IJISEM
INTERNATIONAL JOURNAL OF INNOVATIONS IN SCIENCE ENGINEERING AND MANAGEMENT

International Journal of Innovations In Science Engineering And Management

OPEN ACCESS

Volume: 5

Issue: 2

Month: April

Year: 2026

ISSN: 2583-7117

Published: 11.04.2026

Citation:

Jitendra Yadav, Dr. Brajesh Kumar Arjariya, Praveen Bhawsar "Preparation and Characterization of Fenoprofen Liposomes for Controlled Drug Delivery Applications" International Journal of Innovations in Science Engineering and Management, vol. 5, no. 2, 2026, pp. 88-99

DOI:

10.69968/ijisem.2026v5i288-99

Preparation and Characterization of Fenoprofen Liposomes for Controlled Drug Delivery Applications

Jitendra Yadav[1], Dr. Brajesh Kumar Arjariya[2], Praveen Bhawsar[3]

[1]*Research Scholar, Department of M. Pharma (Pharmaceutics), Malhotra College of Pharmacy, Badwai, Near Karond, Bhopal (M.P.)*

[2]*Professor, Malhotra College of Pharmacy, Badwai, Near Karond, Bhopal (M.P.)*

[3]*Associate Professor, Department of M. Pharma (Pharmaceutics), Malhotra College of Pharmacy, Badwai, Near Karond, Bhopal (M.P.)*

Abstract

The present study focuses on the formulation and evaluation of a liposomal drug delivery system for Fenoprofen HCl to enhance therapeutic efficacy and reduce associated toxicities. Preformulation studies, including organoleptic evaluation, solubility, melting point, partition coefficient, and λmax determination (270.8 nm), were carried out to establish the physicochemical properties of the drug. Compatibility studies using FTIR confirmed the absence of interactions between the drug and excipients. Liposomes were prepared by the thin film hydration technique using soybean lecithin and stabilizers such as dicetylphosphate and stearylamine. The formulated liposomes were evaluated for particle size, zeta potential, surface morphology, drug entrapment, in vitro drug release, and stability. Among all formulations, F6 exhibited optimal particle size, higher stability (zeta potential −23.4 mV), and sustained drug release behavior. SEM analysis confirmed smooth and uniform vesicle morphology. In vitro release studies indicated controlled drug release following zero-order kinetics and Case II transport mechanism. Stability studies demonstrated that the formulations remained stable over 60 days. Overall, the developed liposomal formulation of Fenoprofen showed improved stability, controlled drug release, and potential for effective management of pain and inflammatory conditions such as osteoarthritis and rheumatoid arthritis.

Keywords; Liposomal Drug Delivery System, Fenoprofen HCl, Thin Film Hydration Technique, In Vitro Drug Release, Zeta Potential and Stability Analysis.

INTRODUCTION

The name of liposome is derived from two Greek words "Lipid" meaning fat and "Soma" meaning body. A liposome is a tiny vesicle, composed of the same material as a cell membrane. It can be filled with drugs, and used as drugs deliver carrier for cancer and otherdiseases. Structurally, they are concentric bleeder vesicles in which an aqueous volume is entirely enclosed by a membraneous lipid bilayer. Membranes are generally prepared by phospholipids, which are molecules that have a hydrophilic head group and a hydrophobic tail group. The head is attracted to water, and the tail, which is prepared by long hydrocarbon chain, is repelled by water.

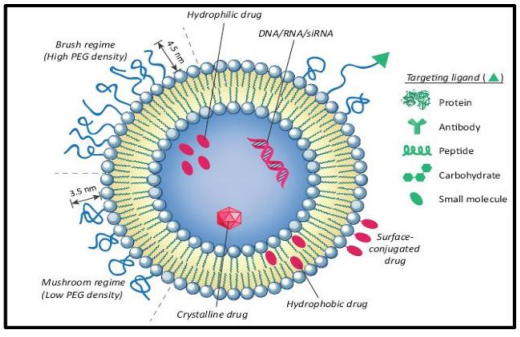


Figure 1: Structural and design considerations for liposomal drug delivery.

The water-soluble drugs are present in aqueous compartments whereas lipid soluble drugs and amphilhilic drugs insert themselves in phospholipids bilayer. The liposomes containing drugs can be administrated by many routes like intervenous, oral inhalation, ocular and local application, used in the treatment of many diseases. It is satisfactory and advanced carrier and has capability to encapsulate hydrophilic as well as lipophilic drugs and shield them from degradation. In general, they are more effective and less toxic than conventional dosage form due to the bilayer composition and structure. Liposomes are usually applied to the skin as liquids or gels and hydrophilic polymers are considered to be suitable thickening agents. Liposomes as a carriers are biocompatible, biodegradable, targeting, and stimulus-responsive. Local anesthetics are also encapsulated into liposomes have longer duration of action, decrease in circulating plasma levels, decrease central nervous system toxicity and cardiovascular toxicity The unfavourable interactions may occur between hydrophilic and hydrophobic phase which prevent by folding into closed concentric vesicles. The large free energy difference develops between the hydrophilic and hydrophobic environment is decreased by the formation of large vesicle. The spherical structures have minimum surface tension and maximum stability. Hence there is maximum stability of self-assembled structure by forming vesicles.

Properties of Liposomes

- Loading of drug and control of drug release rate.
- Overcoming the rapid clearance of liposomes.
- Intracellular delivery of drugs.
- Receptor-mediated endocytosis of ligand-targeted liposomes.
- Triggered release.
- Delivery of nucleic acids and DNA.

Structural Components of Liposomes

The main components of liposomes are phospholipids which are stabilized by cholesterol, with other stabilisers sometimes added to the mixture depending on the specific use of the liposome.

Phospholipids: Phospholipids are the most important structural part of biological membranes. In the structure of the phospholipids on the one end of the molecule are the hydrophobic acyl hydrocarbon chains and the other end of the molecule is also called as phosphate head group, is hydrophilic. It contains the choline group which is the most abundant lipids in nature. The phospholipid mostly used for liposomes preparation is the phosphatidylcholine. Phosphatidylcholines are the generally use due to their suitable stability and their ability to act against changes in pH or salt concentrations in the product and biological environment Sphingolipids are the membrane components made up of sphingoid base. Natural gangliosides class of sphingolipids are added in liposome preparation to provide a layer of surface charged groups, to prolong the lifetime of liposomes in the blood and to prevent their uptake by the reticuloendothelial system (RES). Sphingomyelins are important phospholipids useful in regulation of cholesterol distribution within membranes.

Cholesterol: Cholesterol is one of the chief components in liposomal formulations which increases the rigidity of the lipid bilayer, improves fluidity of the membrane, increase stability and the time of circulation in the blood stream.Cholesterol dose not by itself form bilayer structure, but can be incorporated into phospholipid membranes in very high concentration upto 1:1 or even 2:1 molar ration of cholesterol to phosphatidylcholine. Cholesterol enter into the membrane with its hydroxyl group leaning towards the aqueous surface and aliphatic chain aligent parallel to the acyl chains in the center of the bilayer.

Liposomes Classification

Liposomes classification depend upon size (small, intermediate, or large), number of bilayers (uni- and multi-lamellar), composition and mechanism of drug delivery. Small unilamellar vesicles consist of a single lipid bilayer with an average diameter ranging from 25 to 100 nm. Large unilamellar vesicles also made up of one lipid bilayer and are greater than 100 nm, on other hand multilamellar vesicles are made up of several concentric lipid bilayers and measure of 1-5 µm.

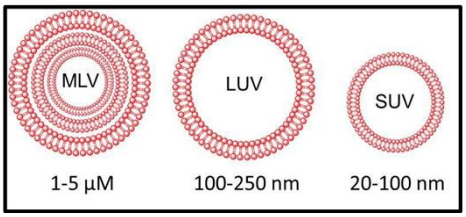


Figure 2: Liposomes classification based on size and lamellarity

According to the composition and mechanism of drug delivery, the liposomes can be classified as conventional liposomes, long-circulating liposomes, polymorphic liposomes (pH-sensitive, thermo-sensitive, and cationic

liposomes), and decorated liposomes (surfacemodified liposomes and immunoliposomes).

DRUG PROFILE

- **Drug name:** Fenoprofen
- **Chemical formula:** C15H14O3
- **IUPAC Name:** 2-(3-phenoxyphenyl)propanoic acid
- **Synonyms:** Fenoprofen, Fenoprofene, Fenoprofeno, Fenoprofenum

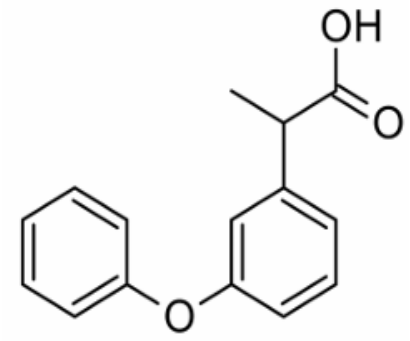


Figure 3: Structure of Fenoprofen

Description

An anti-inflammatory analgesic and antipyretic highly bound to plasma proteins. It is pharmacologically similar to aspirin, but causes less gastrointestinal bleeding.

Pharmacodynamics

Fenoprofen is a propionic acid derivative with analgesic, anti-inflammatory and antipyretic properties. Fenoprofen inhibits prostaglandin synthesis by decreasing the enzyme needed for biosynthesis. In patients with rheumatoid arthritis, the anti-inflammatory action of fenoprofen has been evidenced by relief of pain, increase in grip strength, and reductions in joint swelling, duration of morning stiffness, and disease activity (as assessed by both the investigator and the patient). In patients with osteoarthritis, the anti-inflammatory and analgesic effects of fenoprofen have been demonstrated by reduction in tenderness as a response to pressure and reductions in night pain, stiffness, swelling, and overall disease activity (as assessed by both the patient and the investigator). These effects have also been demonstrated by relief of pain with motion and at rest and increased range of motion in involved joints. In patients with rheumatoid arthritis and osteoarthritis, clinical studies have shown fenoprofen to be comparable to aspirin in controlling the aforementioned measures of disease activity, but mild gastrointestinal reactions (nausea, dyspepsia) and tinnitus occurred less frequently in patients treated with fenoprofen than in aspirin-treated patients. It is not known whether fenoprofen causes less peptic ulceration than does aspirin. In patients with pain, the analgesic action of fenoprofen has produced a reduction in pain intensity, an increase in pain relief, improvement in total analgesia scores, and a sustained analgesic effect.

Mechanism of action

Fenoprofen's exact mode of action is unknown, but it is thought that prostaglandin synthetase inhibition is involved. Fenoprofen has been shown to inhibit prostaglandin synthetase isolated from bovine seminal vesicles.

Absorption

Rapidly absorbed under fasting conditions, and peak plasma levels of 50 µg/mL are achieved within 2 hours after oral administration of 600 mg doses.

Metabolism

About 90% of a single oral dose is eliminated within 24 hours as fenoprofen glucuronide and 4'-hydroxyfenoprofen glucuronide, the major urinary metabolites of fenoprofen.

Half-life

Plasma half-life is approximately 3 hours.

Toxicity

Symptoms of overdose appear within several hours and generally involve the gastrointestinal and central nervous systems. They include dyspepsia, nausea, vomiting, abdominal pain, dizziness, headache, ataxia, tinnitus, tremor, drowsiness, and confusion. Hyperpyrexia, tachycardia, hypotension, and acute renal failure may occur rarely following overdose. Respiratory depression and metabolic acidosis have also been reported following overdose with certain NSAIDs.

Table 1: Dosage Forms

Capsule	Oral	400 mg/1
Capsule	Oral	200 mg/1
Capsule	Oral	300 mg/1
Capsule	Oral	
Tablet	Oral	300 MG
Tablet	Oral	600 MG

AIM

The present study aims to formulate and evaluate a liposomal drug delivery system for Fenoprofen HCl in order to reduce its associated toxicities, enhance therapeutic efficacy, and improve drug targeting. The work focuses on

the development of stable liposomal formulations using various biolipids and stabilizers (both positive and negative) to optimize drug loading and particle size. Additionally, the study aims to investigate the influence of stabilizers on key parameters such as particle size distribution, percentage of free drug, drug assay, in-vitro drug release, release kinetics, and stability. The ultimate objective is to develop a long-circulating, stable liposomal formulation of Fenoprofen HCl with minimized adverse effects and improved drug delivery performance.

MATERIALS AND METHODS

Table 2: List of Materials

S. No.	Materials	Manufacturer
1	Fenoprofen	FDC, Mumbai
2	HCl	SD Fine Chemicals
3	Dichloromethane	Central Drug House (P) Ltd, New Delhi, India.
4	Ethanol	Central Drug House (P) Ltd, New Delhi, India.
5	DMSO	Central Drug House (P) Ltd, New Delhi, India.
6	Soya phosphatidyl choline	Himedia, India
7	Dicetyl phosphate (DCP)	Himedia, India
8	Ethyl Acetate	Himedia, India
9	Butyl Acetate	Himedia, India

Table 3: List of Equipment

S. No.	Equipment	Company
1	Electronic Weighing Balance	Sirtech digital scale, India
2	Mechanical Stirrer	Remi Motors, India.
3	Magnetic Stirrer	MC Dalal& Co India
4	UV Visible Spectrophotometer	Shimadzu, Japan.
5	Particle size analyser	CILAS – 1604L, France
6	SEM	Hitachi, Japan
7	Ultracentrifuge	Eppendorf centrifuge, Germany

Selection of Drug & Excipient

The drug was purchased from Sigma Eldritch Pvt ltd.

Pre formulation

The basic purpose of the Pre formulation activity are to provide a rational basis for the formulation approaches, to maximize the chances of success in formulating an acceptable product and to ultimately provide a basis for optimizing drug product quality and performance. Pre formulation is defined as an investigation of physical & chemical properties of sustained release matrix tablet substance alone and when combined with excipient. A step in time saves nine, so the Pre formulation studies of the new product can away the disaster that is disasters are prevented in advance. (Vilegave et al 2013)

Organoleptic evaluation

It is the initial evaluation during Pre formulation studies which assess the colour, odour and taste of the substance. The appearance was checked visually for colour, homogeneity and transparency. The appearance was checked visually for colour, homogeneity and transparency (Rahman et al., 2018)

Solubility

Aqueous solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy. Solubility of drug was determined in water and methanol, ethanol, chloroform and ethyl acetate (Bala et al., 2004)

Melting point

Melting point of drug was determined by Open capillary method. The melting point of a drug is one of the first and more reliable physical properties measured it can be advantageously used as a guide in early drug discovery and development (Chu and Yalkowsky 2009).

Partition coefficient

Liposome/buffer partition coefficients (Kp) can be determined by different methods, including phase separation (for a comparative review on phase separation methods, consult (Dipali et al. 1996). Since techniques used to separate the free drug from the liposome encapsulated drug can potentially cause leakage of contents and, in some cases, uncertainty in the extent of separation, research using methods that do not rely on separation are of interest.

Determination of λmax

A solution of drug containing the concentration 10 µg/ ml was prepared in 0.1N HCl. The solution was scanned in the range of 200 – 300 nm UV spectrum using Systolic double beam spectrophotometer.

Determination of absorption maximum (λmax): 2 ml of stock solution (100 µg/ml) was taken in 10 ml volumetric flask and volume was made up to 10 ml with solutions of 0.1N HCl (20 ug/ ml) and scanned on a double beam spectrophotometer against respective media blanks. An absorption maximum (λ max) of 270.8 nm was obtained.

This ƛ max was selected for preparation of standard curve of fenoprofen in different media (Chinnala & Panigrahy 2016).

Standard calibration curve of liposome

From the stock solution (100 µg/ml) aliquots of 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, and 5 ml solution were taken and diluted to 10 ml to obtain concentrations from 5 to 50µg/ml with HCl. The absorbance of solutions was determined at ƛ max 270.8 nm against HCl as blank. The experiment was repeated three times and calibration curve was plotted from the mean value (Chinnala & Panigrahy 2016)

Compatibility studies

Compatibility studies by FTIR

Physical changes in the freeze-dried liposomes were studied at a molecular level by FTIR measurements at different temperatures. With this technique, the acyl chain packing in the liposome bilayers can be studied by monitoring the symmetric. Dry sample of drug and potassium bromide was mixed uniformly and filled into the die cavity of sample holder and an IR spectrum was recorded using diffuse reflectance FTIR spectrophotometer (460 plus, Jasco). (Chinnala & Panigrahy 2016).

Preparation of liposomes

The correct choice of liposome preparation method depends on the following parameters:

1) The physicochemical characteristics of the material to be entrapped and those of the liposomal ingredients.
2) The nature of the medium in which the lipid vesicles are dispersed.
3) The effective concentration of the entrapped substance and its potential toxicity.
4) Additional processes involved during application/ delivery of the vesicles.
5) Optimum size, polydispersity and shelf-life of the vesicles for the intended application and
6) Batch-to-batch reproducibility and possibility of large-scale production of safe and efficient liposomal products.

Liposomes are manufactured in majority using various procedures in which the water soluble (hydrophilic) materials are entrapped by using aqueous solution of these materials as hydrating fluid or by the addition of drug/drug solution at some stage during manufacturing of the liposomes. The lipid soluble (lipophilic) materials are solubilized in the organic solution of the constitutive lipid and then evaporated to a dry drug containing lipid film followed by its hydration. These methods involve the loading of the entrapped agents before or during the manufacturing procedure (Passive loading). However, certain type of compounds with ionizable groups, and those which display both lipid and water solubility, can be introduced into the liposomes after the formation of intact vesicles (remote loading). (Dua et al., 2012).

Preparation of drug loaded liposomes

Liposomes are manufactured in majority using various procedures in which the water soluble (hydrophilic) materials are entrapped by using aqueous solution of these materials as hydrating fluid or by the addition of drug/drug solution at some stage during manufacturing of the liposomes. The lipid soluble (lipophilic) materials are solubilized in the organic solution of the constitutive lipid and then evaporated to a dry drug containing lipid film followed by its hydration. These methods involve the loading of the entrapped agents before or during the manufacturing procedure (Passive loading). However, certain type of compounds with ionizable groups, and those which display both lipid and water solubility, can be introduced into the liposomes after the formation of intact vesicles.

Physical characterization of liposomes

Particle size analysis

The particle size of liposomes was determined by using scanning electron microscope. Optimized batch of liposomes were viewed under microscope to study their size. Size of liposomal vesicles was measured at different locations on slide by taking a small drop of liposomal dispersion on it and average size of liposomal vesicles was determined (Chinnala & Panigrahy 2016).

Zeta potential

Zeta potential is a physical property which is exhibited by any particle in suspension. It can be used to optimize the formulations of suspensions and emulsions. Knowledge of the zeta potential can reduce the time needed to produce trial formulation. It is also an aid in predicting long-term stability. The magnitude of the zeta potential gives an indication of the potential stability of the colloidal system. If all the particles in suspension have a large negative or positive zeta potential, then they will tend to repeal each other and there will be no tendency for the particles to come together. However, if the particles have low zeta potential values then there will be no force to prevent the particles coming together and flocculating. The significance of zeta potential is that its value can be related to the stability of

colloidal dispersions. So, colloids with high zeta potential (negative or positive) are electrically stabilized while colloids with low zeta potentials tend to coagulate. Charge on empty and drug loaded vesicles surface was determined using Zetasizer 300HSA (Malvern Instruments, Malvern, UK). Analysis time was kept for 60 s and average zeta potential and charge on the liposome was determined.(Mitkari et., al 2010)

Scanning Electron Microscopy

EM provides high-resolution images with good depth of field and can provide vital information in the research, development, and quality control of pharmaceutical products. Formulations such as controlled-release solid dosage forms are often characterised at various stages during their preparation and also during the in vitro and in vivo testing of drug release from the dosage form and can provide vital information in the research, development, and quality control of pharmaceutical products. Formulations such as controlled release solid dosage forms are characterised at various stages during their preparation and also during the in vitro and in vivo testing of drug release from the dosage form.

They showed that using the freeze-drying method to prepare the liposome samples for SEM resulted in a large proportion of visible lumps and crusted material (Robson et al., 2018).

In vitro characterization

Liposome characterization the extruded pre-lyophilized liposome was characterized by the following methods. Vesicle size measurement immediately after preparation, LEP-ETU formulations were examined for possible aggregation by visual inspection. Thereafter, the liposome mean diameter and particle size distribution for pre-lyophilized and reconstituted LEPETU samples were determined using dynamic light scattering (DLS) technique with a Nicomp 380 Submicron Particle Sizer (Particle Sizing Systems, Santa Barbara, CA, USA) equipped with auto-dilution function. Data were analyzed in terms of intensity, volume and number distributions assuming that the particles are spheres of uniform density which scatter light according to classical Mie Theory. Data were reported as volume weighted distribution and represented as the mean of at least two measurements.

Study on in vitro drug release.

In vitro release of MTO from liposomal formulations was analyzed by membrane dialysis. Pre-experiments were carried out on the in vitro release of MTO from liposomes with or without CH coating in HCl solution (pH 7.4), and less than 5% of MTO was released up to 48 hours from each preparation (data not shown). In this study, equal amount of fetal cattle serum (FCS) was added to the liposome to simulate the in vivo environment. Briefly, 4 mL of CH-coated liposomes mixed with 4 mL of FCS was placed in the cellulose membrane tubing (molecular weight cut-off was 8,000–10,000). For uncoated liposomes, sodium acetate buffer solution (pH 6.0) was added to the liposomes to adjust the concentration. Meanwhile, MTO aqueous solution was treated in the same way and used as control. Then the tubing was tightened and soaked in 200 mL of PBS 7.4 as dissolution medium. The experiments were carried out at 37°C for 48 hours in 3 replicates. At predetermined intervals, 5 mL of the dissolution medium was withdrawn and replaced with the same amount of pre-warmed dissolution medium. The samples of the replicates were pipetted directly into disposal cuvettes and analyzed by an 8453 UV-Visible Spectrophotometer (Agilent Technologies, Santa Clara, CA, USA) at 658 nm (Zhuang et al., 2010)

Release kinetics (Harris Shoaib et al., 2006)

To analyze the in vitro release data various kinetic models were use to describe the release kinetics. The zero order rate Eq. (2) describes the systems where the drug release rate is independent of its concentration. The first order Eq. (3) describes the release from system where release rate is concentration dependent. Higuchi (1963) described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows:

- Zero - order kinetic model – Cumulative % drug released versus time.
- First – order kinetic model – Log cumulative percent drug remaining versus time.
- Higuchi's model – Cumulative percent drug released versus square root of time.

Zero order kinetics

Zero order release would be predicted by the following equation:

$$A_t = A_0 - K_0 t \quad |$$

Where

- At = Drug release at time 't'

- A0 = Initial drug concentration.
- K0 = Zero- order rate constant (hr-1)

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys Zero – order kinetics and its slope is equal to Zero order release constant K0.

First order kinetics

First - order release could be predicted by the following equation:

$$\text{Log } C = \log C_0 - K_t / 2.303$$

Where,

- C = Amount of drug remained at time 't'
- C0 = Initial amount of drug.
- K = First - order rate constant (hr-1).

When the data plotted as log cumulative percent drug remaining versus time, yields a straight line, indicating that the release follow first order kinetics. The constant 'K1' can be obtained by multiplying 2.303 with the slope value.

Higuchi's Model

Drug release from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation:

$$Q = [D\epsilon / \tau (2A - \epsilon Cs)\, Cst]^{1/2}$$

Where,

- Q = Amount of drug release at time't'
- D = Diffusion coefficient of the drug in the matrix.
- A = Total amount of drug in unit volume of matrix.
- Cs = Solubility of drug in the matrix
- Є = Porosity of the matrix.
- τ = Tortuosity.
- t = Time (hrs at which q amount of drug is released.

Above equation can be simplified as if we assume, that 'D', 'Cs' and 'A' areconstant. Then equation: becomes

$$Q = Kt^{1/2}$$

Korsmeyer–Peppas Model

Describes the fraction of drug release relates exponentially with respect to time (Suresh kumar P et al., 2015).

$$Mt / M\infty = K\, tn$$

Where Mt/M∞ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent. In this model, the value of n characterizes the release mechanism of drug. To study the release kinetics, data obtained from In vitro drug release studies are plotted as log cumulative percentage drug release versus log time (Bhatt Neha et al., 2013).

Short term stability studies

The stability of a pharmaceutical delivery system may be defined as the capability of a particular formulation, in a specific container. The short-term stability was conducted to monitor physical and chemical stabilities of the liquid form of Amoxicillin trihydrate liposomal formulations at 40oC and room temperature for up to three months. The stability parameter, such as Assay was determined as function of the storage time Neutral liposomes were produced using microfluidics at a 3:1 FRR and 15 mL/min TFR (4 mg/mL initial lipid concentration) in either MeOH, EtOH or IPA. Solvent was removed by TFF (12 mL wash cycle per mL of sample). Liposome suspensions were then stored at 2–8 °C in the fridge and their size and PDI was measured over 7 days with the Zetasizer Nano ZS (Malvern Instruments Ltd., Worcestershire, UK) using a 1/10 dilution with purified water. (Webb et al., 2019)

RESULTS AND DISCUSSION

Pre-formulation Studies

Pre formulation studies were performed. The result is given below

a) Organoleptic evaluation

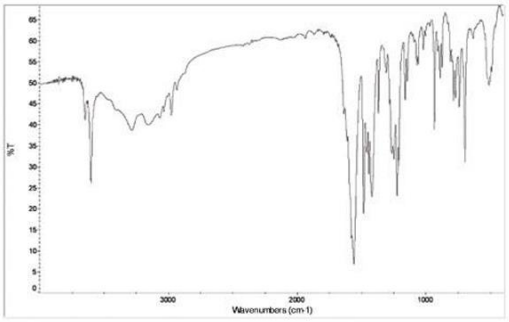
	Name of Drug	inference	Result
Color	Fenoprofen	White and Yellow	White and Yellow
Odor		Unpleasant breath odor	Unpleasant breath
Taste		Metallic taste	Metallic taste
Appearance		Solid	Solid
Melting Point		168-1710C	1700C

Solubility of Cidofovir		
S. No	Solvent	Result
1	Water	Soluble
2	DMSO	Insoluble
3	Methanol	Soluble
Partition co-efficient		

S.No.	Solvent system	Partition Coefficient
1	n-Octanol/Water	3.65± 3.87

Infrared Spectroscopy

It was done by making pellets of the drug in KBr. FTIR spectra was taken at Thermo Instrument. The observed peaks were compared with reported spectra for groups.



Graph 1: Important band frequencies in FTIR spectrum of Fenoprofen

Korsmeyer–Peppas model describes the fraction of drug release relates exponentially with respect to time (Sureshkumar P et al.,2015).

$$Mt / M\infty = K\,tn$$

Where Mt/M∞ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent. In this model, the value of n characterizes the release mechanism of drug. To study the release kinetics, data obtained from In vitro drug release studies are plotted as log cumulative percentage drug release versus log time (Bhatt Neha et al., 2013).

S. No.	Named Group	Reported Band frequency	Band frequency obtained
1	Imidazole C-N stretching	3140-1475	1409
2	Aromatic C-H stretching	3000-3100	3107
3	Aliphatic C-H stretching	2850-3000	2962
4	C=C aromatic	1450-1590	1487
5	C-Cl halogen attached at benzene ring	650-800	754
6	Ether C-O-C stretch ether	1050-1250	1089

Standard Curve of Fenoprofen in HCl Solution (pH 7.4)

All dilutions and measurements were made as above in HCl solution of pH 7.4 made as per formula (I.P.). The absorbance was taken at λmax 293.7nm against a reagent blank. The standard curve was plotted between absorbance and concentration.

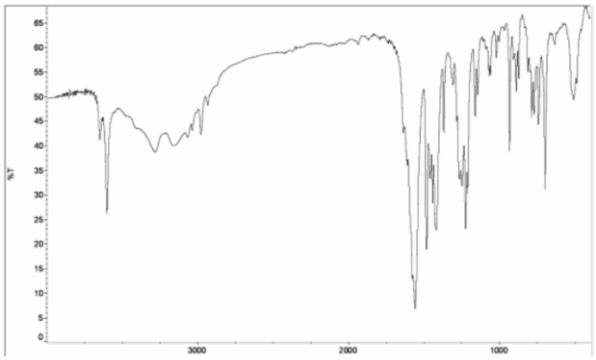
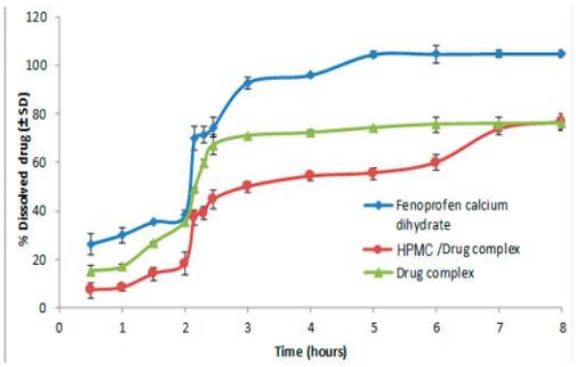


Table 4: Standard Curve of Fenoprofen in HCl Solution (pH 7.4)

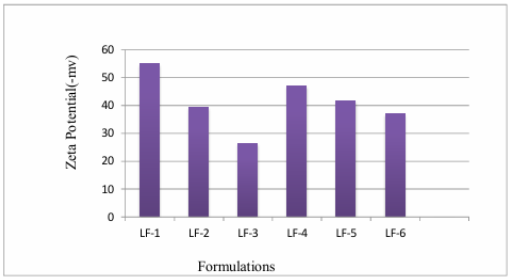
S. No.	Drug Conc. (µg/ml)	Absorbance at 293.7 nm
1	5	0.112
2	10	0.287
3	15	0.452
4	20	0.543
5	25	0.672



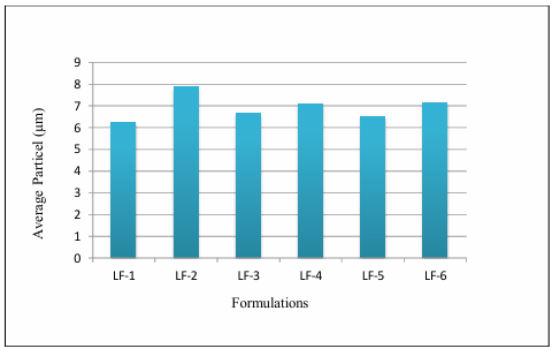
Graph 2: Standard Curve of Fenoprofen in HCl solution (pH 7.4) at 293.7nm

Table 5: Evaluation of Fenoprofen Loaded Liposomal Formulation

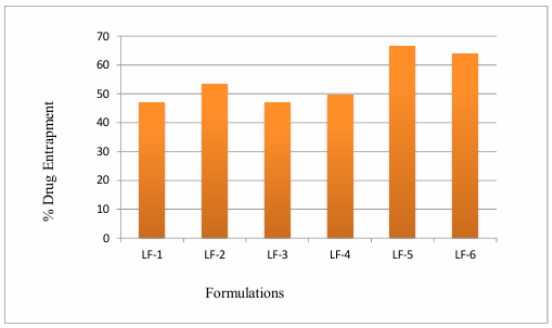
Form. Code	Average Particle (µm)	Zeta potential (mv)	%Drug Entrapment
LF-1	6.24±0.11	54.94±2.27	46.94±0.77
LF-2	7.86±0.20	39.37±1.35	53.45±0.59
LF-3	6.65±0.16	26.39±3.65	47.03±1.38
LF-4	7.10±0.23	47.05±1.45	49.39±2.02
LF-5	6.50±0.18	41.75±4.61	66.32±1.34
LF-6	7.16±0.26	36.99±2.72	63.98±1.47



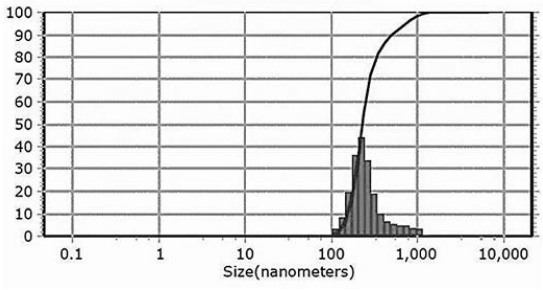
Graph 3: Zeta potential (-mv) of Fenoprofen Loaded Liposomal Formulation.



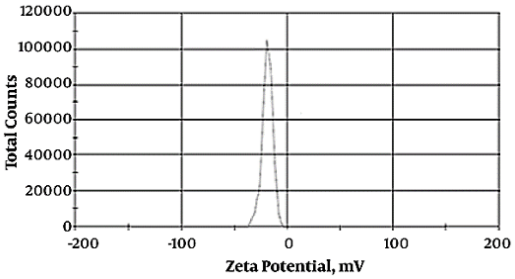
Graph 4: Mean particle size (µm) of Fenoprofenl Loaded Liposomal Formulation



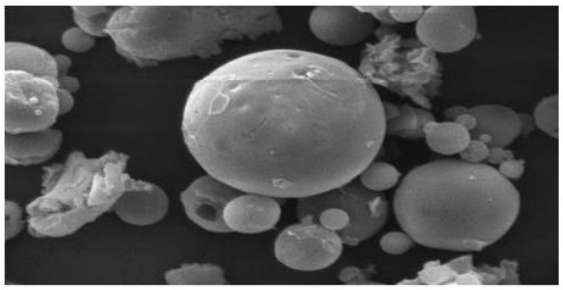
Graph 5: %Drug Entrapment of Fenoprofen Loaded Liposomal Formulation



Graph 6: Particle Size Distribution of Fenoprofen Loaded Liposomal Formulation.



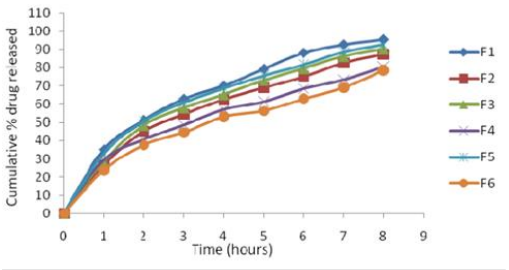
Graph 7: Zeta Potential of Fenoprofen Loaded Liposomal Formulation



Graph 8: SEM Photograph of Fenoprofen Loaded Liposomal Formulation

Table 6: Cumulative % of Drug Release of Fenoprofen Loaded Liposomal Formulation

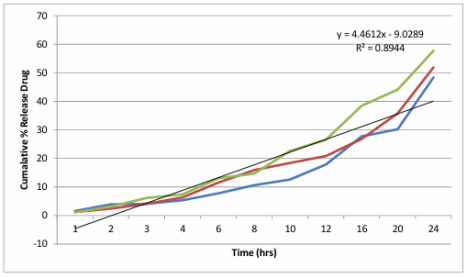
FC/T	Cumulative % of Drug Release					
	LF-1	LF-2	LF-3	LF-4	LF-5	LF-6
2	2.24±1.56	2.8±1.33	2.88±1.18	4.43±2.23	4.26±1.66	2.45±1.35
4	7.48±1.32	9.11±1.67	9.22±2.09	11.72±1.86	12.53±1.53	7.88±1.66
6	12.42±1.98	15.27±1.54	16.09±1.08	19.67±2.06	20.96±1.79	13.58±1.39
8	18.31±2.15	22.39±1.17	23.18±2.62	29.23±1.56	29.95±1.43	19.58±1.21
10	25.34±2.28	28.74±2.15	31.15±1.32	37.69±2.98	40.13±3.08	25.99±1.63
24	47.89±1.06	59.68±2.18	64.51±2.67	71.61±1.54	67.79±1.69	52.39±2.52



Graph 9: Cumulative % of Drug Release of Fenoprofen Loaded Liposomal Formulation

Table 7: Zero order release model of Fenoprofen liposomal Optimized formulations

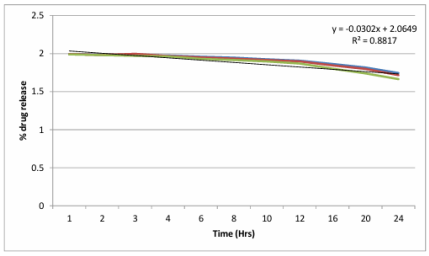
Time (hrs)	Cumulative % Drug Release		
	F2	F4	F6
1	1.58	1.24	1.15
2	3.92	2.37	3.07
3	4.12	4.11	6.19
4	5.33	6.32	7.43
6	7.77	11.5	13.01
8	10.65	15.9	14.62
10	12.63	18.38	22.62
12	17.91	20.86	26.56
16	27.73	26.82	38.47
20	30.25	35.78	44.07
24	48.31	51.84	57.67



Graph 10: Comparison of Zero order release studies for optimized formulation

Table 8: First order release model of Fenoprofen liposomal Optimized formulations.

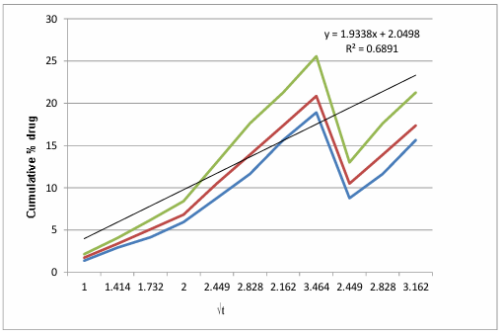
Time (hrs)	Log Remaining % drug release		
	F2	F4	F6
1	1.993	1.992	1.990
2	1.987	1.985	1.981
3	1.980	1.977	1.972
4	1.973	1.969	1.961
6	1.960	1.951	1.931
8	1.946	1.935	1.915
10	1.926	1.917	1.896
12	1.908	1.898	1.871
16	1.864	1.846	1.802
20	1.817	1.800	1.739
24	1.745	1.717	1.665



Graph 11: Comparison of First order release studies for optimized formulations LF-2, LF-4 and LF-6

Table 9: Higuchi release model of Fenoprofen liposomal Optimized formulations

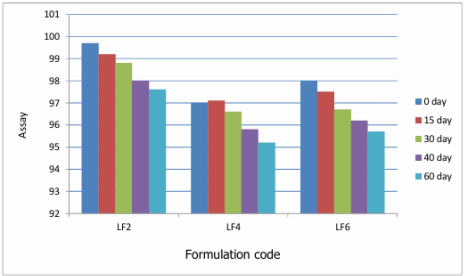
√t	Cumulative % drug release		
	F2	F4	F6
1	1.38	1.74	2.15
1.414	2.92	3.37	4.07
1.732	4.14	5.11	6.19
2	5.93	6.82	8.43
2.449	8.77	10.5	13.01
2.828	11.65	13.9	17.62
3.162	15.63	17.38	21.26
3.464	18.91	20.86	25.56
2.449	8.77	10.5	13.01
2.828	11.65	13.9	17.62
3.162	15.63	17.38	21.26



Graph 12: Comparison of Higuchi's order plot for optimized formulations LF-2, LF-4 and LF-6

Table 10: Effect of temperature on Assay of Fenoprofen at 4°C

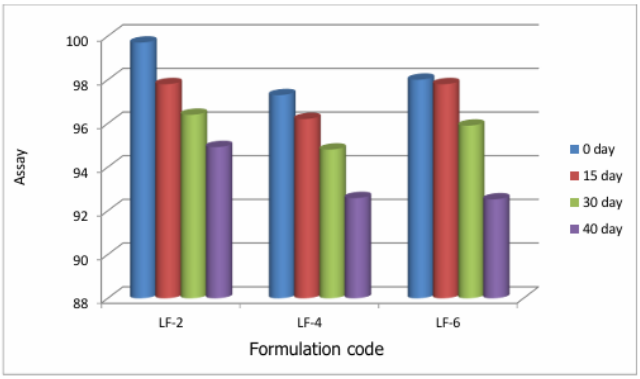
Formulation code	Effect of stability on Assay at 4oc				
	0 day	15 day	30 day	40 day	60 day
LF-2	99.7±0.65%	99.2±0.47%	98.8±0.72%	98±1.0 %	97.6±0.65 %
LF-4	97.3±0.96%	97.1±0.73%	96.6±1.12%	95.8±0.43%	95.2±0.96 %
LF-6	98±1.3 %	97.5±1.0%	96.7±0.9%	96.2±0.63%	95.7±1.3 %



Graph 13: Stability plot for LF2, LF-4 and LF-6 Formulations at 4° C

Table 11: Effect of temperature on Assay of Fenoprofen at room temperature

Formulation code	Effect of stability on Assay at room temperature.			
	0 day	15 day	30 day	40 day
LF-2	99.7±0.65 %	97.8±0.48	96.4±0.54	94.92±0.32
LF-4	97.3±0.96 %	96.2±0.92	94.8±0.62	92.58±0.58
LF-6	98±1.3%	97.8±0.65	95.9±0.69	92.52±0.86



Graph 14: Stability plot for F1, F2 F3, F4, F5, F6 Formulations at Room temperature

DISCUSSION

The UV absorbance of Fenoprofen standard solution in the range of 10-50 µg/ml of drug in buffer, pH 7.4 showed linearity at λ max 270 nm. The linearity was plotted for absorbance against concentration with R2 value 0.9995 and with the slope equation y = 0.0179x-0.003. The compatibility between the drug and the selected lipid and other Excipient was evaluated using the FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-lipid mixture, which confirmed the absence of any chemical interaction between the drug, lipid and other chemicals. The Liposomes were prepared by dried thin film hydration technique using a rotary evaporator with drug and carrier (soybean lecithin). The formulation containing Fenoprofen was prepared with different stabilizers like Dicetylphosphate and Stearylamine and all other parameters like temperature, vacuum and RPM were kept constant. The particle size distribution was analyzed for F2, F4, F6 formulations of Fenoprofen Liposomes by wet method. The particle size was optimum in F6 Formulation, When compared to F2 and F4. The Morphology and surface appearance of Liposomes were examined by using SEM. The SEM photographs of F2 and F6 formulation showed that the particles have smooth surfaces. The zeta potential report of liposomal solution for F2, F4, F6 formulations are 5.21mV, 24.66mV, -23.4 which lies near to the arbitrary value. The report shows good stability value for formulated liposomal solution. The release kinetics of F2, F4, F6 formulations were studied. All formulations follow Zero order release kinetics and follow case II transport. The stability of the Fenoprofen Liposomes was evaluated after storage at 40c and room temperature for 60 days. The assays of the samples were determined as a function of the storage time. The Liposomes stored at 40c were found to be stable for a duration of 60 days.

SUMMARY AND CONCLUSION

The main objective of this work was designed to prepare and evaluate the Fenoprofen Liposomes. This formulation will target the site of action with effect of various stabilizers on drug entrapment efficiency, and to reduce the side effects by formulating non-pegylated Liposomes. The Liposomes were prepared by dried thin film hydration technique using a rotary evaporator with drug, carrier, ammonium sulphate and stabilizers. The parameters like temperature, vacuum and RPM were maintained accordingly. After preparation, the Liposomes were stored in freeze condition, and given for further evaluation The prepared Liposomes of LF-1, LF-2, LF-3, LF-4, LF-5 and LF-6 formulations were evaluated for physical and chemical characteristics like average vesicle size, shape and zeta potential. The prepared Liposomes of F1 to F6 were evaluated for % free drug and Assay, The % Free drug was optimum in F6 (Negative) formulation when compared to other formulations of F1, F2, F3, F4 and F5. The Assay was optimum in F2 (Neutral) formulation when compared to other formulations of F1, F3, F4, F5 and F6. This developed liposomal drug delivery system was also evaluated for dissolution study by pH 7.4 HCl using membrane diffusion method. The release of drug from F6(Negative) formulation was found to be sustained to a certain extent when compared to F1, F2, F3, F4 and F5 formulations. The release kinetics of F2, F4 and F6 Formulations were studied. All formulations follow Case II transport when it applied to the Korsmeyer – Peppas model for mechanism of drug release. F6 (negative) formulation has better kinetic results when compared to F2 and F4 formulations. The stability of the Fenoprofen Liposomes was evaluated after being stored at 4oC and room temperature for 60 days. The assay of the samples was determined as a function of the storage at different time intervals. The Liposomes stored at 4oc were found to be stable for duration of three months from the results of physical characterization, in-vitro evaluation, release kinetics and stability studies, it was found that charged Liposomes containing Fenoprofen might be used for the

treatment osteoarthritis or relieve pain, tenderness, swelling, and stiffness caused by (arthritis caused by a breakdown of the lining of the joints) and rheumatoid arthritis (arthritis caused by swelling of the lining of the joints). Fenoprofen is also used to relieve mild to moderate pain from other causes.

REFERENCES

[1] Poggi JC, Barissa GR, Donadi EA, Foss MC, Cunha FQ, Lanchote VL, dos Reis ML: Pharmacodynamics, chiral pharmacokinetics, and pharmacokinetic pharmacodynamic modeling of fenoprofen in patients with diabetes mellitus. J Clin Pharmacol.

[2] Fresta M, Villari A, Puglisi G, & Cavallaro G, 5-FU various kinds of loaded liposomes, encapsulation efficacy, storage stability and fusogenic properties, Int J Pharm.1993;99:145-156

[3] Shukla, K., & Singh, B. (2020). TO EVALUATE THE METHOTREXATE DRUG WITH ITS PREFORMULATION METHOD CONFIRMING FOR THE PREPARATION OF NANO-FORMULATION OPTIMIZATION.

[4] Srinivas, P., & Babu, D. R. (2014). Formulation and evaluation of parenteral methotrexate nanoliposomes. International Pharmaceutical Sciences, 295-300. Journal of Pharmacy and

[5] Dua, J. S., Rana, A. C., & Bhandari, A. K. (2012). Liposome: methods of preparation and applications. Int J Pharm Stud Res, 3(2), 14-20.

[6] El Maghraby, G. M. M., Williams, A. C., & Barry, B. W. (2005). Drug interaction and location in liposomes: correlation with polar surface areas. International journal of pharmaceutics, 292(1-2), 179-185.

[7] Zhuang, J., Ping, Q., Song, Y., Qi, J., & Cui, Z. (2010). Effects of chitosan coating on physical properties and pharmacokinetic behavior of mitoxantrone liposomes. International journal of nanomedicine, 5, 407.

[8] Mitkari, B. V., Korde, S. A., Mahadik, K. R., & Kokare, C. R. (2010). Formulation and evaluation of topical liposomal gel for fluconazole. Indian J Pharm Educ Res, 44(4), 324-333.

[9] Chinnala, K. M., & Panigrahy, R. (2016). Formulation and Evaluation of Fenoprofen Liposomes.

[10] Danaei, M., Dehghankhold, M., Ataei, S., Hasanzadeh Davarani, F., Javanmard, R., Dokhani, A., & Mozafari, M. R. (2018). Impact of particle size and polydispersity index on the clinical systems. Pharmaceutics, 10(2), 57. applications of lipidic nanocarrier

[11] Webb, C., Khadke, S., Tandrup Schmidt, S., Roces, C. B., Forbes, N., Berrie, G., & Perrie, Y. (2019). The impact of solvent selection: strategies to guide the manufacturing of liposomes using microfluidics. Pharmaceutics, 11(12), 653.

[12] Robson, A. L., Dastoor, P. C., Flynn, J., Palmer, W., Martin, A., Smith, D. W., & Hua, S. (2018). Advantages and limitations of current imaging techniques for characterizing liposome morphology. Frontiers in pharmacology, 9, 80.

[13] Dua, J. S., Rana, A. C., & Bhandari, A. K. (2012). Liposome: methods of preparation and applications. Int J Pharm Stud Res, 3(2)