JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

PROLIPOSOMES-LOADED LIPOSOME TO IMPROVE PANTAPRAZOLE STABILITY

[1]Shubam Sharma, [2]Kaushalya Bains, [3]Raveena Devi, [4]Dr. Sakshi

[1]Student, [2]Guide, [3]Mam, [4]Mam

[1]Himalyan Institute Of Pharmacy

[1]Himalyan Group Of Professional Institute, Kala-Amb, H.P. India.

ABSTRACT

A new medicine delivery method termed a target drug delivery system uses liposomes. Noveldrug delivery systems are a cutting-edge technology that solves the issues with traditional medication administration systems. Liposomes are self-assembling (phospho)lipid-based drug vesicles with a core aqueous compartment enclosed in a bilayer (uni-lamellar) or a concentric series of several bilayers (multi-lamellar).In the present investigation, we have tailored pantoprazole sodium-loaded eudragit S 100 coated proliposomes to control the release of drug and to improve the stability of pantoprazole sodium and GIT tract fluid.pantoprazole sodium was enclosed in proliposomes that were then coated with Eudragit S100 to resist denaturation by the severe circumstances of the stomach and to deliver the medication to the intestinal environment. proliposomes loaded with pantoprazole sodium and covered in eudragit S 100 showed minimal release. The percentage of drug release increases but depends on the buffer's ph when the buffer is changed after two hours. The greatest release of pantoprazole sodium from coated proliposomes, 93%, was recorded at ph 7 buffer medium, respectively up to 24 hours, while a percentage release of 23% was seen at ph 5–6 medium.

Key words: Lipids, Proliposomes, Pantoprazole, Lamellar

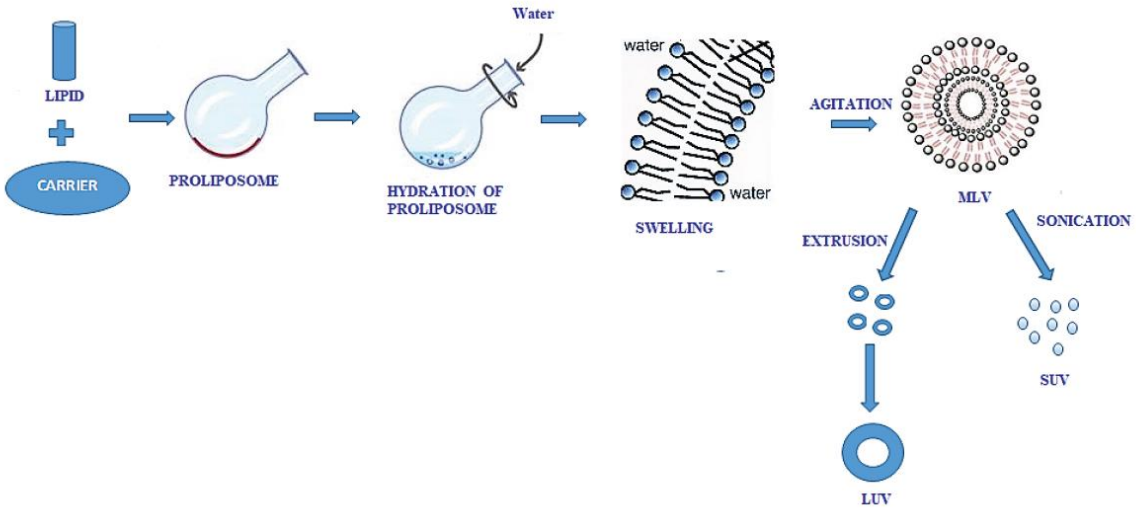
1.Introduction

Since the discovery of liposomes in 1965 by Bangham et.al, they continue to be the most Promising, broadly applicable, and highly researched of all the novel delivery systems. (Hiremath et al. 2009)

Structurally they are composed of phospholipids which are biodegradable, nontoxic and devoid of any antigenic, pyrogenic or allergic reactions, and with careful selection, allows encapsulation of matter that is as small as the lithium ion up to macromolecules as large as genetic material of several hundred thousand Daltons. (Jain SK and Jain 2008; Margalit and Yerushalmi 2006) These properties of liposomes have been extensively investigated for drug delivery, drugs targeting, controlled release and increased solubility. However, liposomes are relatively unstable colloidal system manifested by physical and chemical instability. Physical instability is evidenced by vesicle aggregation and fusion, which is associated with changes in vesicle size and loss of entrapped material. Chemical stability is of more importance as it is associated with phospholipids which form the backbone of the bilayer. It is of two types namely hydrolysis of the ester bonds linking the fatty acids to the glycerol backbone and peroxidation of unsaturated acyl chains (if present) which accelerates liposome breakdown and alters drug-release characteristics. (Yadav et al. 2011; Taylor and Elhissi 2007) These factors influence the in vivo performance and storage behaviour of liposomes. (Stark et al. 2010) For

liposomes to enter the market, they must be stable during the storage period, and remain intact before reaching their targeted tissues to produce action. Various approaches have been used to overcome these problems, some of which include, control of particle size and lamellarity, altering the lipid composition, lyophilisation, electrosteric stabilization etc. One such approach which helped overcome the stability issue associated with liposome and led to the development of a new drug delivery system is the Proliposome (PL). Discovered by Payne et.al in 1986, Proliposomes (pls) are dry, free-flowing granular products composed of drug and phospholipids which, upon addition of water, disperse to form a multi-lamellar liposomal suspension. (Payne et al. 1986) It is one of the most cost-effective and widely used methods for producing commercial liposome products. It is based upon the intrinsic property of hydrated membrane lipids to form vesicles on contact with water. Being available in dry powder form, they are easy to distribute, transfer, measure and store making it a versatile system. Liposomes can either be formed in vivo under the influence of physiological fluids or can be formed in vitro prior to administration using a suitable hydrating fluid. The liposomes formed on reconstitution are similar to conventional liposomes and more uniform in size. (Janga et al. 2012)

The proliposome methodology was created as a straightforward, repeatable, and trustworthy manufacturing method for the mass production of liposome dispersions. The method is based on hydrated membrane lipids' inherent ability to form vesicles when in contact with water. Dry powders are created by stacking the phospholipids over a particle support that has been finely split. Phospholipids on the solid substrate quickly disperse when the dry powders are hydrated with an aqueous solution and then gently mixed to produce a liposomal suspension in an aqueous solution. A appropriate hydration fluid can be used to create liposomes in vitro prior to delivery or in vivo under the influence of physiological fluids. The liposomes formed on reconstitution are similar to conventional liposomes and more uniform in size. The mechanism of formation of liposome from proliposome is demonstrated in Figure 1.1. (Muneer et al. 20017; Payne et al. 1986; Hiremath et al. 2016)



1.

Figure 1.1: Mechanism of formation of Liposomes from Proliposome

2. Experimental work

2.1 Preformulation studies

2.1.1 Organoleptic properties

The drug's organoleptic characteristics (API) were demonstrated:

Table 2.1: Organoleptic properties of pantoprazole sodium in bulk form

S.No.	Test	Specification	Observation
1.	Colour	Off white	Off white
2.	Odour	Odourless	Odourless

2.1.2 Melting point

Pantoprazole sodium's melting point was found to be between 138^0C±1.0-140.67^0C±1.154, which is quite close to the reported in the literature.

Table 2.2: Melting point of pantoprazole sodium

Drug	Specification	Observation
Pantoprazole sodium	139-141°C	138^0C±1.0-140.67^0C±1.154

2.1.3 Determination of λ_{max} and calibration curve of pantoprazole sodium in 0.1nnaoh determination of λ_{max} of pantoprazole sodium

By scanning a solution of pantoprazole sodium at a known concentration of 12µg/ml between 200 and 400 nm, the absorption maxima was discovered to be at 295 nm, in accordance with published data as shown in Figure 2.1.

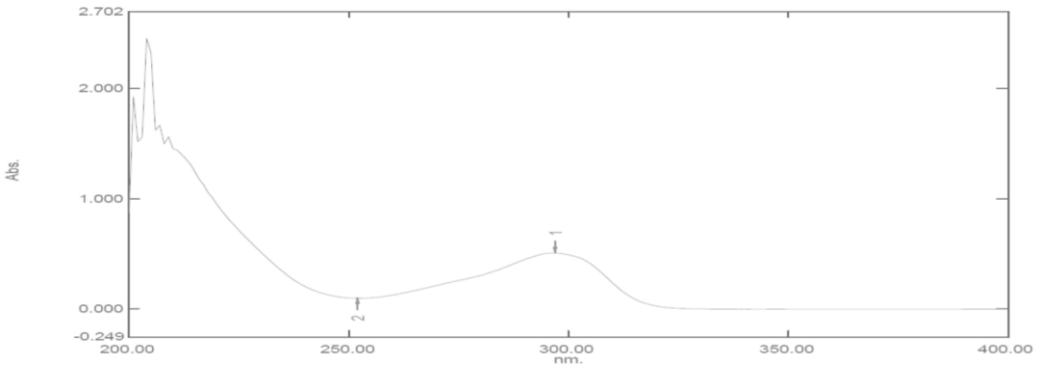


Figure 2.1: UV spectrum Graph of pantoprazole sodium

2.1.4 Standard calibration curve of pantoprazole sodium

The amount of Pantoprazole sodium in a sample that was unknown was measured using a standard calibration curve. It was charted together with their absorbance and concentration. Due to the Lambert Beer Rule, the range of 2-20µg/ml was utilized in the current activity. As can be seen in table 6.3, the linear relationship between absorbance and concentration was also determined by measuring the absorbance of all solutions at a given concentration. The regression equation Y = 0.0462x -0.0059 and R^2 value of 0.999, which exhibited good linearity, were suggested by the calibration curve for pantoprazole Sodium.

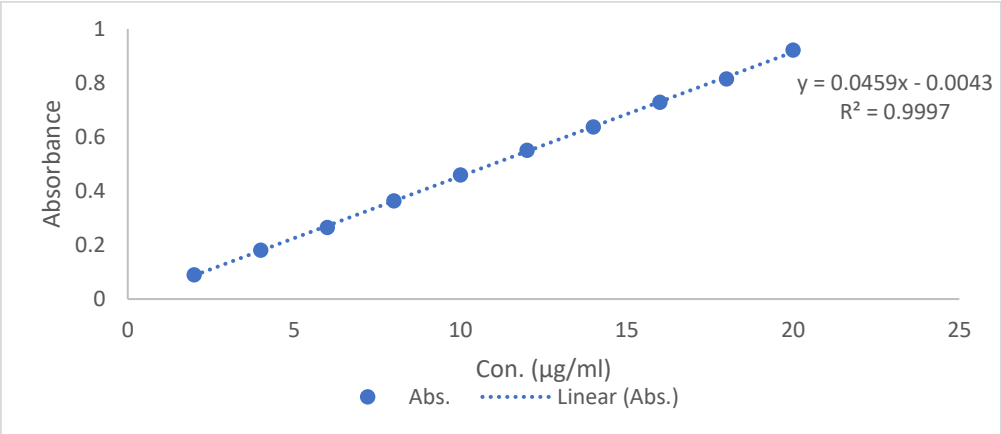


Figure 2.2: Linearity Graph of Pantoprazole sodium

2.1.5 Solubility studies of drug

The solubility of Pantoprazole sodium in different aqueous and non-aqueous solvent was shown in table 2.3

Table 2.3: Solubility (mg/ml) of Pantoprazole sodium in different solvents.

Solvent	Solubility(mg/ml)
Water	95.52±0.35
Methanol	97.75±0.62
Ethanol	96.78±0.017
Chloroform	0.36±0.01
0.1nhcl	29.61±0.27
Phosphate buffer 6.8ph	61.21±0.17
0.1nnaoh	99.95±0.35

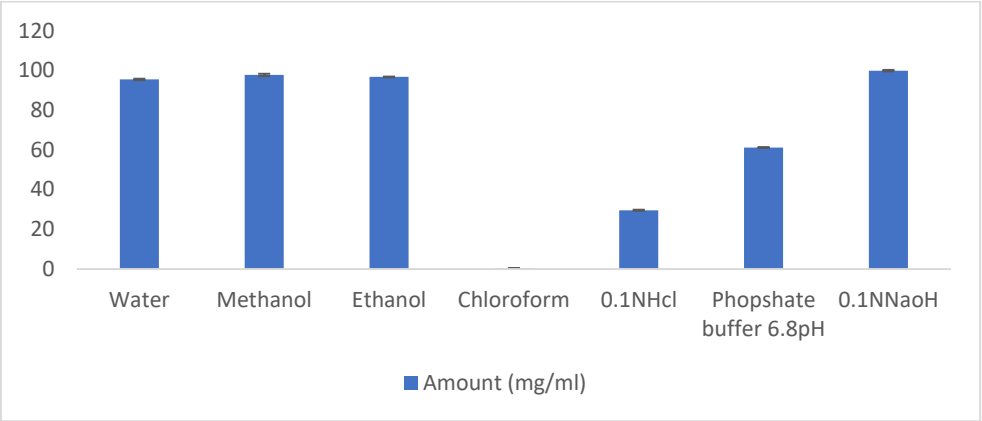


Figure 2.3: Bar Graph of Solubility data of Pantoprazole sodium in different solvent medium

According to figure 6.6, pantoprazole sodium was most soluble in 0.1nnaoh, then in alcohols, and in distilled water, where its solubility was 95.520.35mg/ml.

2.1.6 Partition coefficient of drug

Partition coefficient reveals a drug's hydrophilic and lipophilic properties. Drugs having partition coefficient values more than one are considered to be lipophilic, while those with partition coefficient values lower than one are considered to be hydrophilic. As shown in table 6.8, the partition coefficient of Pantoprazole sodium was calculated in a solution of n-octanol and water. The hydrophilic nature of Pantoprazole sodium is indicated by the value of the partition coefficient, which was determined to be 1.32 ± 0.32.

Table 2.4: Reference and observed value of partition coefficient of pantoprazole sodium

S. No.	Drug	Reference partition coefficient	Observed Partition coefficient (Log P)
1.	Pantoprazole sodium	1.30	1.31 ± 0.32

2.1.7 Identification of pure drug (FT-IR spectra):-

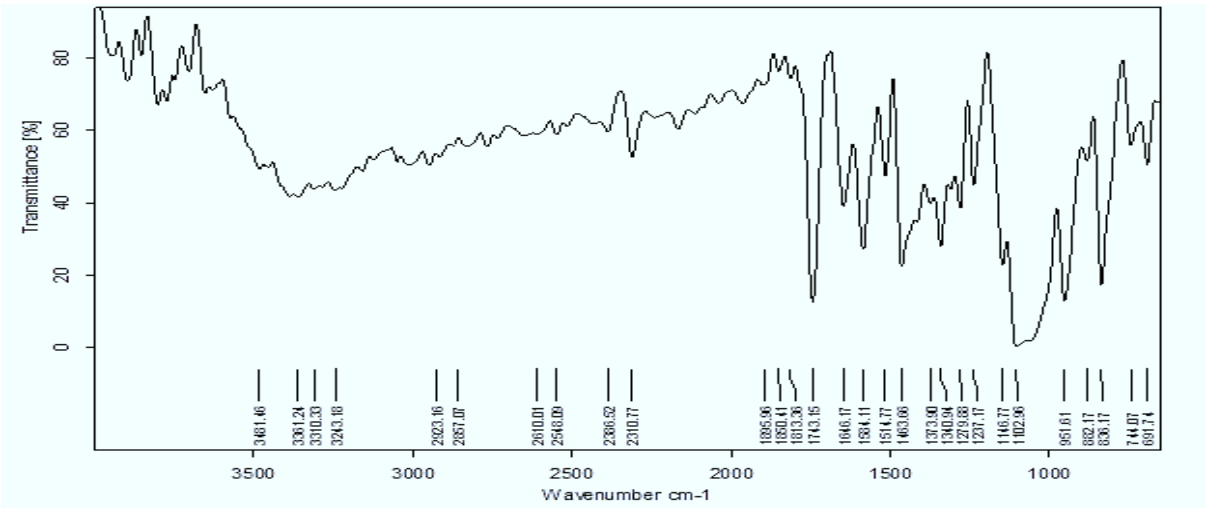


Figure 2.4: Graph of FTIR spectrum of pantoprazole sodium

The IR spectra of pure drug pantoprazole sodium revealed its characteristic peaks at 3481.46, 1584.11, 1102.96, 1146.77 and 951.61 cm^{-1} due to N-H, C-O, C-F, C-S and Sp^2 C-O aromatic ether stretch. (Nasef et al. 2017)

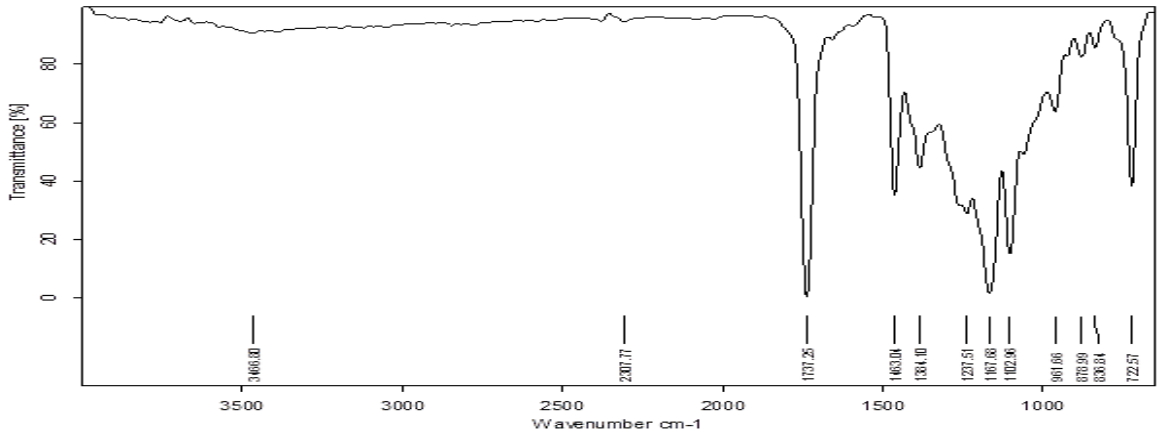


Figure 2.5: Graph of FT-IR Spectra of Pantoprazole sodium loaded eudragit S 100 coated proliposome

FITR spectrum of optimized formulation displayed that the major characteristic peak of the pantoprazole sodium was appeared with less intensity, confirmed the encapsulation of the drug into the proliposome and coating of the eudragit S 100.

2.2 Optimization of pantoprazole sodium loaded proliposomes

In the current study, pantoprazole sodium was enclosed in proliposomes that were then coated with Eudragit S100 to resist denaturation by the severe circumstances of the stomach and to deliver the medication to the intestinal environment

Screening of the process parameters for the preparation of the pantoprazole loaded proliposomes

2.2.1 Effect of the molar ratio of the soy lecithin and cholesterol

Different soy lecithin and cholesterol molar ratios (ranging from 50 to 300 µm) were tested, while other variables such the amount of solid carrier mannitol and temperature remained constant.

Table 2.5: In vitro characterization parameters of the pantoprazole sodium loaded proliposomes under presence of the different soy lecithin and cholesterol

Formulation code	% Yield	Percentage drug entrapment (%)	Percentage drug loading (%)	Carrs index (%)	Hausner ratio
PL1	66.15±0.97	37.46±1.74	4.15±0.19	9.07±2.90	1.10±0.03
PL2	92.37±0.67	59.87±0.11	6.09±0.02	3.26±1.09	1.03±0.01
PL3	95.20±0.78	98.90±0.01	8.65±0.04	5.18±2.18	1.05±0.02
PL4	95.23±0.40	98.38±0.02	7.54±0.02	23.33±4.81	1.31±0.08
PL5	86.72±1.16	55.31±0.41	5.92±0.05	11.03±0.92	1.12±0.01
PL6	97.92±0.58	81.61±0.20	7.56±0.03	15.60±3.47	1.19±0.05
PL7	95.54±0.32	69.43±0.19	5.9±0.04	22.08±0.96	1.28±0.02

Both percentages of yield and drug entrapment increased simultaneously as soy lecithin and cholesterol concentrations rose, but after a certain point, further increases had no effect. In contrast, percentages of drug entrapment decreased as a result of cholesterol competing with the drug and taking up less space for the pantoprazole sodium to be enclosed. For the PL3 formulation, the maximum percentages of drug entrapment and drug loading were found to be 98.90±0.01and 8.65±0.04, respectively. The values of the Carrs index and Hausner ration were found to be between 3.26±1.09 to 23.33±4.81 and 1.03±0.01 to 1.31±0.08 respectively. (Xu et al. 2009)

2.2.2 Optimization of the pantoprazole sodium loaded proliposomes

Using the Response Surface Methodology (RSM), a central composite design was created with the aim of detecting the interactions between the factors such as soy lecithin quantity (100-200 µm) and cholesterol amount (50-100µm). The goal was to enhance the amount of Pantoprazole sodium that was trapped inside the proliposomes.

The screening study's findings suggest that X1 soy lecithin and X2 cholesterol had a significant impact on this system, leading to high drug loading and encapsulation efficiency.

The effect of factors over the response was shown in table no.10

Table 2.6: Summary of central composite design

Factor	Name	Units	Low Actual	High Actual
X1	Amount of soy lecithin	µm	100	200
X2	Amount of cholesterol	µm	50	100
Response (Y) : Percentage drug entrapment Model : Quadratic				

Table 2.7: Composition of different formulation with response as per CCD design

Formulation code	Factor X1: Amount of lipid Micromolar	Factor X2: Amount of cholesterol Micromolar	Response Y: Percentage drug entrapment (%)
Pls1	150	75	85.99
Pls2	79.28932188	75	42.04
Pls3	100	100	59.87
Pls4	220.7106781	75	89.10
Pls5	200	50	81.05
Pls6	200	100	98.90
Pls7	150	39.64466	74.58
Pls8	150	75	87.68
Pls9	100	50	55.31
Pls10	150	75	86.69
Pls11	150	110.3553	91.22
Pls12	150	75	88.02
Pls13	150	75	84.67

According to Table 2.7, the quadratic models had the greatest fit for each of the replies Y1 (Encapsulation efficiency); in contrast to the linear model and the quadratic model, the two-factor model had the highest r^2 values across all responses. To represent the impacts of the variables, a quadratic model with quadratic and interactional components was chosen. The quadratic Eq. (1) of the response surface can be used to describe all experimental responses:

$$Y= 86.61+16.41X1+5.74X2+3.32X1X2-10.63X1^2-1.98X2^2 \quad \text{.....(1)}$$

The software was used to obtain Figure 2.6, also known as the response surface, in accordance with the predict equation. Figure 2.6 showed that the most significant factor affecting the proliposome powders' ability to entrap particles was the amount of soy lecithin present. Not that the entrapment efficiency would increase significantly with the amount of soy lecithin present. Figure 6.9 clearly demonstrates that while entrapment efficiency increases as soy lecithin concentration rises, the opposite is true at higher soy lecithin concentrations. Similar to this, the amount of cholesterol played a role in the effectiveness of the trapping. Figure 6.9 shows that the entrapment efficiency declined as the amount of cholesterol increased past 100 mg. There can be two factors. First off, the addition of the cholesterol may cause the liposomes' diameter to shrink, resulting in a smaller interspace between the bilayers. Second, the cholesterol occupied the gap between the two layers of the bilayer or competed with the medication.

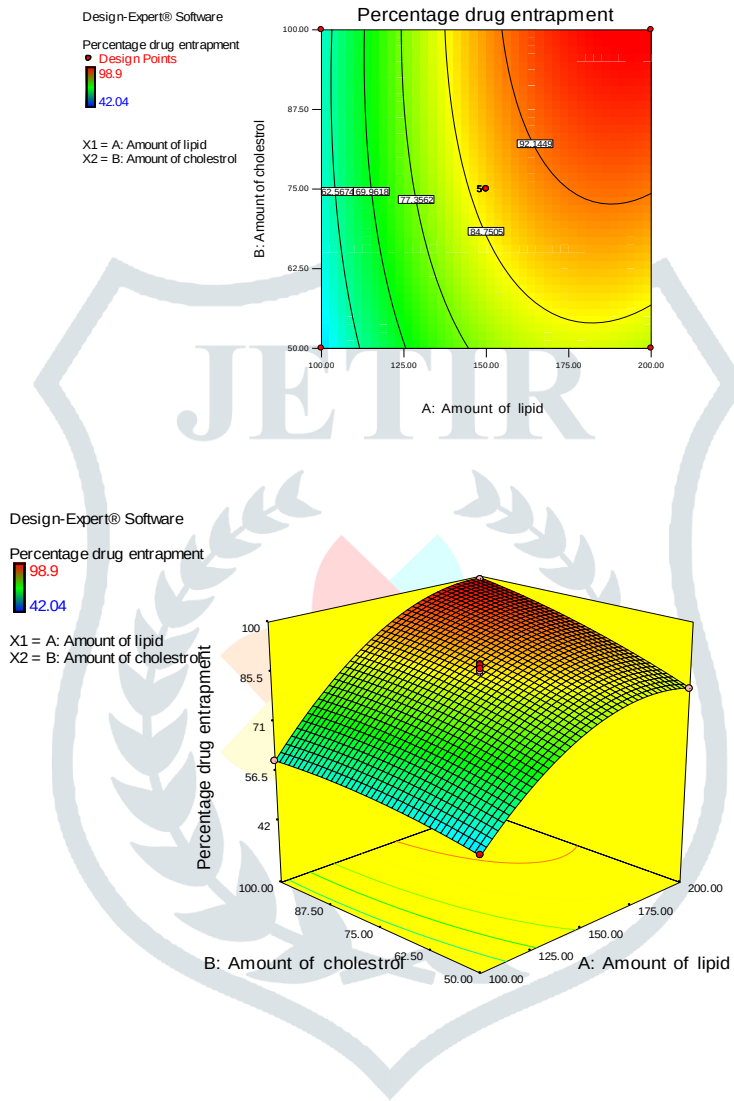


Figure 2.6: Effect of soy lecithin and cholesterol combined over the proportion of drug content is shown in a counter plot and 3D surface graph.

The goal of pharmaceutical formulation optimization is typically to identify the variables' levels of influence on the selected responses and to establish the variables' levels from which a reliable product with high-quality properties may be generated. The optimization process took into account all measured responses that could have an impact on the product's quality.

The following standards were used after "trading off" various response variables: Increased drug content percentage. On the other hand, the accuracy of the prediction of ideal values was evaluated by calculating the relative and absolute errors between the answers observed experimentally under optimal conditions and those anticipated by the model. The equation not only predicts the possible formulation of the proliposomes, but it also reacts on the response surface. Soy lecithin was expected to be 175.61 µm, cholesterol to be 94.76 µm, and EE to be 96.68% in the formulation. With the above-mentioned formulation, the real EE could reach 95.51±0.14%, indicating that the model equation has an excellent capacity for prediction. The optimal formulation has the following ingredients.

Table 2.8: Composition of optimized formulation and percentage drug entrapment

Formulation code	Factor 1 A: Amount of soy lecithin µm	Factor 2 B: Amount of cholesterol µm	Predicted Percentage drug entrapment (%)	Observed Percentage drug entrapment (%)
Pls14	175.61	96.67	96.68	95.51±0.14

2.3 Evaluation of pantoprazole sodium loaded Prolipsomes

2.3.1 Percentage yield

Table 2.9 displays the percentage yield for all prepared formulations.

Table 2.9: Value and states of percentage yield of all prepared pantoprazole sodium loaded proliposomes

Formulation code	Percentage yield (%)
Pls1	95.50±0.74
Pls2	93.16±1.09
Pls3	92.37±0.67
Pls4	92.21±0.99
Pls5	96.97±0.80
Pls6	95.20±0.78
Pls7	96.32±0.66
Pls8	96.28±0.24
Pls9	86.72±1.16
Pls10	94.28±0.61
Pls11	95.54±0.84
Pls12	95.72±0.37
Pls13	95.80±0.64

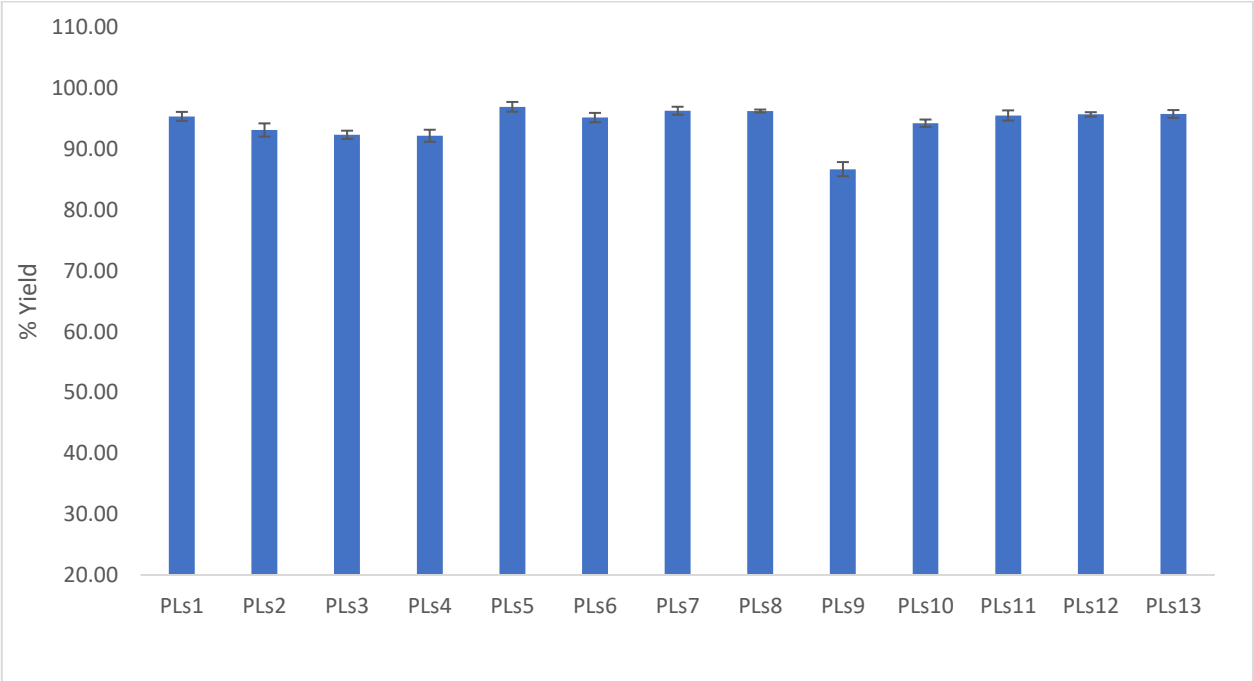


Figure2.7: Bar Graph of percentage yield of all prepared Pantoprazole sodium loaded proliposomes

The range of the total prepared formulation's percentage yield was discovered to be between 86.72±1.16% to 96.97±0.80%.

2.3.2 Percentage drug entrapment and percentage drug loading

Table 2.10 displays the percentage drug loading and percentage drug entrapment of all produced formulations.

Table 2.10: Value and states of percentage drug entrapment and percentage drug loading of all prepared Pantoprazole sodium loaded proliposomes formulations

Formulation code	Percentage drug entrapment (%)	Percentage drug loading (%)
Pls1	85.99±0.19	8.28±0.02
Pls2	41.970.62	4.54±0.07
Pls3	59.87±0.11	6.09±0.01
Pls4	89.11±0.08	7.73±0.04
Pls5	81.05±0.03	7.40±0.02
Pls6	98.90±0.01	8.65±0.01
Pls7	74.57±0.20	7.42±0.02

Pls8	87.58±0.30	8.43±0.03
Pls9	55.31±0.41	5.92±0.05
Pls10	86.69±0.05	8.35±0.02
Pls11	91.22±0.08	8.50±0.01
Pls12	88.03±0.17	8.48±0.02
Pls13	84.69±0.11	8.16±0.03

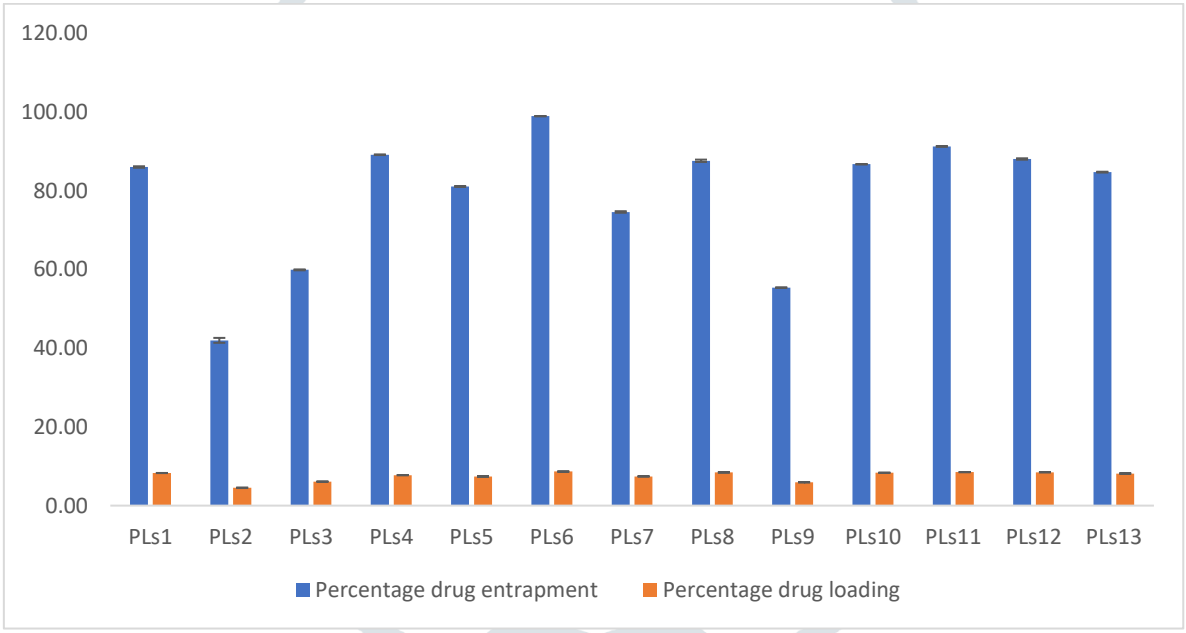


Figure 2.8: Bar Graph showing the percentage drug entrapment and percentage drug loading

The percentage drug entrapment and percentage drug loading of all prepared formulation was found to be in the range of 41.970.62 to 98.90±0.01% and 4.54±0.07 to 8.50±0.01%.

2.3.3Micromeritic property

The formulas' carrs index, and Hausner ratio are all displayed in 2.11.

Table 2.11 :Carrs index and Hausner ration of the all prepared formulations

Formulation code	Carr's index (%)	Hausner ration
Pls1	4.56±1.04	1.06±0.01
Pls2	12.97±2.10	1.14±0.02
Pls3	3.26±1.09	1.03±0.01
Pls4	4.56±1.04	1.04±0.01
Pls5	3.90±1.97	1.03±0.02
Pls6	5.18±2.18	1.05±0.02
Pls7	8.51±2.80	1.09±0.03
Pls8	5.79±1.85	1.06±0.04
Pls9	11.03±0.92	1.12±0.06
Pls10	8.44±1.17	1.09±0.01
Pls11	3.87±0.1156	1.02±0.02
Pls12	5.83±1.8859	1.06±0.03
Pls13	3.82±0.1156	1.01±0.02

All prepared formulations had respective Carrs indices and Hausner rations in the ranges of 3.26±1.09 to 11.03±0.92 and 1.01±0.02 to 1.14±0.02 respectively.

2.4 EUDRAGIT S 100 COATING OF THE OPTIMIZED FORMULATION

The eudragit S100 polymer was used to create the optimized formulation pls14, which was then further examined for its particle size, zeta potential, shape, and in-vitro drug release of pantoprazole sodium.

2.5 *IN-VITRO* Characterization of the eudragit s 100 coated pantoprazole sodium s100 loaded Proliposomes

2.5.1 Percentage drug entrapment and percentage drug loading

Table 2.12 lists the percentages of drug entrapment and loading for the pantoprazole sodium S100 loaded proliposomes coated with Eudragit S 100.

Table 2.12: Percentage drug entrapment and percentage drug loading of the of the formulation ES-pls14

S.No.	Formulation code	Percentage drug entrapment	Percentage drug loading
1	ES-pls14	94.95±0.17	8.75±0.08

For both uncoated and coated systems, the percentages drug entrapment efficiency and drug loading were roughly 94–95% and 8.70–8.90%, respectively (Table 6.18).

2.5.2 Transmission electron microscopy

Eudragit S 100 coated proliposomes formulation under TEM inspection showed that tiny, spherical vesicles had formed. Figure 2.9 shows that there was no indication of free pantoprazole sodium.

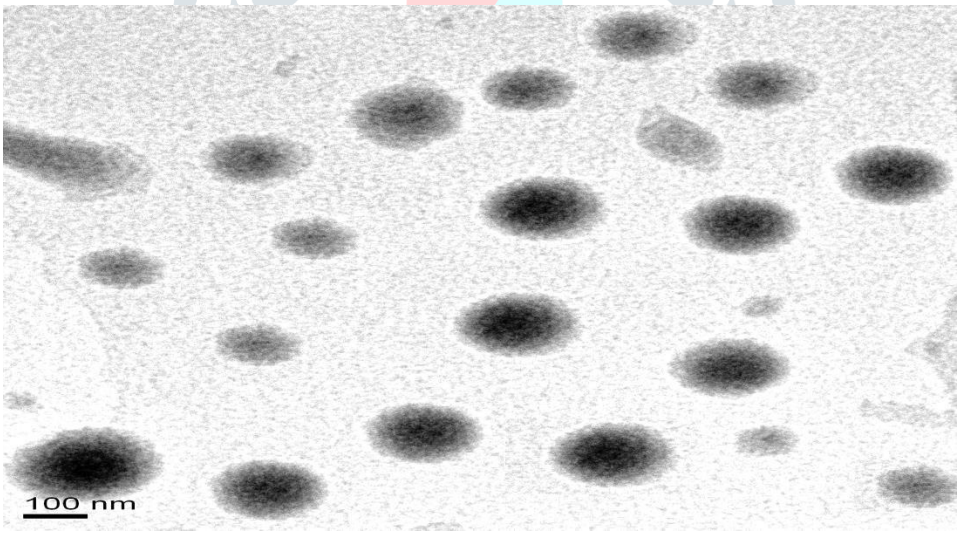


Figure 2.9: TEM micrograph of optimized formulation ES-pls14

2.5.3*IN-VITRO*drug release study

Table 2.13 presents the in vitro drug release data for the pure drug pantoprazole, uncoated drug loaded proliposomes, and coated drug loaded proliposomes.

Table 2.13: Comparison of the in vitro drug release of the pure drug, uncoated proliposomes and coated proliposomes

Time (Hr.)	Percentage drug release of Pure drug	Percentage drug release of pls14	Percentage drug release of ES-pls14
0.5	3.09±0.1	3.67±0.03	1.29±0.03
1	63.99±2.41	5.52±0.17	1.6±0.07
2	65.70±0.69	8.57±0.14	1.87±0.1
3	63.99±1.03	12.68±0.31	2.97±0.21
4		18.50±0.28	3.96±0.24
5		22.28±0.24	7.84±0.14
6		26.56±0.10	23.25±0.25
7		39.20±0.21	38.88±0.17
8		74.71±0.34	58.39±0.69
12		90.54±0.69	91.75±0.34
24		92.48±1.38	92.24±1.03

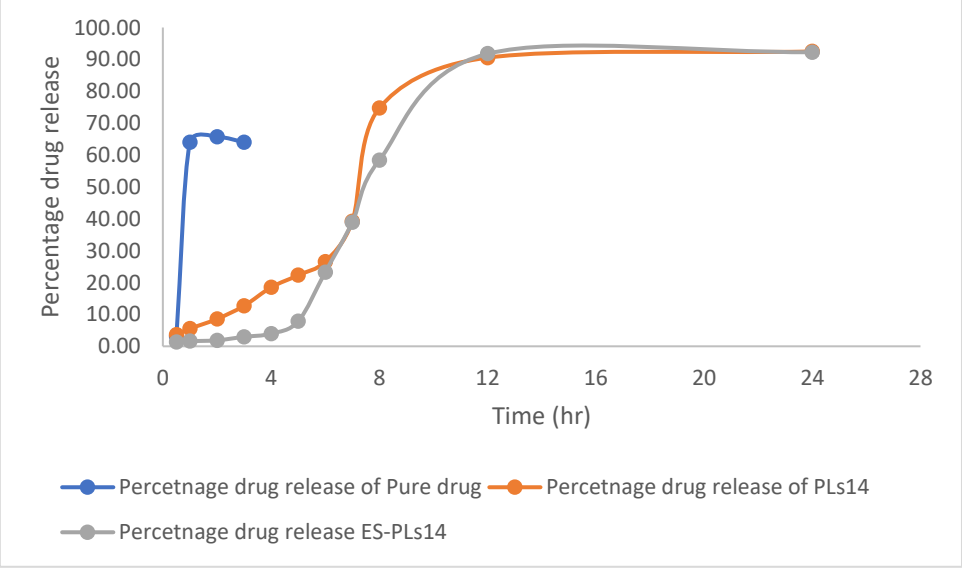


Figure 2.10: Comparison of the in vitro drug release of the pure drug, uncoated proliposomes and coated proliposomes

Pure pantoprazole sodium contained in an uncoated gelatin capsule released 65.7% of the medicine within two hours of being consumed under gastric circumstances (ph1.2). (Figure 6.17). On the other hand, proliposomes loaded with pantoprazole sodium and covered in eudragit S 100 showed minimal release. The percentage of drug release increases but depends on the buffer's phwhen the buffer is changed after two hours. Very little sodium pantoprazole is released at ph4.5. The greatest release of pantoprazole sodium from coated proliposomes, 93%, was recorded at ph7 buffer medium, respectively up to 24 hours, while a percentage release of 23% was seen at ph5–6 medium. A methacrylic acid and phsensitive polymer called Eudragit S100 permits the release of medicinal moiety above ph7.0. Chemically, Eudragit S100 is an anionic copolymer made of methyl methacrylate and methacrylic acid. Due to its high phthreshold and well-established polymeric backbone, Eudragit S 100 offers great gastric resistance.

3.Discussion

In preformulation studies, the melting point of pantoprazole sodium was found to be 138^0C±1.0-140.67^0C±1.154. Absorption maxima of Pantoprazole sodium was determined to be 295nm. Standard calibration of pantoprazole sodium was plotted between concentration and their absorbance in the range of 2-20µg/ml. With regression equation Y = 0.0462x -0.0059 and R^2 value 0.999, showed good linearity. The value of partition coefficient of pantoprazole sodium was found to be 1.32 ± 0.32.In the current study, pantoprazole sodium was enclosed in proliposomes that were then coated with Eudragit S100 to resist denaturation by the severe circumstances of the stomach and to deliver the medication to the intestinal environment. Different molar ration of the soy lecithin (50µm to 300 µm) and cholesterol (50µm to 300 µm) were investigated, while the other parameters like amount of solid carrier mannitol, temperature were remained constant.Among all formulation the percentage drug entrapment and percentage drug loading were found to be maximum 98.90±0.01and 8.65±0.04 for the PL3 formulation.Using the Response Surface Methodology (RSM), a central composite design was created with the aim of detecting the interactions between the factors such as soy lecithin quantity (100-200 µm) and cholesterol amount (50-100µm). The goal was to enhance the amount of Pantoprazole sodium that was trapped inside the proliposomes. On validation, Soy lecithin was expected to be 175.61 µm, cholesterol to be 94.76 µm, and EE to be 96.68% in the formulation the real EE could reach 95.51±0.14%, indicating that the model equation has an excellent capacity for prediction. The optimal formulation has the following ingredients. The range of the total prepared formulation's percentage yield was discovered to be between 86.72±1.16% to 96.97±0.80%. The percentage drug entrapment and percentage drug loading of all prepared formulation was found to be in the range of 41.970.62 to 98.90±0.01% and 4.54±0.07 to 8.50±0.01%. All prepared formulations had respective Carrs indices and Hausner rations in the ranges of 3.26±1.09 to 11.03±0.92 and 1.01±0.02 to 1.14±0.02 respectively. Uncoated proliposomes had a tiny size of about 189 nm, good homogeneity (P.I. 0.147), and a negative zeta potential (-15.8mv), which was caused by the negative charge of the soy lecithin. The coating of liposomes with eudragit resulted in an increase in size and polydispersity (230 nm and P.I. 0.162), with zeta potential (-17.2.mv) because of the polymer's negative charge. TEudragit S 100 coated proliposomes formulation under TEM inspection showed that tiny, spherical vesicles had formed. Pure pantoprazole sodium contained in an uncoated gelatin capsule released 65.7% of the medicine within two hours of being consumed under gastric circumstances (ph1.2). On the other hand, proliposomes loaded with pantoprazole sodium and covered in eudragit S 100 showed minimal release. The percentage of drug release increases but depends on the buffer's phwhen the buffer is changed after two hours. Very little sodium pantoprazole is released at ph4.5. The greatest release of pantoprazole sodium from coated proliposomes, 93%, was recorded at ph7 buffer medium, respectively up to 24 hours, while a percentage release of 23% was seen at ph5–6 medium. A methacrylic acid and phsensitive polymer called Eudragit S100 permits the release of medicinal moiety above ph7.0. Chemically, Eudragit S100 is an anionic copolymer made of methyl methacrylate and methacrylic acid. Due to its high phthreshold and well-established polymeric backbone, Eudragit S 100 offers great gastric resistance. Higuchi's model has a greater regression coefficient 0.811 than other drug release models, the release of Pantoprazole sodium from formulation ES- pls 4 follows it.

4.Conclusion:

In the present investigation, we have tailored pantoprazole sodium-loaded eudragit S 100 coated proliposomes to control the release of drug and to improve the stability of pantoprazole sodium and GIT tract fluid.pantoprazole sodium was enclosed in proliposomes that were then coated with Eudragit S100 to resist denaturation by the severe circumstances of the stomach and to deliver the medication to the intestinal environment. Different molar ration of

the soy lecithin (50µm to 300 µm) and cholesterol (50µm to 300 µm) were investigated, while the other parameters like amount of solid carrier mannitol, temperature were remained constant.Among all formulation the percentage drug entrapment and percentage drug loading were found to be maximum 98.90±0.01and 8.65±0.04 for the PL3 formulation.Pure pantoprazole sodium contained in an uncoated gelatin capsule released 65.7% of the medicine within two hours of being consumed under gastric circumstances (ph 1.2). On the other hand, proliposomes loaded with pantoprazole sodium and covered in eudragit S 100 showed minimal release. The percentage of drug release increases but depends on the buffer's ph when the buffer is changed after two hours.The greatest release of pantoprazole sodium from coated proliposomes, 93%, was recorded at ph 7 buffer medium, respectively up to 24 hours, while a percentage release of 23% was seen at ph 5–6 medium.

5.References:

Hiremath, R., Gowda, D., Raj, A., Shamant, B.S., & Srivastava, A. (2016). Proliposomes: A novel approach to carrier drug delivery system. Journal of Chemical and Pharmaceutical Research, 8, 348-354.

Hiremath, P. S., Soppimath, K. S., &Betageri, G. V. (2009). Proliposomes of exemestane for improved oral delivery: Formulation and in vitro evaluation using PAMPA, Caco-2 and rat intestine. International Journal of Pharmaceutics, 380: 96–104.

Jain, S. K., & Jain, N. K. (2008). Liposomes as Drug Carriers, Controlled and Novel Drug Delivery, CBS, New Delhi, 304-345.

Jain, A.; Jain, S.K.; Ganesh, N.; Barve, J.; Beg, A.M. Design and development of ligand-appended polysaccharidic nanoparticles for the delivery of oxaliplatin in colorectal cancer. Nanomedicine 2010, 6, 179–190

Janga, K. Y., Jukanti, R., &Velpula, A. (2012). Bioavailability enhancement of zaleplon via proliposomes: Role of surface charge. European Journal of Pharmaceutics and Biopharmaceutics. 80(2), 347-357.

Jeon, D., Kim, K. T., Baek, M. J., Kim, D. H., Lee, J.Y., & Kim, D.D. (2019). Preparation and evaluation of celecoxib-loaded proliposomes with high lipid content. European Journal of Pharmaceutics and Biopharmaceutics, 141, 139–148.

Matthias, H. M. K., Sarah, T., Hristo, P. V., Doris, H., Verena, P., Markus, G., Samuel, M M., & Bernhard, K., (2018). Development and Validation of Liquid Chromatography-Based Methods to Assess the Lipophilicity of Cytotoxic Platinum (IV) Complexes, Inorganics, 6,130.

Muneer, S., Masood, Z., Butt, S., Anjum, S., & Zainab, H. (2017) Proliposomes as Pharmaceutical Drug Delivery System: A Brief Review. Journal of Nanomedicine & Nanotechnology. 2017, 8, 448-450.

Payne, N. I., Browning, I., & Hynes, C.A. (1986). Characterization of proliposomes. Journal of Pharmaceutical Sciences.75(4): 330-333.

Payne, N. I., Timmis, P., Ambrose, C. V., Warel, M.D., & Ridgway, F. (1986). Proliposomes: a novel solution to an old problem, Journal of Pharmaceutical Sciences, 75(4), 325–329.

Raffin, R. P., Colome, L. M., Hoffmeister, C. R. D., Colombo, P., Rossi, A., Sonvico, F., & Costa, T. D. (2010). Pharmacokinetics evaluation of soft agglomerates for prompt delivery of enteric pantoprazole-loaded microparticles. European Journal of Pharmaceutics and Biopharmaceutics, 74(2), 275–280.

Raffin, R. P., Jornada, D. S., Re, M. I., Pohlmann, A. R., & Guterres, S. S. (2006). Sodium pantoprazole-loaded enteric microparticles prepared by spray drying: Effect of the scale of production and process validation. International Journal of Pharmaceutics, 324(1), 10–18.

Rojanarat, W., Nakpheng, T., Thawithong, E., Yanyium, N., &Srichana, T. (2012). Levofloxacin-Proliposomes: Opportunities for Use in Lung Tuberculosis. Pharmaceutics, 4(3), 385–412.

Stark, B., Pabst, G., &Prassl, R. (2010). Long-term stability of sterically stabilized liposomes by freezing and freeze-drying: Effects of cryoprotectants on structure. European Journal of Pharmaceutical Sciences, 41, 546–555.

Yadav, A. V., Murthy, M. S., Shete, A. S., &Sakhare, S. (2011). Stability Aspects of Liposomes. Indian Journal of Pharmaceutical Education and Research, 45(4), 402-413.