Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 12 [6] May 2023 : 82-91

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Development and characterization of a novel nano-liposomal formulation of famotidine-loaded nano-sized liposomal with biodegradable polymer

Shakti Jaiswal, Alok Kumar Dash,*Jhansee Mishra
Institute of Pharmacy Veer Bahadur Singh Purvanchal Universty,Jaunpur,Uttarpradesh

ABSTRACT

The primary objective of this study was to develop and optimize a nano-liposomal formulation of Famotidine for sustained drug delivery in the treatment of gastric ulcers. Nano-liposomes were prepared using the thin-film hydration method followed by sonication. The effect of the amount of soyaphosphatidyl choline and cholesterol in the formulation of nano-liposomal was determined by using evaluation parameters such as vesicle size and drug entrapment efficiency. The Famotidine liposomal formulation was optimized using 32 factorial designs to achieve stable nano-liposomal with small vesicle size and maximum entrapment efficiency. Compatibility studies conducted was done with FT-IR and DSC method. The compatibility studies results were revealed that there were no significant interactions between the drug and the excipients. The formulated liposomal preparations were evaluated for various parameters, and the results obtained for the optimized batch (F3) showed a vesicle size of 217.86 nm, zeta potential ranging from -77.8mV to -82.8mV, entrapment efficiency of 89.65%, and drug release of 92.07% over a period of 12 hours. Liposomal drug delivery can target drug concentration at the site of action and provide sustained drug release according to the Higuchi-matrix model, ultimately reducing dosing frequency and minimizing side effects related to high drug intake. Nano-liposomes provide a range of options and opportunities for designing and implementing site-specific, targeted drug therapy.
Keywords: *Famotidine, nano-liposomal, drug entrapment, in-vitro drug release, Release kinetics.*

Received 11.03.2023 Revised 16.04.2023 Accepted 21.05.2023

INTRODUCTION

Cancer treatment commonly involves chemotherapy, but chemotherapeutic agents can cause serious side effects due to their toxicity to healthy cells. Thus, the development of new drug delivery systems with high anticancer activity and reduced side effects is crucial. Nano-sized drug delivery systems offer several advantages in cancer treatment, such as improved pharmacokinetic parameters and reduced side effects. Nano-liposomes, a class of nanoparticles with one or more phospholipid bilayers enclosing an aqueous core, are a widely studied drug delivery system with biocompatibility and biodegradability. However, nano-liposomes have low encapsulation efficiency (EE%) for water-soluble drugs due to low affinity for phospholipids. Therefore, selecting an appropriate nano-liposomes preparation method to achieve high EE% and narrow size distribution is crucial. In this study, two different methods were investigated to enhance hydrophilic drug encapsulation. Famotidine, a potent H2 receptor antagonist used in the treatment of gastric ulcers and reflux disease, has limited bioavailability and a short half-life. Prolonged-release formulations can improve its absorption and bioavailability, and proniosome-derived niosomes may offer improved bioavailability of poorly soluble drugs with poor solubility. Liposomal drug delivery systems offer a promising avenue for cancer therapy with targeted drug delivery and sustainable drug release [1-2].Liposomal drug delivery systems have been widely investigated for the treatment of various types of cancer and several liposomal products have been approved for clinical use [3]. Despite their biocompatibility and biodegradability advantages, the encapsulation efficiency (EE%) of nano-liposomes for water-soluble drugs remains a challenge due to their low affinity for phospholipids [5]. Therefore, the selection of a suitable nano-liposomes preparation method that achieves a high EE% and a narrow size distribution is critical. In order to enhance EE%, both passive and active strategies have been investigated. There are several reported nano-liposomes preparation methods that enhance the encapsulation of hydrophilic drugs. In the present study, two different methods were investigated to achieve high EE%, and the thin film hydration method (TFH) was selected as one of the simplest ways to prepare nano-liposomes [8].Famotidine (FAM) is a highly potent antagonist of H2 receptors that is commonly prescribed for the treatment of gastric ulcers, duodenal ulcers, Zollinger-Ellison syndrome,

and gastroesophageal reflux disease. It has been found to be 7.5 and 20 times more potent than ranitidine and cimetidine, respectively, among other H2 receptor antagonists. However, famotidine is constrained by its poor solubility, low bioavailability, and rapid elimination from the body. [9] Famotidine, a potent H2 receptor antagonist commonly used to treat gastric ulcers, duodenal ulcers, ZollingerEllison syndrome, and gastro esophageal reflux disease, has demonstrated relative freedom from side effects despite its high potency. However, famotidine suffers from low and variable bioavailability (20-40%) and short biological half-life (2.54 hours). The conventional dose of 20 mg can inhibit gastric acid secretion for up to 5 hours, but not for up to 8-10 hours. Formulating famotidine into a prolonged-release formulation could improve its absorption from the proximal small intestine due to the prolongation of residence time in the stomach. The low bioavailability (40-45%) and short biological half-life (2.54 hours) of famotidine following oral administration support the development of a prolonged-release formulation. Proniosome-derived niosomes have been shown to offer more controlled drug release than conventional niosomes and may therefore improve the bioavailability of some poorly soluble drugs with poor solubility [10].

The objective of this investigation was to evaluate the influence of the preparation technique used to produce nano-liposomes loaded with Famotidine drug on the physicochemical properties of the vesicles. Various variables, including hydration volume for the Thin Film Hydration (TFH) method, drug quantity, and incubation volume for passive loading, were identified to enhance the encapsulation of Famotidine in nano-liposomes.

MATERIAL AND METHODS

Materials

Famotidine, and Cholesterol was purchased from Himedia and Merck, respectively. All other reagents and solvents were of analytical grade.

Compatibility studies by FTIR

The FT-IR spectra of the pure drug and physical mixture were obtained using a FT-IR spectrophotometer (Agilent Technologies, Cary 630 FTIR) and the potassium bromide (KBr) disk technique. A KBr disk containing famotidine and physical mixture was prepared and scanned at a wavelength range of 4000 to 400 cm-1.

Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) analysis was conducted to evaluate the compatibility of pure famotidine and physical mixture with polymers. The analysis was performed using a Mettler-Toledo DSC 821e instrument, with temperature and enthalpy scale calibration carried out with indium and zinc standards. The samples were hermetically sealed in aluminum containers and heated at a constant rate of 10°C/min over a temperature range of 25-250°C. An inert atmosphere was created using nitrogen gas at a flow rate of 50 mL/min.

Preparation of famotidine-loaded-nano-liposomes

Famotidine-loaded nano-liposomes were prepared using TFH method as described below.

Thin film hydration (TFH) method

Preparation of nano-liposomes

Nano-liposomes were prepared using the thin film hydration technique, where various weight ratios of soya phosphatidylcholine and cholesterol were dissolved in chloroform to achieve a concentration of lipid phase in a rotary flask. A film was formed by attaching the flask to a rotary evaporator at a temperature of 40°C and rotating it at 50 rpm under vacuum for an hour. The formed film was then hydrated with a phosphate buffer solution (pH 7.4) containing famotidine, followed by hand shaking for 10 minutes to produce nano-liposomes. In order to obtain small uniform nano-liposomes preparations and were subjected to sonication for a 20 minute cycle, with 20 seconds of working and 10 seconds of rest at a low frequency of 30 kHz and a temperature of 37°C. The resulting nano-liposomes were then allowed to settle undisturbed at room temperature for 1-2 hours, followed by storage at 4°C under an inert atmosphere for 24 hours to allow for complete vesicle formation [10]. The final liposomal dispersion was then transferred to sterile glass vials for further processing. The composition of liposomal formulation was shown in Table 1. The general scheme for the preparation of nano-liposomes is shown in Figure 1.

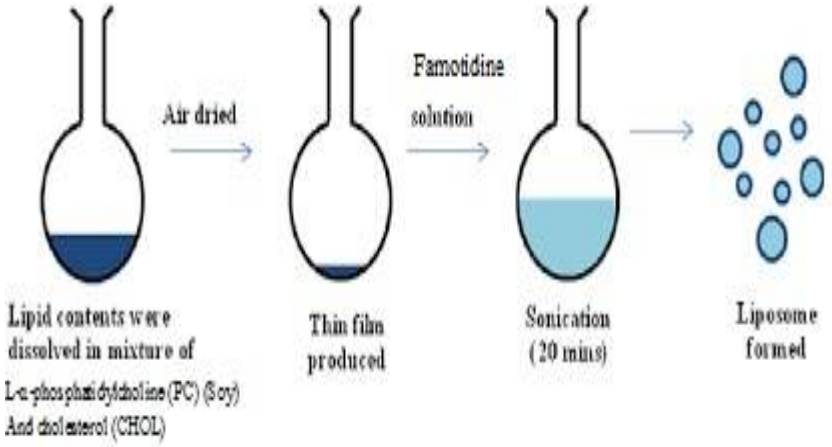

Figure 1. Schematic preparation of nano-liposomes.

Table 1: Optimization of Famotidine loaded nano-liposomal formulation.

Formulation code	SPC:CH Ratio (mg)	Drug (mg)	Chloroform (mL)	Methanol (mL)
F1	60:10	50	30	15
F2	90:10	50	30	15
F3	120:10	50	30	15
F4	60:20	50	30	15
F5	90:20	50	30	15
F6	120:20	50	30	15
F7	60:30	50	30	15
F8	90:30	50	30	15
F9	120:30	50	30	15

Optimization of nano-liposome preparation

Speed of the rotary evaporator

Achieved a thin and uniform film is crucial for obtaining optimal results in nano-liposomal preparation. The speed of rotation was adjusted between 60 and 100 rpm during the film formation and hydration stages to optimize the final outcome of the nano-liposomal preparation.

The ratio and volume of solvent system

The optimization of the solvent system was conducted by testing various combinations of organic solvents, namely chloroform and methanol. Different ratios of the solvents were evaluated to determine the uniformity of the resulting film.

pH of the hydrating media

The impact of pH of the phosphate buffer on the formulation was evaluated to assess its effect on drug entrapment in nano-liposomes. The pH of the hydrating buffer was adjusted to values proximate to the pKa of the drug, and the entrapment efficiency was determined. Methanol and phosphate buffer pH 5.2, 6.8, and 7.4 were employed as hydrating media, and formulations were evaluated in terms of entrapment efficiency.

Evaluation of Famotidine Loaded Nano-Liposome [11]

Particle size

The size distribution and mean vesicle size of nano-liposomes loaded with Famotidine were determined using the HORIBA scientific SZ-100 instrument based on the principle of photon correlation spectroscopy. The size analysis was performed at room temperature with an angle of detection of 90° for 100 seconds.

Zeta potential

The surface charge of Famotidine loaded nano-liposomes was measured using a Zetasizer instrument (HORIBA scientific SZ-100). The liposomal formulations were diluted with deionized water at a ratio of 1/10 (w/v) and placed in the measurement cell for analysis. The zeta potential and charge on the nano-liposomes surface were determined by allowing the sample to equilibrate for 60 seconds.

Entrapment efficiency

To determine the actual drug loading in the nano-liposomes, 5 mL of the drug-loaded liposomal preparation was mixed with 5 mL of ethanol to rupture the nano-liposomes, and then centrifuged at 9500 rpm at 1°C for 45 min using a cooling centrifuge (REMI C30, Mumbai). The supernatant was carefully

separated and suitably diluted with 10 mL of phosphate buffer solution pH 7.4. The diluted dispersion was then filtered through a micro syringe filter (0.2µm) and the absorbance of the filtrate was recorded at 304 nm using a UV/Visible spectrophotometer (Shimadzu, Japan).

The total amount of drug present in the formulation was determined by suspending 5 mL of nano-liposomes in 5 mL of ethanol to destroy the liposomal structure. The formed pellet was washed with 1 mL of phosphate buffer solution pH 7.4 and vortexed to remove the free drug adsorbed on the surface of nano-liposomes. The resulting dispersion was then diluted with 10 mL of phosphate buffer solution pH 7.4 and filtered through a microsyringe filter (0.2µm). The filtrate was analyzed for Famotidine by measuring the absorbance at 265 nm using a UV/Visible spectrophotometer. The entrapment efficiency was calculated by using a formula,

$$\textbf{Entrapment efficiency} = \frac{A-B}{A} \times 100 \quad (1)$$

Where 'A' is total amount of drug that is detected both in the supernatant layer and resident layer and 'B' is the amount of drug detected only in the supernatant**.** The percentage drug entrapped in the vesicles was then calculated using the following Eq. (1):

Transmission Electron Microscopy

The structural morphology of Famotidine nano-liposomes was examined using transmission electron microscopy (TEM) images obtained with a Hitachi S-7500 instrument. The images were captured at a magnification of 30,000× and at an accelerating voltage of 100 kV, by placing a drop of diluted liposomal dispersion on a 200-mesh carbon-coated copper grid.

In-vitro drug release study

In vitro drug release studies of all nano-liposomes batches were conducted using a modified USP XXI dissolution model. A glass tube, opened from both ends, was tied at one end with treated cellulose membrane (molecular weight cut off [MWCO] 10 kDa, Thermo Fisher Scientific) and dipped into a 250 mL beaker containing a mixture of water and ethanol (70:30) as the dissolution medium, with temperature maintained at 37±1℃. A volume of 10 mL of liposomal preparation was added to the tube, and the dissolution medium was stirred at 100 rpm using a magnetic stirrer. At various time intervals up to 12 hours, 2 mL samples were withdrawn from the receiver compartment and replaced with equal volumes of fresh dissolution medium. The samples were spectrometrically assayed for drug content at 304 nm using a UV-Visible spectrophotometer. All readings were taken in triplicates. The study was performed to evaluate the drug release profiles of the liposomal formulations.

Kinetic Modeling of Release Profiles

The drug release data obtained from liposomal formulations were analyzed using various kinetic models such as zero order, first order, Higuchi matrix, Korsmeyer-Peppas, and Hixson-Crowell. The correlation coefficient values of each model were compared, and the model with the highest correlation coefficient was chosen as the best fit model [12].

Stability of nano-liposomes

The physical stability assessment of drug-loaded liposomal formulation was conducted by monitoring the physical appearance, changes in vesicle size distribution, and mean vesicle size over time. A volume of 5 mL of the formulation was stored at three different temperatures, namely refrigerated (4°C ± 2°C), room temperature (24°C), and physiological temperature (37°C), as per the International Conference on Harmonization (ICH) guidelines. Samples were taken at specific intervals of 1, 2, and 3 months and analyzed for their physical appearance, mean vesicle size, size distribution, and percent drug entrapment, as described above.

RESULTS AND DISCUSSION

Compatibility studies

The compatibility of Famotidine with other excipients was assessed by means of Fourier-transform infrared (FTIR) spectroscopy. The FTIR spectra of the pure drug and its physical mixture with the excipients were obtained using the KBr disc method and presented in Figure 1. The characteristic peaks of famotidine, cholesterol and phosphatidyl choline were present in the physical mixture, thus indicating no significant evidence of chemical interaction between drug and lipid, which confirms the stability of drug. The major peaks (NH_2)g peak at 3401cm^{-1}, $(CH_2–S)$ peak at 2917 cm^{-1}, (C=N) peak at 1639 cm^{-1}, (NH_2) peak at 1600cm^{-1} and SO_2 peak at 1147 cm^{-1} which were present in pure drug famotidine are also present in the physical mixture. No appearance or disappearance of peaks was observed in the physical mixture of the drug and the excipients, indicating the absence of any chemical interaction between them.

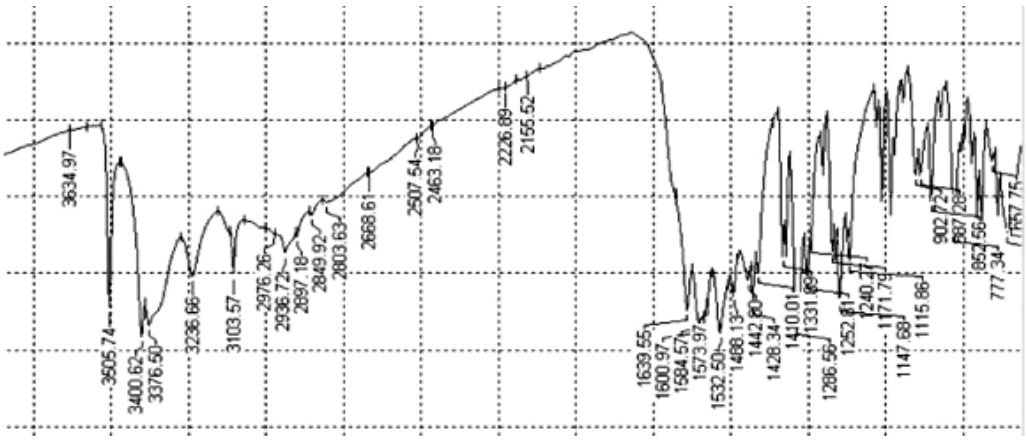

Figure 2: FTIR spectra of Pure Famotidine.

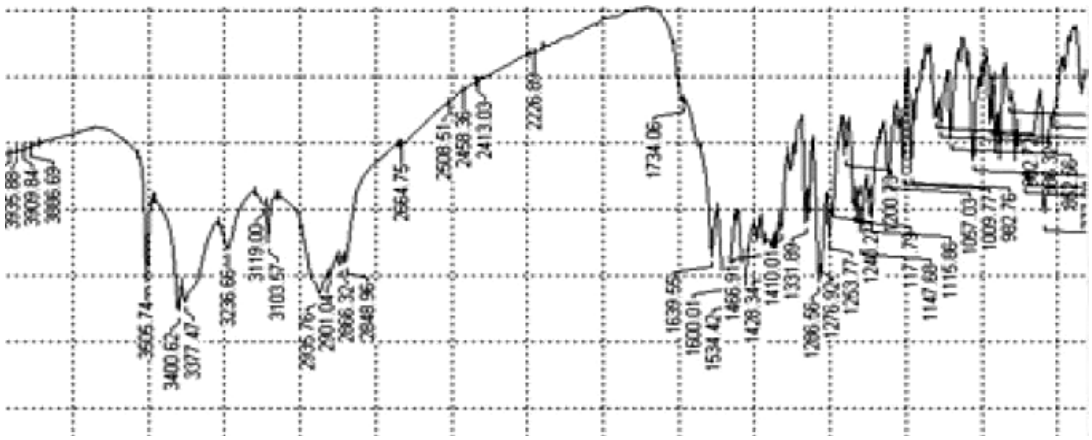

Figure 3: FTIR spectra of Pure Famotidine and physical mixture

Differential scanning colorimetry

The thermal behavior of pure Famotidine and its physical mixture with cholesterol and phosphatidyl choline were investigated using differential scanning calorimetry (DSC) analysis. The results are presented in Figure 8. The DSC thermogram of pure Famotidine exhibited a sharp endothermic peak at 121°C, which was attributed to the melting of pure Famotidine during the DSC run. The DSC thermal profile of the drug when mixed with cholesterol and phosphatidyl choline indicated a negligible shift in the peak to 118°C, confirming the absence of any interactions between the drug and the polymers.

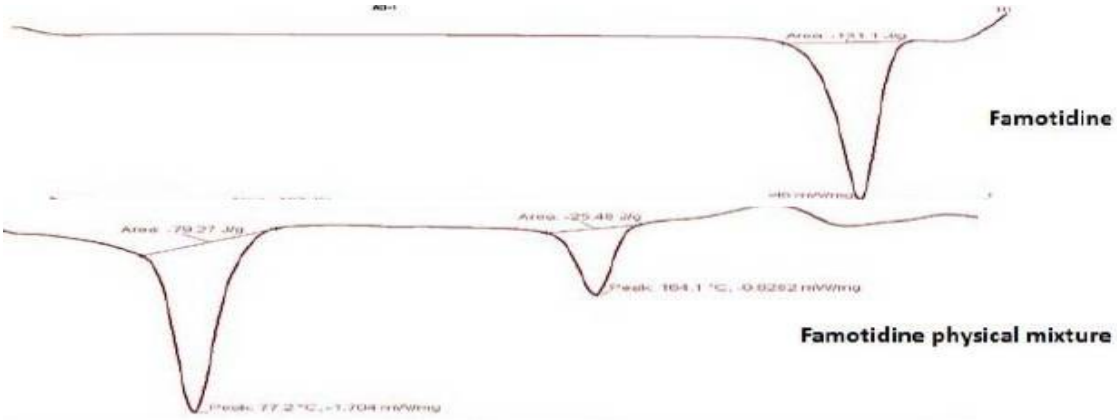

Figure 4: DSC thermogram of pure drug Famotidine **and Physical mixture.**

Optimization of formulation

Saturated phospholipids (SPC) have been found to possess stability and biocompatibility advantages over unsaturated phospholipids. In light of preliminary investigations, the concentrations of soyaphosphatidyl choline and cholesterol were selected to yield stable nano-liposomes that are devoid of aggregation,

fusion, and possess small vesicle size and high percent drug entrapment. This observation suggests that the quantity of soya phosphatidyl choline and cholesterol is a crucial factor influencing nano-liposomes formation. The optimized concentrations of soyaphosphatidyl choline (60-120 mg) and cholesterol (10-30 mg) were found to be sufficient for generating nano-liposomes devoid of aggregation and sedimentation with small vesicle size and excellent drug entrapment.

Particle size and particle size distribution

The liposomal formulations containing 60-120 mg of soya phosphatidylcholine and 10-30 mg of cholesterol exhibited mean vesicle sizes in the range of 198-378.2 nm. The polydispersity index values between 0.29-0.41 suggested a narrow range of vesicle size distribution for the drug-loaded nano-liposomes (Table 2). All the formulations showed a relatively uniform size distribution. The vesicle size of the drug-loaded formulations was directly proportional to the concentrations of soya phosphatidyl choline and cholesterol. The addition of cholesterol to the formulation increased the rigidity of the liposomal membrane in comparison to the lipid concentration in the liposomal dispersion. A typical particle size distribution profile observed for prepared nano-liposomes is shown in Figure 2, 3.

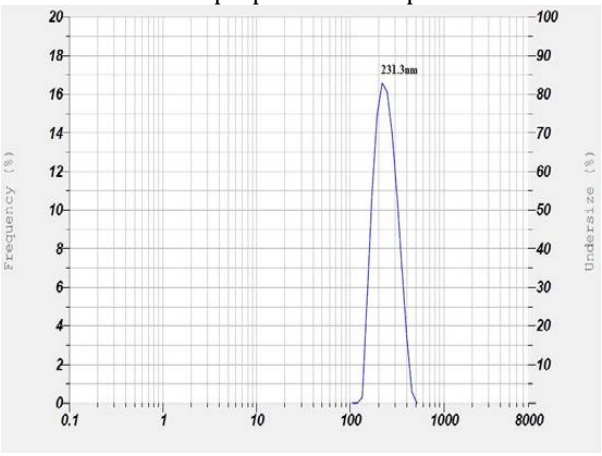

Figure 5: Particle size distribution in nano-liposomes without sonication (F3).

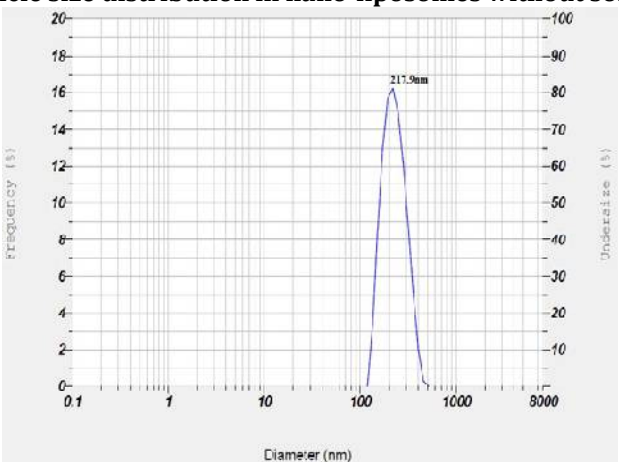

Figure 6: Particle size distribution of sonicated nano-liposomes (F3).

Zeta Potential determination

The zeta potential of nano-liposomes provides valuable information about the particle charge and dispersion stability. In this study, the zeta potential of the optimized formulation (F3) was determined and found to be in the range of -77.8mV to -82.8mV, as shown in Figure 5 and 6. This result indicates that the nano-liposomes possess sufficient charge and mobility to prevent aggregation of vesicles, thus indicating good dispersion stability.

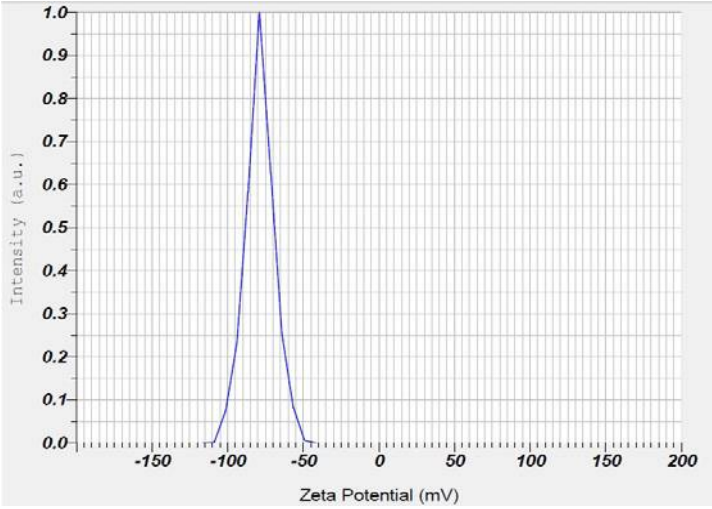

Figure 7: Zeta potential in nano-liposomes formulation without sonication (F3).

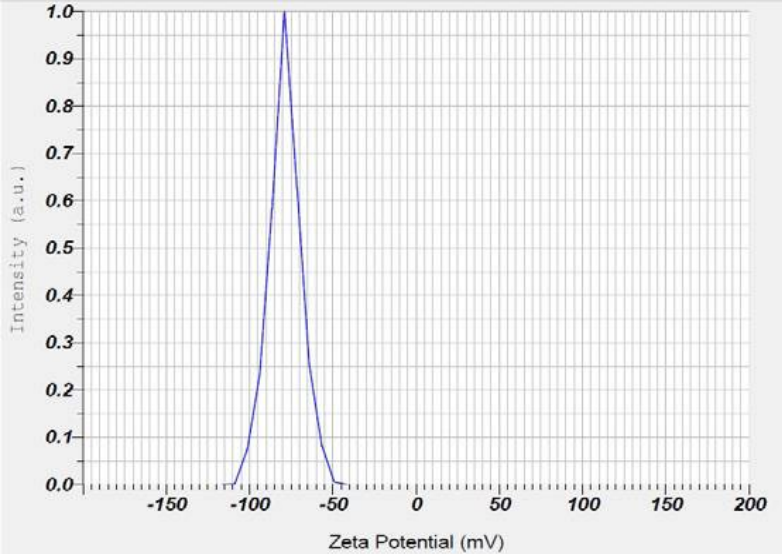

Figure 8: Zeta potential in nano-liposomes formulation sonication (F3).

Percentage Drug Entrapment

The percent drug entrapment (PDE) is defined as the ratio of the amount of drug encapsulated in the nano-liposomes to the total amount of drug used. In this study, the PDE for all the formulations ranged from 18.16% to 79.86%. The optimization of the concentration of soyaphosphatidyl choline and cholesterol for the liposomal formulation was based on the parameters of vesicle size and drug entrapment efficiency, as these parameters are crucial in determining drug deposition. Formulation code F3 was found to be significant based on its high drug entrapment and low vesicle size.

Table 2: Vesicle size and percent drug entrapment of different batches of liposomal preparation

Formulation codes	**Vesicle size (nm)**		**Percentage Drug Entrapment (PDE)**	
	Thin film hydration	Sonication	Thin film hydration	Sonication
F1	232.3	198.07	18.42±0.931	25.05±0.012
F2	274.4	230.52	61.37±1.051	58.05± 0.047
F3	230	**217.8**	**89.65±0.522**	**72.36±0.002**
F4	313	298.11	36.98±0.638	33.28±0.012
F5	318	331.08	45.12±1.211	49.71±0.192
F6	341	204.03	66.24±1.230	61.62±0.061
F7	287	231.08	25.16±1.125	41.24±0.095
F8	375	274.92	38.79±0.731	51.83±0.358
F9	377	374.12	40.05±0.561	36.89±0.792

*Each value represent Mean ± SD, *n* = 3.

Transmission Electron Microscopy

TEM analysis was conducted to examine the morphology and appearance of Famotidine loaded nano-liposomes. The optimized batch F3 was evaluated and the results revealed smooth, spherical-shaped nano-liposomes with small vesicle size. The TEM image of the nano-liposomes was shown in Figure 7, which supports the results obtained from particle size analysis.

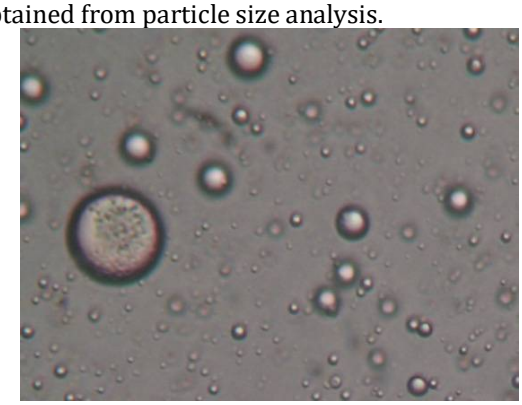

Figure 9: TEM micrograph of Famotidine loaded nano-liposomes (F3).

In-vitro drug release studies [12-13]

The drug release profiles were successfully customized by manipulating the concentration of phospholipid and cholesterol. All formulations demonstrated sustained release for a period of 12 hours. With the exception of formulation F2, all other formulations exhibited a drug release exceeding 90%. Formulation F9 (94.08%) show maximum release compared to other formulations shown in Figure 9.

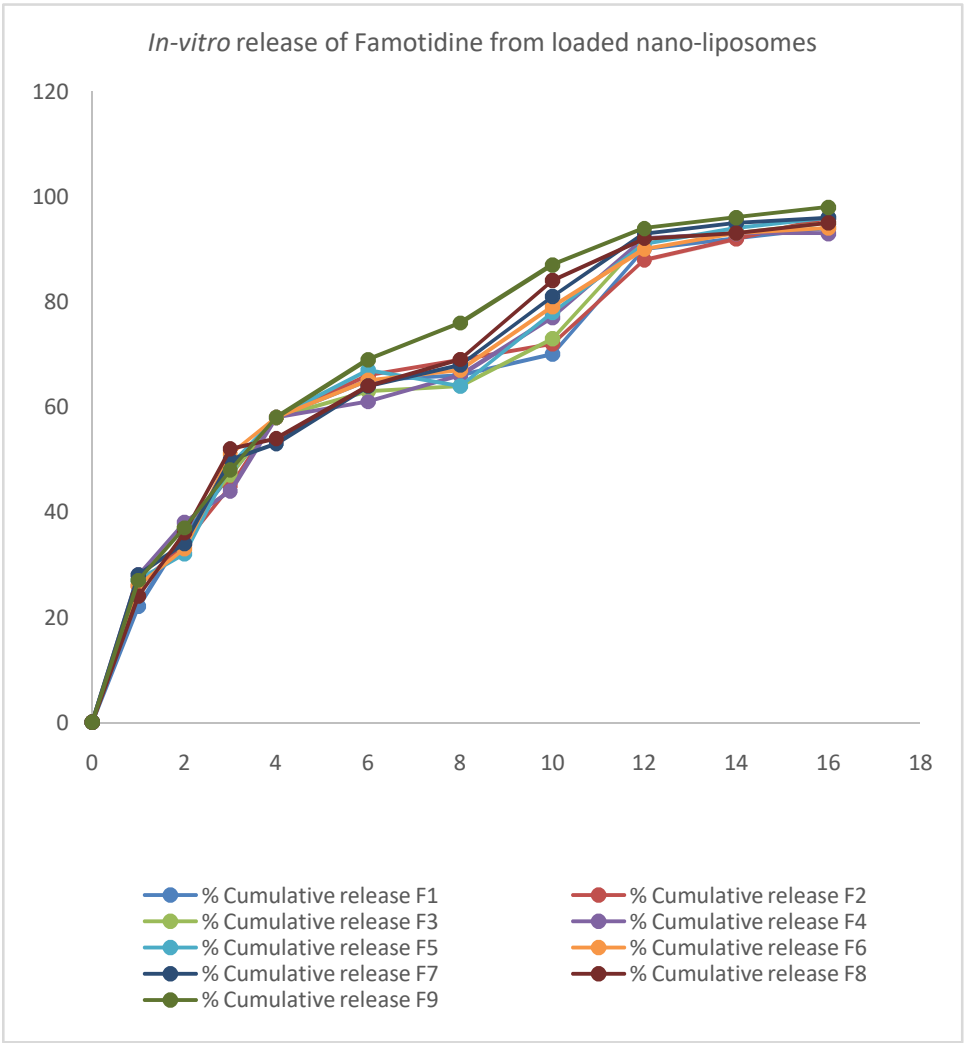

Figure 9: Drug Release profile of Famotidine loaded nano-liposomes

Release Kinetic

To elucidate the mechanism underlying drug release, data acquired from in vitro drug release investigations of nano-liposomes under development were subjected to fitting in kinetic models. The coefficient of correlation (R2) was employed as an indicator of optimal fitting, with regression values for each formulation ranging between R2 = 0.8340 to 0.9982. Upon evaluating the regression values for different models of all formulations, it was observed that the in vitro release of famotidine from nanoliposomes was best described by the Higuchi matrix kinetic model, except for formulation codes F7 and F9. Moreover, the exponent values (n) in the Korsmeyer-Peppas equation for all formulations examined were less than 0.5 under the study conditions. All the formulations showed Fickian release mechanism i.e. release due to diffusion of drug from matrix except formulation F7 and F9 (Table 3).

The *in vitro* release of famotidine nano-liposomes exhibited zero order kinetics for the F9 formulation and Hixson-Crowell kinetics for the F7 formulation. The zero order release pattern implies the drug release to be independent of its initial concentration. The Hixson-Crowell model proposes the drug release to occur in planes, which may be attributed to the adsorption of famotidine on the surface of nano-liposomes.

Table 3: Mathematical models in drug release kinetics of famotidine loaded liposomal formulation

Formulation codes	Zero order (*R*2)	First order (*R*2)	Higuchi (*R*2)	Hixon crowell (*R*2)	Korsmeyer-peppas	
					(*R*2)	n
F1	0.988	0.973	0.994	0.993	0.982	0.457
F2	0.985	0.982	0.993	0.992	0.988	0.483
F3	0.992	0.972	0.994	0.992	0.987	0.468
F4	0.989	0.964	0.992	0.986	0.988	0.402
F5	0.978	0.991	0.998	0.997	0.987	0.437
F6	0.987	0.982	0.997	0.989	0.981	0.436
F7	0.971	0.974	0.987	0.994	0.958	0.409
F8	0.974	0.947	0.987	0.986	0.958	0.421
F9	0.991	0.987	0.989	0.998	0.974	0.438

Stability study

The physical appearance of liposomal formulation F3 was assessed after storage at temperatures of 4°C, 24°C, and 37°C for intervals of 1, 2, and 3 months. The liposomal formulation F3 was observed to remain stable when stored at 4°C and 24°C, while instability was noted upon storage at 37°C. Furthermore, the mean particle size and percent entrapment of the formulation were examined as a function of temperature. There is no significant change in mean particle size of the nano-liposomes stored at 4°C and 24°C except for storing at 37°C (Table 4).

Table 4: The mean particle size and percent drug entrapment (PDE) of formulation (B3) stored at different temperature conditions.

Storage temperature	4°C		24°C		37°C	
Parameter	**Vesicle size**	**PDE***	**Vesicle size**	**PDE***	**Vesicle size**	**PDE**
Initial	217.8	79.86±0.522	217.8	79.86±0.522	217.8	79.86±0.522
1 Month	218.3	79.20±0.223	220.2	78.42±0.232	224.2	77.26±0.181
2 Month	222.2	78.32±0.132	228.1	77.63±0.341	234.2	76.41±0.525
3 Month	224.32	78.77±0.421	232.2	77.44±0.132	242.3	74.12±0.422

CONCLUSION

In the current study, we have developed a method for encapsulating the water-soluble anticancer agent famotidine within a stable nanoliposomal formulation to improve tumor targeting and minimize undesired side effects on normal tissues. The physicochemical characteristics of the nano-liposomes, including vesicle size, zeta potential, and entrapment efficiency, were optimized to maintain their stability during long-term storage in refrigerated conditions and incubation at 37°C. Various lipid (soy phosphatidylcholine) and cholesterol compositions were tested to obtain nano-sized nano-liposomes with sustained drug release at the target site. Surface response plots and regression equations revealed that different concentrations of SPC and CH exhibited a positive correlation with respect to the vesicle

size of famotidine-loaded nano-liposomes. The increase in lipid concentration into the liposomal bilayer was responsible for the observed size enlargement, while cholesterol conferred stiffness to the bilayer membrane. The *in-vitro* drug release and drug release kinetics studies of famotidine nano-liposomes demonstrated a diffusion mechanism followed by the Higuchi matrix model over an extended period. Stability studies showed that the liposomal formulation remained stable under refrigerated storage conditions (4ºC). Hence, the nanoliposomal formulation of famotidine has the potential to reduce dosing frequency and target the site of action, thereby minimizing the side effects associated with high dosing and non-targeted delivery of famotidine. Further in-vivo bioavailability studies can be performed to develop a promising drug delivery system and investigate pharmacokinetic and pharmacodynamic parameters.

ACKNOWLEDGEMENT

The authors express gratitude to Veer Bahadur Singh Purvanchal University, Jaunpur-222003, India, for providing the necessary facilities to conduct this research.

CONFLICT OF INTEREST

The authors declare no conflicts of interest in relation to this research.

ABBREVIATIONS

The abbreviations used in this study are as follows: FTIR, Fourier Transform Infrared Spectroscopy**; PDE,** Percent drug entrapment**; SPC,** Soya phosphatidyl choline**; CH,** Cholesterol**; TEM,** Transmission Electron Microscopy**; DSC,** Differential scanning calorimetry**; HCL,** Hydrochloric acid.

REFERENCES

1. Davoudi, E.T., Noordin, M.I., Farjam, A.S., Javar, H.A. [2013]. Preparation and Characterization of a Gastric Floating Dosage Form of Capecitabine. *Bio Med Res Int*:2013:1-8.
2. Padamawar, M.N., Pokharkar, V.B. [2006]. Development of vitamin loaded topical formulation using factorial liposomal formulation, drug deposition and stability. *Int J Pharm*; 320(1-2):37-44.
3. Jain, N.K. [1997]. Advances in controlled and novel drug delivery. 1st edition, *CBS Publishers*; 304-52.
4. Bangham, A.D., Standish, M.M., Watkines, J.C. [1965]. Diffusion of univalent across the lamella of swollen phospholipids. *J Mol Biol*; 13(1):238-52.
5. Vyas, S.P., Khar, R.K. [2002]. Targeted and controlled drug delivery. 1st edition, *CBS Publishers*.
6. Qingguo, X.U., Yasuhiro, T., Jan, T.C. [2007]. Encapsulation and release of a hydrophobic drug from hydroxyapatite coated liposomes. *Biomaterials*; 28(16):2687-94.
7. Daraee, H., Etemadi, A., Kouhi, M., Alimirzalu, S., Akbarzadeh, A. [2016]. Application of liposomes in medicine and drug delivery. *Artif Cells Nanomed Biotechnol*; 44(1):381-91.
8. Ong, S.G., Ming, L.C., Lee, K.S., Yuen, K.H. [2016]. Influence of the Encapsulation Efficiency and Size of Liposome on the Oral Bioavailability of Griseofulvin- Loaded Liposomes. *Pharmaceutics*; 8(3):25.
9. Ammara, H.O., Ghorab, M., El-Nahhasc, S.A. [2011]. Proniosomes as a carrier system for transdermal delivery of tenoxicam. *Int J Pharmaceutics*; 405:142-152.
10. Mokale, V.J., Patil, H.I., Patil, A.P., Shirude, P.R., Naik, J.B. [2016]. Formulation and optimisation of famotidine proniosomes: an in vitro and ex vivo study. *Journal of Experimental Nanoscience*; 11(2):97-110.
11. Panwar, P., Pandey, B., Lakhera, P.C., Singh, K.P. [2010]. Preparation, characterization and in vitro release study of albendazole-encapsulated nanosize liposomes. *Int J Nanomedicine*; 5:101-108.
12. Dash, S., Murthy, P., Nath, L., Chowdhury, P. [2010]. Kinetic Modeling on Drug Release from Controlled Drug Delivery Systems. *Acta Pol Pharm*; 67(3):217-23.
13. Muppidi, K., Pumerantz, A., Wang, J., Betageri, G. [2012]. Development and Stability Studies of Novel Liposomal Vancomycin Formulations. *ISRN Pharmaceutics*;1-8.

CITATION OF THIS ARTICLE

Shakti Jaiswal, Alok Kumar Dash,*Jhansee Mishra. Development and characterization of a novel nano-liposomal formulation of famotidine-loaded nano-sized liposomal with biodegradable polymer. Bull. Env. Pharmacol. Life Sci., Vol 12[6] May 2023: 82-91.