanning the solution (Naproxen+Methanol) of a drug over a range (230 nm – 350 nm), the Etodolac drug showed a maxima at 271.6 nm, which are compared with the reference spectrum of the drug given in I.P. 2010 and table 1.

Table 1: Standard and observed maxima of Naproxen.

Standard (I.P.2010)	Observed
271,	271.6

2. FTIR. Spectroscopy. [48]

1. C=O vibrations

Carboxylic acids typically exhibit a C=O stretching peak around 1700–1725 cm^{-1}, In the case of Nap, the C=O stretching mode of the carboxylic acid group was observed at 1690 cm^{-1}

2. C–O vibrations

C–O stretching vibrations typically occur in the 1000–1300 cm^{-1} region. For alcohols and ethers, these vibrations are generally observed between 1050 and 1150 cm^{-1}, while carboxylic acids and esters show C–O stretching in the 1200–1300 cm^{-1} range. In Nap, the C–O stretching of the carboxylic acid group was observed at 1250 cm^{-1}. (as shown in fig 2)

3. C=C vibrations

In aromatic compounds such as benzene, C=C stretching vibrations typically occur around 1500–1600 cm^{-1} due to the conjugation of double bonds within the ring, which generally lowers the vibrational frequency. In the case of Nap, the C=C stretching vibration of the benzene ring was observed at 1490 cm^{-1}. (as shown in fig 3)

4. C-H_3 bending vibrations

In aromatic compounds such as benzene, CH_3 stretching vibrations typically occur around 1404–1445 cm^{-1}. In the case of Nap, the CH_3stretching vibration of the benzene ring was observed at 1490 cm^{-1}.

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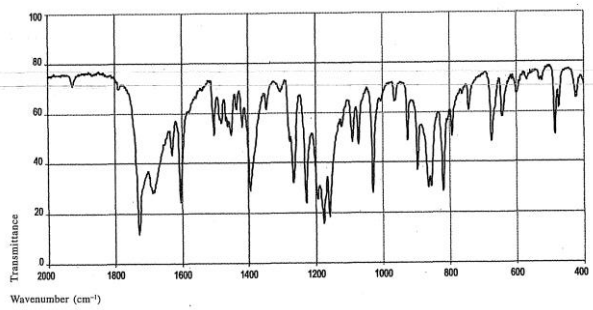

Figure 2: Reference FTIR Spectrum of Drug (Naproxen)

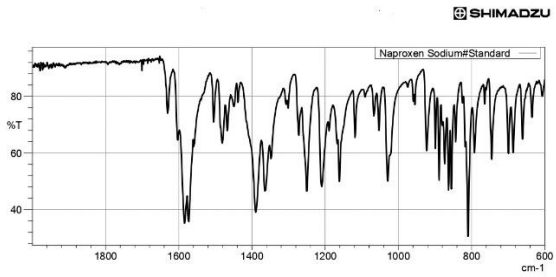

Fig 3: FTIR Spectrum of pure Drug (Naproxen)

3. Melting point.

The melting point of the drug sample was found 155 ± 1°C, which complies with the standard melting point range of drug 154-156°C given in IP, 2010.

4. Solubility Analysis.

The solubility profile of the drug was analysed in various solvents at different temperature. The drug was found soluble freely in ethanol, soluble in DMSO, chloroform, and insoluble in Polyethylene Glycol (PEG) and water.

5. Partition Coefficient.

The partition coefficient of Naproxen was found to be 4.1.

All these observations confirm the identity of Naproxen.

6. Compatibility studies of Drug and Excipients.

The possible interaction of Drug (Naproxen) and excipients were detected by the FTIR studies. The FTIR spectra were analyzed for any change/deviation in the principle peaks of Naproxen. The FTIR spectra of Naproxen + lecithin, drug + tristearin, drug + stearylamine and drug + soya lecithin + tristerain + sterylamine were shown in Figure 4 to 7. In all the spectra Naproxen pure drug spectrum was incorporated to compare any deviations of principle peaks (1690, 1490, 1250, 1150, 1050,). From the study, it was concluded that Naproxen was found compatible with other excipients and they can be used for further studies.

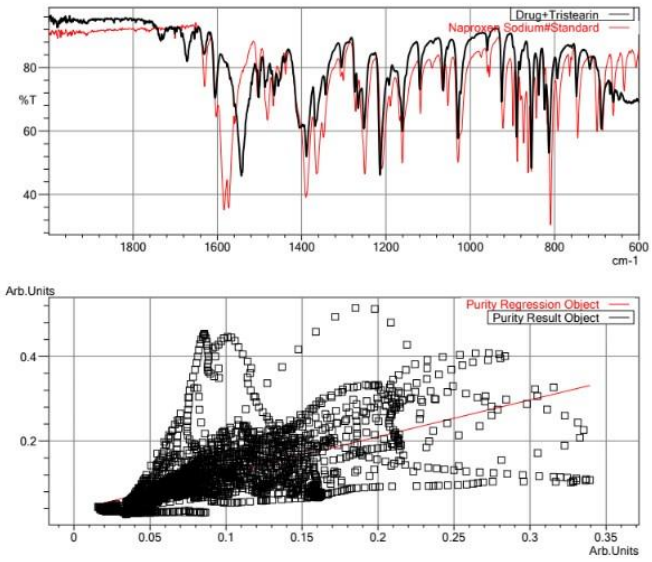

Fig 4: Shows the compatibility Drug + Tristearin

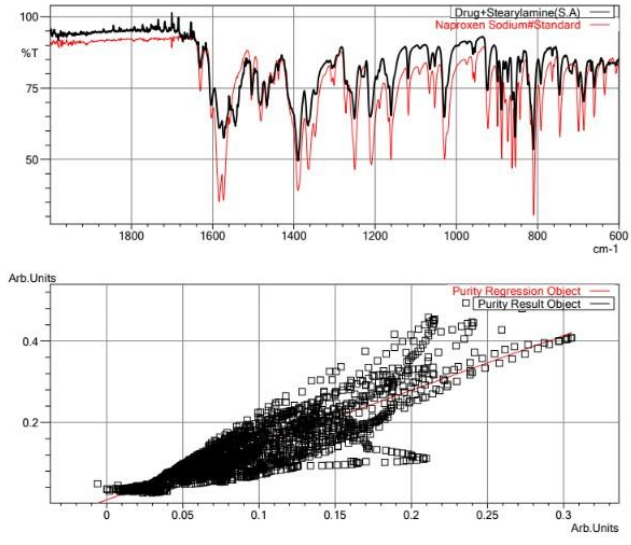

Fig 5: Shows the compatibility Drug + Stearyl amine

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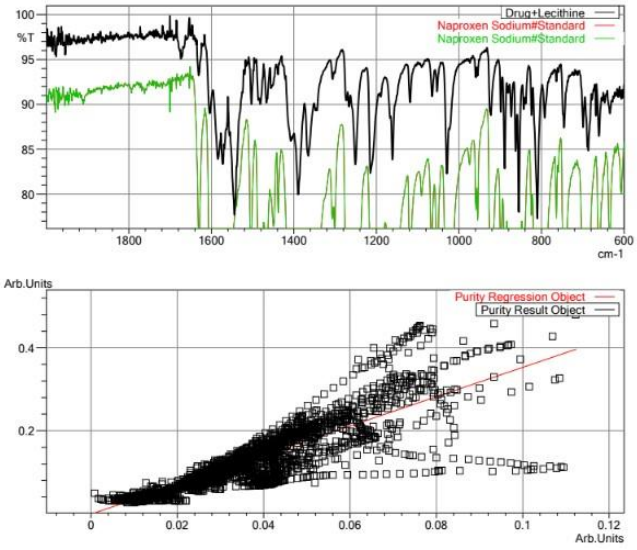

Fig 6: Shows the compatibility Drug + Lecithine

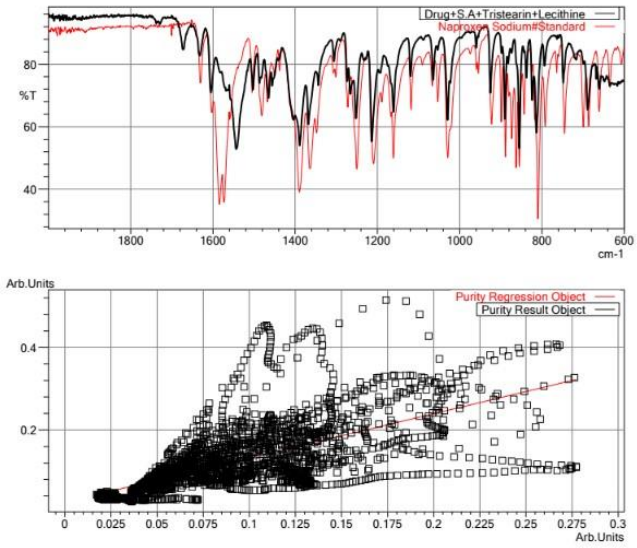

Fig 7: Shows the drug compatibility with all the excipient.

7. Formulation development.

1 Method of preparation.

Emulsomes were prepared by the method of film hydration followed by sonication. Some initial trial batches were formulated to check the feasibility of the method of preparation as per laboratory conditions. The evaluation of trial batches was done for the formation of the vesicle (Emulsomes) dispersed in an aqueous medium by using a digital compound microscope as shown in Figure 8 The round-shaped globule (vesicles) formed confirms the formation of the vesicular structure of Emulsomes and justified the method of preparation.

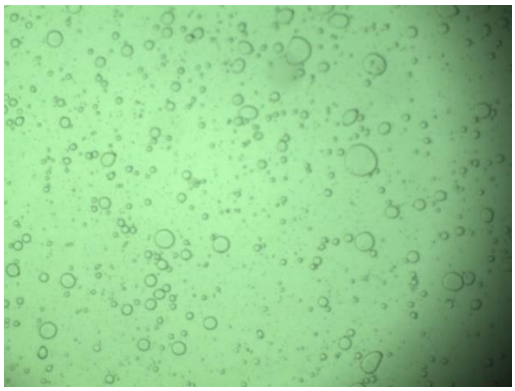

Fig 8: Microscopic image of trial batch of Emulsomes.

8. Characterization of optimized batch of Emulsomes.

1. Morphology.

The optimized batch (OB) of Emulsomes formulation is evaluated for surface morphology by using electron microscopy using the transmission electron microscopy (TEM). The micrograph of TEM reveals that the prepared Emulsomes were spherical, smooth, and vesicular structure. The TEM micrographs are shown in Figure 9.

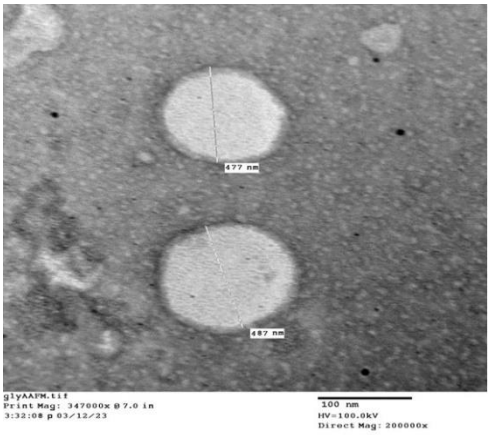

Fig 9: TEM images of optimized batch of Emulsomes.

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2. Particle size.

The values of particle size observed with particle size analyzer are given in Table 2. The particle size of Emulsomes formulation varies from 495 nm to 580 nm as shown in Figure 10. The particle size values of an optimized batch are shown in triplicate and an average value was 545.1 ± 43.31 nm as shown in Table 2. The particle size evaluation graph is shown in Figure 10

Table 2: Particle Size of Optimized batch

Readings	Particle Size (nm)
1	495.2
2	567.6
3	572.6
Average	545.1333
Standard Deviation	43.31574

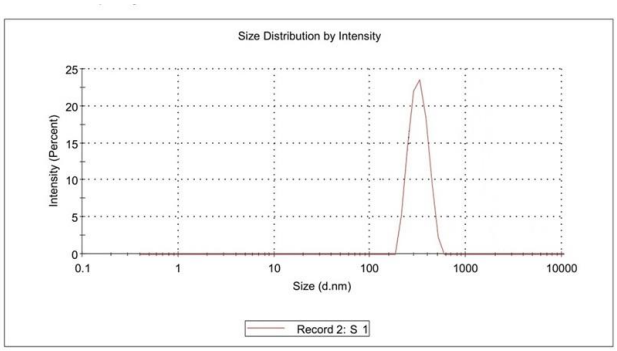

Fig 10: Particle Size of Optimized batch

3. Surface Charge.

The surface charge (zeta potential) of Emulsomes formulation varies from 22.6 mV to 68.5 mV as shown in the Figure 10. The zeta potential values of the optimized batch are shown in triplicate and an average value was 47.2 ± 1.8 mV, which is similar to that of the predicted value given by the design of experiment i.e. 45.000 mV. Zeta potential graph is shown in Figure 11.

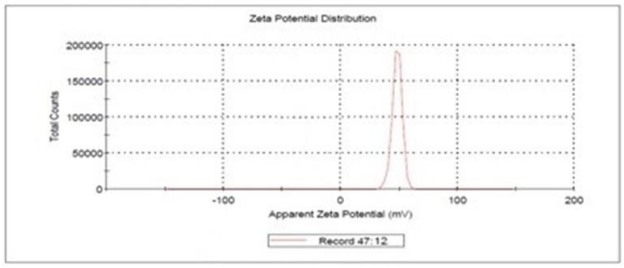

Fig 11: Zeta Potential of Optimized batch

4. Drugs Entrapment Efficiency (%).

Preparation of Sephadex G-50 Column.

The drug entrapment efficiency value of emulsomes of optimized batch was found to be 77.8%.

5. In vitro Drug release study.

***In vitro* drug release study**.

The filtered formulation was packed in a dialysis membrane and suspended in a dialysis medium and *in vitro* drug release study has been carried out for 16 hours to evaluate the drug release pattern from the Emulsomes formulation. The results are shown in Table 3 and Figure 12

The *in vitro* drug release study of an optimized batch (OB) was carried out using a dialysis membrane. The dialysis membrane allows drug molecules to diffuse through but restricts the diffusion of emulsomes vesicles. *In vitro* drug release study has been carried out for 16 hours to understand the drug release pattern from the Emulsomes formulation. The results are given in Table 3. The cumulative drug release during 1st hour of 29.92% indicated the initially burst release, which could possibly be due to the initial drug release from the phospholipid bilayer. After 1 h the release pattern showed slow release of the drug over 16 h study up to 96.69± 3.63 %. The sustained release of drug is due to the slow release of drug entrapped in solid lipid core composed of tristearin. The overall release study confirms the release of drug in way of controlled manner up to 16 h with a cumulative drug release of 96.69± 3.63%.

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Table 3: In vitro drug release of optimized batch of Emulsomes formulation.

Time (h)	Reading 1	Reading 2	Reading 3	Average (%)	Standard Deviation
0.5	11.46	15.67	12.98	13.37	2.13
1	31.87	27.92	29.97	29.92	1.97
2	37.42	31.36	33.79	34.19	3.05
4	42.55	45.23	38.52	42.1	3.38
6	54.23	48.34	49.45	50.67	3.13
8	61.77	62.43	58.36	60.85	2.18
10	74.28	79.57	82.99	78.95	4.39
12	91.43	85.93	88.38	88.58	2.75
16	98.38	92.53	99.18	96.69	3.63

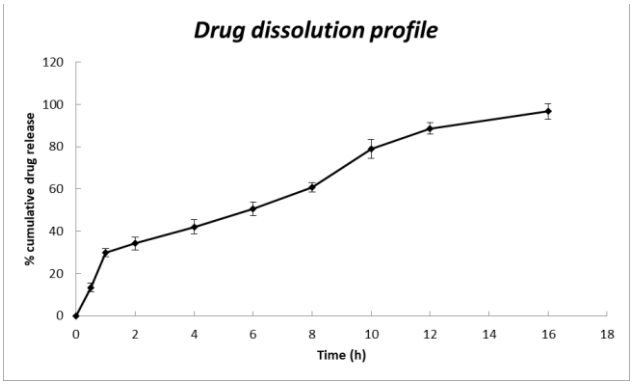

Fig 12: In vitro drug release Profile of optimized batch of Emulsomes formulation

6. Stability Studies.

6.1. Effect of storage on average particle size.

The optimized Emulsomes formulation has been chosen for evaluation of stability data based on the *in vitro* performance. Short term stability studies were carried out according to ICH guidelines for short term stability studies. The formulations were kept at the different temperatures (4 ± 1˚C and 25 ± 2˚C) for time period of six months and formulations were examined for residual drug content (%) and particle size. The stability study has been performed for the evaluation of the potential of the prepared Emulsomes to check their suitability to withstand the environmental challenges under stress conditions. The changes in particle size of formulations were observed after storing at different temperatures (4 ± 1ºC and 25 ± 2ºC) and no significant change in particle size was observed after storage at 4 ± 1˚C for six months and was recorded 545.13 ± 43.3, 629.63 ± 52.9 and 719.73 ± 68.8 nm as shown in table 4 and fig 13. But there has been an increase in the value of particle size of 1019.83.3 ± 87.2 after 6 months when stored at temperature of 25 ± 2˚C. This effect may be a cause of fusion of the bilayer membrane of particles at a higher temperature.

Table 4: Effect of storage conditions on particle size.

S. No	Initial Particle Size (nm)	4 ± 1ºC		25 ± 2ºC	
		3 Months	6 Months	3 Months	6 Months
1	495.2	592.4	649.6	824.3	1102.4
2	567.6	606.2	722.4	682.9	928.7
3	572.6	690.3	787.2	611.6	1028.4
Average	545.1333	629.6333	719.7333	706.2667	1019.833
Standard Deviation	43.31574	52.99003	68.83875	108.2581	87.1663

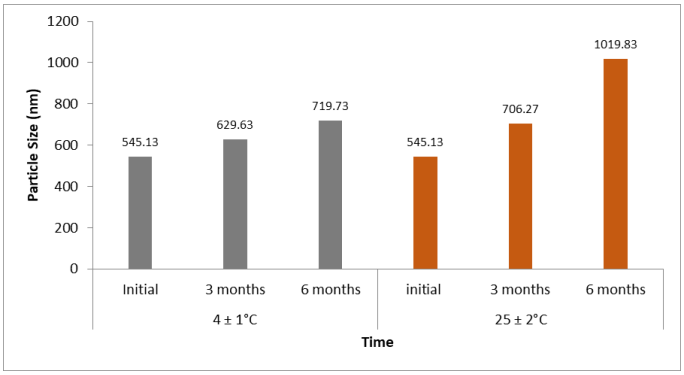

Figure 13: Effect of storage conditions on particle size

6.2. Effect of storage on residual drug content.

The residual drug content (%) of Emulsomes were determined periodically (after 0, 3, 6 months) after the storage of formulations at 4 ± 1ºC and 25 ± 2ºC. The residual drug content recorded after 6 months was 96.9

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± 0.9 at 4 ± 1ºC and the figure is not significant, but significant change in residual drug content at 25 ± 2ºC and was found to be 89.4 ± 1.95.

The data indicate that the change in particle size was not significant at 4 ± 1ºC but a significant level of increase in the value of particle size has been observed at 25 ± 2˚C. Similarly, a significant level of decrease in value of drug content has been observed at 25 ± 2˚C but no significant decrease in the value of drug content has been found at 4 ± 1ºC. The results showed that 4 ± 1 º C temperatures has been considered to be suitable for the storage of Emulsomes as shown in table 5 and and fig 14.

Table 5: Effect of storage conditions on residual drug content.

S. No	Initial Drug Content	4 ± 1ºC		25 ± 2ºC	
		3 Months	6 Months	3 Months	6 Months
1	100%	98.8	97.5	95.3	87.5
2	100%	98.1	96.8	96.7	89.3
3	100%	99.5	96.4	94.9	91.4
Average	100%	98.8	96.9	95.63333	89.4
Standard Deviation	00	0.7	0.556776	0.945163	1.951922

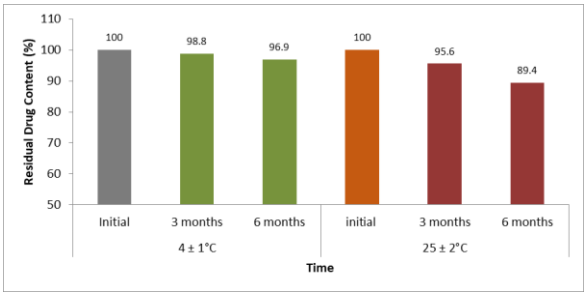

Figure 14: Effect of storage conditions on residual drug content

Conclusion

The present investigation successfully developed and optimized naproxen-loaded emulsomes to overcome the drug's inherent solubility limitations and associated gastrointestinal side effects. Utilizing the thin-film hydration technique followed by sonication, the emulsomes were prepared with biocompatible lipid excipients such as lecithin, cholesterol, tristearin, and stearylamine. The formulation exhibited desirable physicochemical characteristics, including an average particle size of 545.1 ± 43.3 nm, a high zeta potential of 47.2 ± 1.8 mV ensuring colloidal stability, and a substantial entrapment efficiency of 77.8%. The morphology confirmed through TEM revealed uniform, spherical vesicles, ideal for consistent drug delivery.

In vitro release studies demonstrated a sustained drug release pattern, with 96.69 ± 3.63% of naproxen released over 16 hours. This indicates a well-controlled release mechanism, likely attributed to the lipidic core and phospholipid bilayer structure. Stability studies under varied storage conditions validated the robustness of the emulsomal system, with minimal alterations in drug content and particle size when stored at 4 ± 1°C.

Overall, the emulsomal formulation provided a promising delivery platform for enhancing naproxen's solubility, bioavailability, and therapeutic performance. The study supports the potential of emulsomes as a viable carrier for other poorly water-soluble drugs, addressing key formulation challenges. Future research may explore in vivo evaluations, scalability, and clinical translation of this system to fully harness its benefits in therapeutic applications.

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