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Development of docetaxel loaded phospholipid based polymeric mixed micelles forcontrolled delivery

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Abstract

Phospholipid-containing mixed micelles are better at delivering drugs because they can better bind, load, and penetrate drugs through lymphatic drug absorption pathways, increasing the drug's systemic bioavailability. Hence the drug like docetaxel can be incorporated and deliver using phospholipid based polymeric mixed micelles (Ph-PmM). Present work represents the enhanced solubility and bioavailability of poorly aqueous soluble docetaxel. The Box-Behnken design was used for optimization of formulation and processing parameters like concentration of phospholipid, surfactant and drug. Prepared docetaxel loaded Ph-PmM were characterized for physicochemical and functional properties. The particle size of the Ph-mM was found to be 180 nm. The Ph-PmM were found to be thermodynamically stable which was confirmed by negative zeta potential value of about -40 mV. The drug was compatible with the other excipients, confirmation was done by DSC and FTIR. The drug released study of the drug loaded Ph-mM and pure drug showed that the sustained release of drug from the Ph-PmM. The solubility of drug was also increased due to Ph complex formation. Hence the Ph-mM has thepotential to improve the bioavailability of docetaxel.

Keywords: Docetaxel; mixed micelles; bioavailability; drug release; physical stability

Introduction

Micelles are used as a drug delivery vehicle which is made up of surfactants at a certain concentration in the water phase and self-assemble into specialized structures. Because they are thermodynamically unstable, alternative systems known as mixed micellar systems—which combine lipid and surfactant in the water phase—are being utilized more and more in drug delivery applications [1, 2]. With their nanometric-sized particles, these formulations can be applied to two-phase or three-phase systems to produce micelles and offer improved

thermodynamic stability and biocompatibility characteristics. Phospholipid-containing nanomixed micelles are better at delivering drugs because they can better bind, load, and penetrate drugs through lymphatic drug absorption pathways, increasing the drug's systemic bioavailability [3]. Furthermore, these micellar formulations help decrease the P-gp efflux of drugs that prevent Cytochrome P450 isozymes from catalyzing terminal metabolism because they contain phospholipids and surfactants [4-6]. In recent years, several studies have demonstrated the effectiveness of nanomixed micellar formulations for the oral administration of different drug classes.

Several studies in the literature have indicated that poor solubility, limited permeability, and variable systemic availability are just a few of the potential causes of issues with oral docetaxel delivery. Thus, while some reports emphasize active drug targeting using nanocarrier systems to specific receptors, a number of research findings deal with the development of novel formulation approaches, such as supersaturated systems and inclusion complexes, nanoemulsifying systems, nanoparticulate systems, etc. for passive drug targeting. Undoubtedly, a number of these innovative formulations have shown promising results in both in vitro and in vivo studies, highlighting the importance of creating cutting-edge drug delivery techniques to enhance the medication's therapeutic efficacy. However, when stored for a long time, some of the nanostructured systems—especially the nanoparticles—show limited fruition in terms of formulation stability. There are many reports in the literature on nanostructured systems based on phospholipids. Among these are nanomixed micelle formulations, which hold great promise for enhancing the biopharmaceutical properties of a range of medications.

To create nanostructured systems with reliable product and process performance, systematic development based on the quality by design (QbD) idea has gained importance [6]. High variability and inconsistent quality are common problems with nanoformulations, in particular,

because they necessitate a logical combination of multiple excipients and procedures to produce final products with dimensional properties in the nanometric range. Because QbD places a strong emphasis on understanding the product and process through the use of risk assessment techniques and the scientific foundation of development, it offers a high yield for incorporating quality into pharmaceutical products. In development of products exercises, risk analysis is used to figure out crucial variables, which are then optimized through the use of multifaceted tools and design of experiments [8, 9]. Singh and coworkers' recent creation [6] of numerous literature reports covering the last ten years on QbD-based development of nanostructured drug carriers attests to its importance in producing drug products with consistent quality over time.

Antineoplastic drug docetaxel (DTX) works by preventing cells from going through mitosis and interphase [10-12]. The concentration and length of exposure of docetaxel affect its anticancer activity. Despite being widely used in cancer chemotherapy, there are still a number of unresolved issues with its clinical use [13, 14]. Owing to its low solubility in water, DXT is delivered continuously via intravenous injection in conjunction with lipophilic solvents. According to Nie et al. (2011) [15], this formulation has a limited stability and is linked to significant toxicities related to vehicles. Our study's objective was to create and assess polymeric mixed micelles based on phospholipids that were loaded with docetaxel and had better formulation stability. Using a high-pressure self-assembly technique and basic excipients, docetaxel-loaded polymeric mixed micelles (DTX-Ph-PmM) were created. Water was utilized as a dispersion preparation medium. The drug docetaxel exhibited controlled release after being encapsulated in polymeric mixed micelles based on phospholipids.

1. Material and methods

We received a gift sample of docetaxel from Scino Pharmaceutical Pvt., Taiwan. Otto Chemie in Mumbai, India provided the soy lecithin. The source of phospholion 90H was Lipoid GmbH Frigenstr Ludwigshafen GERMANY. Thermo Fisher Scientific India Pvt. Ltd. supplied the ethanol, dimethyle sulfoxide (DMSO), and dimethylformamide (DMF), while Research Lab Fine Chem Industries, Mumbai, India, supplied Pluronic® F127 (PF127).

1.1 Preparation of DTX-Ph-PmM

The phospholipid-based polymeric mixed micelles were produced by hydrating a thin-film of a drug-phospholipid mixture dissolved in an organic solvent and applying the self-assembly

method as previously reported in research [8, 9]. Stirring at room temperature, the docetaxel (5 mg), Tween 80 (125 μL), and phospholipid (30 mg) were mixed together in 0.3 mL of getting dehydrated ethanol. After that, the mixture above received an addition of poloxamer F127 (0.25–1% w/v) solution. To create a clear mixed micelle solution with a final volume of 10 mL, the above-obtained identical phase was quickly injected into the 5% glucose solution. The mixed micelle solution was then filtered through a filter membrane with an aperture of 0.22-μm for additional research. After being produced, the polymeric mixed micelles based on phospholipids were gathered.

1.2 Quality by Design (QbD) based design of experiment

The best means of developing experiments for the methodical approach for formulation is the QbD-based design of experiment. Thus, in order to achieve the study's proposed goal, a trial with a QbD-based design was used, and the impact of the process and formulation elements were measured using the associated reaction properties.

1.3 Experimental Design

The systemic maximizing the efficiency of the formula and processing parameters was carried out in the present research using the Box-Behnken type of design of experiment approach [16]. In order to optimize the formula, variables that are independent such as the individual concentrations of phospholipid (X1, %v/v), surfactant (X2, %w/v), and drug (X3, %w/v) have been taken into account. Their impact on the size of particles and effectiveness of entrapment was also measured. To obtain an optimal formulation with the highest efficiency of entrapment and the smallest particle size, seventeen different batches, as indicated in Table 3, containing every possible combination of lipid, surfactant, and drug, were created.

Equation (1), which employs a statistical model with interactive and polynomial terms, was utilized to assess the response.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_{11}X_1^2 + b_{22}X_2^2 + b_{33}X_3^2 + b_{12}X_1X_2 + b_{23}X_2X_3 + b_{13}X_1X_3 \quad \text{Eq. (1)}$$

Where, the predicted coefficient for the factor X_1 is b_1, the variable that is dependent is Y, and b_0 is the arithmetic mean response of the 20 runs. The mean outcome of adjusting each factor one at a time from a low to a high value was represented by the main effects (X_1, X_2, and X_3). When all three factors were changed at once, the response changed as indicated by the

interaction terms (X_1X_2, X_2X_3, and X_1X_3). To look into on-linearity, the polynomial terms (X_{12}, X_{22}, and X_{32}) were added.

The level values of three factors and the composition of the Box-Behnken design batches were shown in **Table 1**.

Table 1: Coded levels and "Real" values for each factor under study

Variables	**Levels**				
	-1.68179	-1	0	+1	+1.68179
Independent	**Real values**				
Conc. of Phospholipid (X_1, mg)	0.591036	20	30	40	17.409
Conc. of Surfactant (X_2, %w/v)	-0.181793	0.25	0.625	1	3.18179
Conc. of Drug (X_3, mg)	0.318207	5	7.5	10	3.68179
Dependent					
Particle size (Y, nm)					
Entrapment efficiency (Y, % w/w)					

Table 2: Box-Behnken design of experiment formulation batches

Sr. No.	**Batches**	**X1**	**X2**	**X3**
1.	F1	30	0.625	7.5
2.	F2	40	0.25	7.5
3.	F3	30	0.25	10
4.	F4	30	0.625	7.5
5.	F5	30	1	10
6.	F6	40	0.625	10

7.	F7	30	0.25	5
8.	F8	30	0.625	7.5
9.	F9	40	1	7.5
10.	F10	30	1	5
11.	F11	30	0.625	7.5
12.	F12	40	0.625	5
13.	F13	20	0.625	10
14.	F14	20	1	7.5
15.	F15	30	0.625	7.5
16.	F16	20	0.25	7.5
17.	F17	20	0.625	5

1.4 Characterization of DTX-Ph-PmM

1.4.1 Particle Size and zeta potential analysis

Using photon correlation spectroscopy (PCS) and dynamic light scattering on a Zetasizer® nano (Model: Zen 3600, Malvern Instruments, Malvern, UK) outfitted with a 5-mW helium neon laser with an output wavelength of 633 nm, the particle sizes of the docetaxel-loaded phospholipid-based polymeric mixed micelles were analysed [17, 18]. The measurements were done for at least 40–80 seconds, at 25 °C, and at a 90° angle. The dispersant was water. Smoluchowski's equation was utilized to determine the zeta potential based on the electrophoretic mobility of polymeric mixed micelles based on phospholipids [19]. Every measurement was done in triplicate.

1.4.2 DSC analysis

The polymorphism state of docetaxel, phospholipon® 90H, their physical mixture of was examined by DSC. As a purge gas, dried nitrogen gas was applied at a rate of 80 mL/min. An aluminum pan containing around 5 milligrams of powdered substance was within the

instrument chamber. a single heating cycle that raised the temperature from 40 °C to 400 °C at a rate of 10 °C per minute [19]. TA software was utilized to examine the peaks.

1.4.3 FTIR

Docetaxel, Phospholipon® 90H, and their physical mixing IR spectra were obtained, and the interaction between the components required to produce the DTX-Ph-PmM was examined. The FTIR spectra of docetaxel, phospholipon® 90H, and their physical combination were recorded using an FTIR spectrophotometer (FTIR-8300). In order to get ready for FTIR analysis, pretreatment was briefly applied to the docetaxel, Phospholipon® 90H, and their physical combinations. These materials were mixed uniformly with FTIR-grade potassium bromide (KBr) at a ratio of 1:100. Following that, they were subjected to 45 scans at a resolution of 4 cm^{-1} and analyses spanning from 4,500 to 400 cm^{-1} [19].

1.4.4 Entrapment efficiency

A variety of techniques previously reported in the literature were used to assess the entrapment efficiency, or the docetaxel-loaded polymeric mixed micelles [20, 21]. In summary, 1 milliliter of polymeric mixed micelles based on phospholipids and containing docetaxel was introduced into the Centricon® reservoir (Model: YM-100, Amicon, Millipore, Bedford, MA, USA). Following a 40-minute centrifugation of the polymeric mixed micelles based on phospholipids at 15,000 rpm, the filtrate containing free docetaxel was extracted. The filtered dispersion was then diluted with methanol and subjected to a UV analysis to determine the amount of docetaxel. The total concentration of docetaxel (Ct) and the concentration of docetaxel in the filtrate after centrifugation (Cf) were calculated using the UV-spectrophotometric analysis.

The entrapment efficiency was calculated using the following equation (2);

$$\text{Entrapment efficiency (\%)} = \frac{C_t - C_f}{C_t} \times 100 \qquad \text{Eq. (2)}$$

1.4.5 Drug content

The polymeric mixed micelles based on phospholipids and loaded with docetaxel were identified using the UV method previously reported by Rarokar et al in 2022 [19]. Vibrant shaking was used for 20 minutes to dissolve phospholipid-based polymeric mixed micelles, which were equivalent to 10 mg of docetaxel in 100.0 mL of ethanol. For five minutes, the

solution sonicated. Following a 0.45 µ filter filtering of the solution, 1.0 mL of the filtrate was removed, diluted with 10 mL of distilled water, and subjected to spectrophotometric analysis at 230 nm.

1.4.6 Scanning electron microscopy

After the spheres formed, a drop of the optimized formulation of polymeric mixed micelles based on phospholipids and loaded with docetaxel was placed on a glass slide and allowed to dry [22]. Using an auto fine coater (Model: JFC1600, Jeol Ltd., Tokya, Japan), a thin layer of palladium was applied to the sphere's surface on the glass slide. Using a scanning electron microscope (Model: JSM-6390LV, Jeol Ltd., Tokyo, Japan) with a digital camera and an accelerating voltage of 10 KV, the palladium-coated samples were examined.

1.5 *In-vitro* docetaxel release study

By using a Franz diffusion cell to measure the drug's diffusion across a cellophane membrane, the docetaxel release from the docetaxel-loaded phospholipid-based polymeric mixed micelles was assessed. The donor compartment and the receptor compartment were the two compartments that made up the cell. These two compartments were separated by a semipermeable membrane that had been previously activated. The formulation of polymeric mixed micelles based on phospholipids was incorporated into the donor compartment situated above the membrane. 18 mL of phosphate buffer saline solution (PBS, pH 7.4), kept at 37±0.5°C, served as the release medium within the receptor compartment. Aliquots of the release medium were taken out and replaced with an equivalent volume of brand-new release medium at prearranged intervals. UV light was used to examine the drug concentrations in the release medium at different times [22].

1.6 Statistical analysis

The mean±standard deviation (SD) was used to express all the data. Using GraphPad® Prism® software version 5.03 (San Diego, CA), a two-way analysis of variance (ANOVA) and a Bonferroni post test were used for the statistical analysis. If there were significant differences between the means, the P value was deemed less than 0.05.

2. Results and discussion

2.1 Responses correspondent to Experimental Design

Table 5 presents the Box-Behnken design matrix along with the experimental responses that were obtained. SAS software is used to analyse the experimental design's results, and it can yield a wealth of insightful data that supports the value of using statistical design in experimentation. The data are fitted using the following quadratic model, with the final equation being expressed in terms of the coded factors found in equations 3 and 5 whereas actual values in equations 4 and 6;

2.1.1 Response 1: Particle size

For Particle Size,

Coded equation, Particle Size= +178.60+8.75A+0.8750B+9.13C-0.2500AB 2.25AC +3.50BC-10.05A^2-0.8000B^2+6.70C^2 Eq. (3)

It is possible to predict the response for specific levels of each factor by using the equation expressed in terms of coded factors. The factors' high levels are automatically coded as +1 and their low levels as -1. By comparing the factor coefficients, the coded equation can be used to determine the relative impact of the factors.

Actual equation,

Particle Size= +87.14444+7.62167-16.55556-12.06333-0.066667-0.090000+3.73333-0.100500-5.68889+1.07200 Eq. (4)

Predictions regarding the response for specific levels of each factor can be made using the equation expressed in terms of the actual factors. In this case, each factor's levels ought to be stated in their original units. Because the intercept is not in the centre of the design space and the coefficients are scaled to account for the units of each factor, this equation should not be used to calculate the relative impact of each factor.

Table 3: Actual values of XA, XB and XC

Particle Size =	
+87.14444	
+7.62167	Conc. of Phospholipid

-16.55556	Conc.of Surfactant
-12.06333	Conc. of Drug
-0.066667	Conc. of Phospholipid * Conc.of Surfactant
-0.090000	Conc. of Phospholipid * Conc. of Drug
+3.73333	Conc.of Surfactant * Conc. of Drug
-0.100500	Conc. of Phospholipid^2
-5.68889	Conc.of Surfactant^2
+1.07200	Conc. of Drug^2

2.1.2 Response 2: Entrapment efficiency

The difference between the predicted R^2 of 0.5981 and the adjusted R^2 of 0.9347 is greater than 0.2, as one might typically anticipate. This could point to a significant block effect or a potential issue with your data or model. Model reduction, response transformation, outliers, and other issues should be taken into account. Confirmation runs ought to be used for testing any empirical model. Adequate precision calculates the ratio of signal to noise. Ideally, the ratio should be higher than 4. With a ratio of 18.856, you have a sufficient signal. The design space can be navigated with the help of this model.

When all other factors are held constant, the coefficient estimate shows the expected change in response for each unit change in factor value. The total average response of all the runs is the intercept in an orthogonal design. Based on the factor settings, the coefficients represent adjustments made around that average. VIFs are 1 when the factors are orthogonal; VIFs greater than 1 denote multi-colinearity; the higher the VIF, the stronger the factor correlation. VIFs of less than 10 are generally acceptable.

For Entrapment Efficiency,

Coded equation, $EE=+84.40+8.00A+4.13B-3.63C-1.25AB-0.7500AC-2.50BC+0.0500A^2-2.20B^2-1.20C^2$ Eq (5)

It is possible to predict the response for specific levels of each factor by using the equation expressed in terms of coded factors. The factors' high levels are automatically coded as +1 and their low levels as -1. By comparing the factor coefficients, the coded equation can be used to determine the relative impact of the factors. Phospholipid concentration (mg) is represented by XA, Pluronic F127 concentration (%w/v)

by XB, and docetaxel concentration (mg) by XC in coded values. One quadratic equation can be used to represent each experimental response, Y.

Actual equation, EE=+22.43889+1.20333+60.55556+3.99667-0.333333-0.030000-2.66667+0.000500-15.64444- 0.192000 Eq (6)

Table 4: Actual values of XA, XB and XC

EE =	
+22.43889	
+1.20333	Conc. of Phospholipid
+60.55556	Conc.of Surfactant
+3.99667	Conc. of Drug
-0.333333	Conc. of Phospholipid * Conc.of Surfactant
-0.030000	Conc. of Phospholipid * Conc. of Drug
-2.66667	Conc.of Surfactant * Conc. of Drug
+0.000500	Conc. of Phospholipid^2
-15.64444	Conc.of Surfactant^2
-0.192000	Conc. of Drug^2

The equation defined in terms of the real factors may be used to predict the response for particular amounts of each element. The levels of each element in this instance should be expressed in their original units. This equation should not be utilized to determine the relative influence of each element since the intercept is not in the centre of the design space and the coefficients are scaled to accommodate for the units of each factor.

2.2 ANOVA for response surface Quadratic model

The response surface quadratic model of particle size and entrapment efficiency's ANOVA findings are shown in equations 3, 4, 5 and 6. When the p value was less than 0.005, the model was considered significant.

The three-dimensional (3D) response surface graphs that show the interactions between the independent variables and the responses are shown in Figure 1. The Design Expert® program generated an optimal formula that produced the experimental and expected results. When the p value was less than 0.005, the model was considered significant.

Table 5: Box-Behnken design for formulation batches with respect to particle size and entrapment efficiency

Sr. No.	**Batches**	X_1	X_2	X_3	Response 1	Response 2
		A: Conc. of Phospholipid (mg)	**B: Conc. of PF127 (%w/v)**	**C: Conc. of** docetaxel **(mg)**	**Particle Size (nm)**	**% Entrapment efficiency (%)**
1.	F1	30	0.625	7.5	178	85
2.	F2	40	0.25	7.5	180	87
3.	F3	30	0.25	10	190	74
4.	F4	30	0.625	7.5	180	84
5.	F5	30	1	10	195	78
6.	F6	40	0.625	10	186	89
7.	F7	30	0.25	5	181	79
8.	F8	30	0.625	7.5	178	85
9.	F9	40	1	7.5	185	92
10.	F10	30	1	5	172	93
11.	F11	30	0.625	7.5	175	85
12.	F12	40	0.625	5	170	95

13.	F13	20	0.625	10	185	73
14.	F14	20	1	7.5	156	80
15.	F15	30	0.625	7.5	182	83
16.	F16	20	0.25	7.5	150	70
17.	F17	20	0.625	5	160	76

2.2.1 Model F and P- value

The model F-value of 26.45 indicates that it is considered significant. The likelihood of noise being the cause of this type of big F-value is 0.01%.

Model terms with P-values less than 0.0500 are deemed significant. In this case, key model terms are A, B, C, BC, and B2. If the value is more than 0.1000, the model terms are not important. If your model has a lot of unimportant model terms (apart from those required to support hierarchy), model reduction could improve it.

The lack of fit is considerable, as indicated by the 8.65 F-value. The likelihood of noise causing a significant Lack of Fit F-value is 3.19%. We want the model to fit, thus a notable misfit is not what we want.

2.2.2 Validation of Model

To evaluate the optimization capability of models generated based on the results of the central composite design, DTX-Ph-PmM were prepared using optimized concentrations of phospholipid (Phospholipon 90H), surfactant (Pluronic® F127), and drug (docetaxel) of 40 mg, 0.625%w/v, and 5 mg, respectively. As can be seen from table 6 the model's importance was demonstrated by the percentage bias for the observed and predicted values of particle size and entrapment efficiency for docetaxel-loaded polymeric mixed micelles based on phospholipid being less than ±3.0% [24].

$$Bias\ (\%) = \frac{predicted\ value - observed\ value}{predicted\ value} \times 100$$

Eq (6)

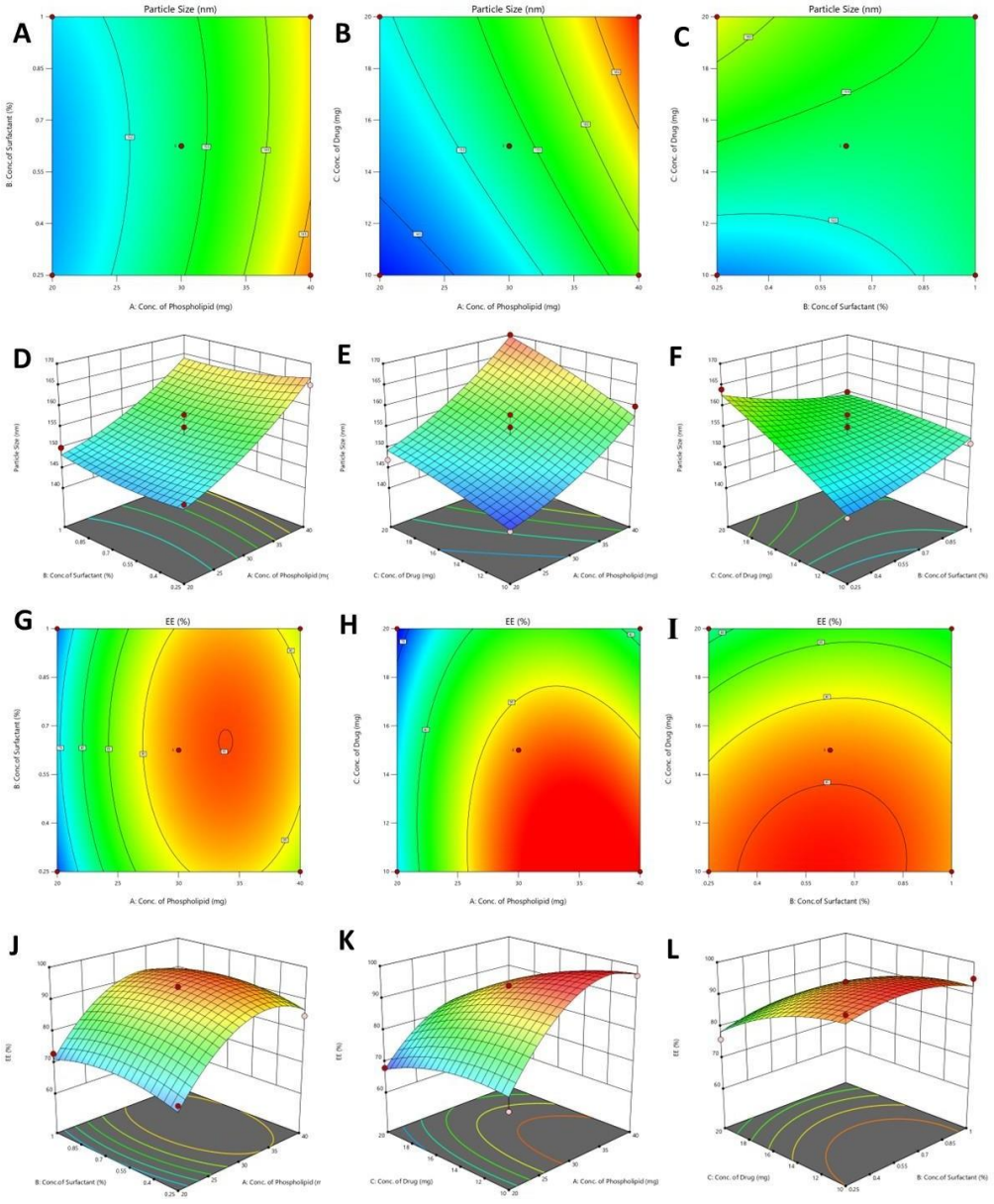


Figure 1: The contour plots (A, B, C) and response surface plot (D, E, F) based on the particle size for factors conc. of phospholipids and surfactant, conc. of drug and phospholipids, conc. of drug and surfactant respectively. The contour plots (G, H, I) and response surface plot (J, K, L) based on the entrapment efficiency for factors conc. of phospholipids and surfactant, conc. of drug and phospholipids, conc. of drug and surfactant respectively.

Table 6: Comparison of the observed and predicted values in docetaxel-loaded phospholipid-based polymeric mixed micelles under predicted optimum conditions

Response Variable	**Predicted Value**	**Observed value***	**Bias (%)**
Particle size (nm)	178	180.8±2.6 nm	-1.57
Entrapment efficiency (%)	97	95±2.32	2.06

* Values represent mean ± standard deviation (n=3)

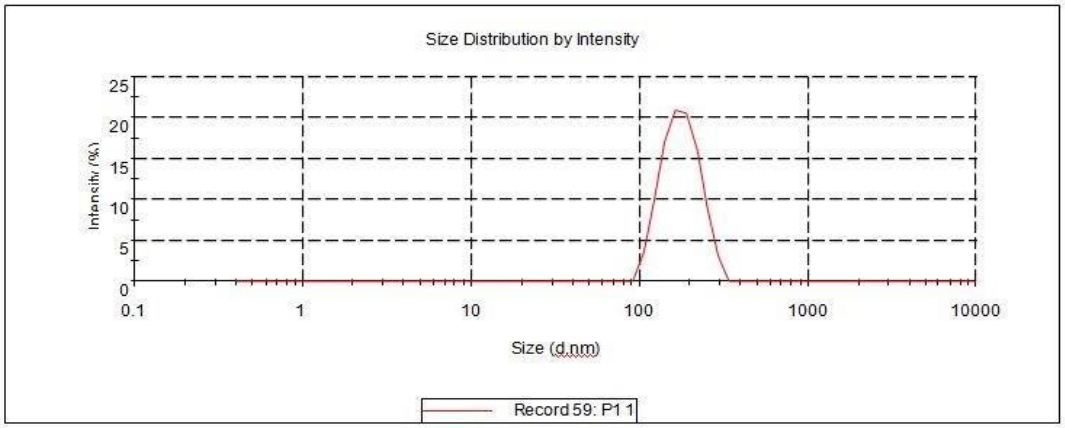
2.3 Physicochemical characterization

2.3.1 Particle size and zeta potential analysis

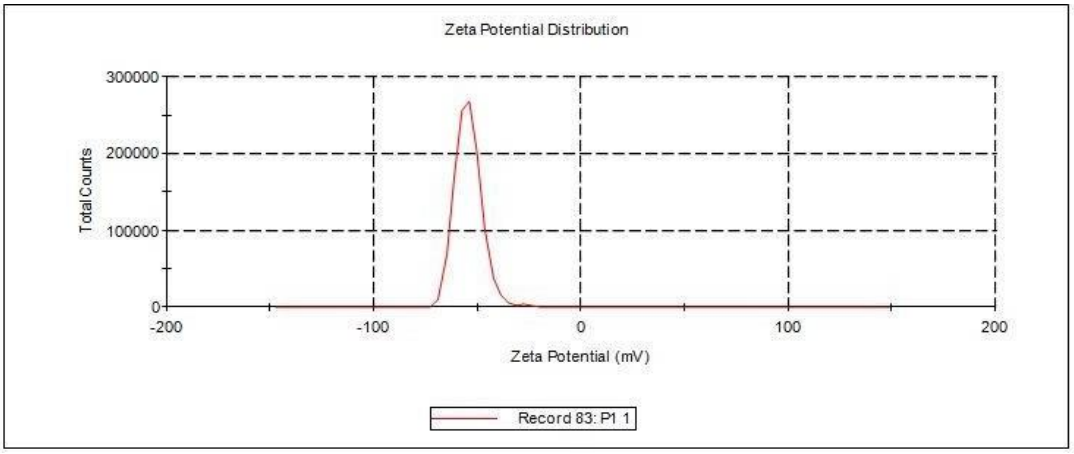
Smaller particles have a higher surface area/volume ratio, which facilitates the drug's release from the phospholipid-based polymeric mixed micelles through surface erosion and diffusion. Additionally, smaller particles have the advantage of allowing the drug-loaded polymeric mixed micelles to pass through physiological drug barriers. Previous research has indicated that smaller particles (less than 500 nm) can pass through endocytosis to cross the membrane of epithelial cells, while larger particles (less than 5 mm) would be absorbed through the lymphatics [25].

It was discovered that the mean particle sizes of the docetaxel-loaded phospholipid-based polymeric mixed micelles was 180.8±2.6 nm. Consequently, it was discovered that the docetaxel loading only slightly raised the mean particle size of the polymeric mixed micelles based on phospholipids. Furthermore, a narrow particle size distribution was indicated by the low polydispersity index values (0.172±0.020) for docetaxel-loaded phospholipid-based polymeric mixed micelles [26].

Another crucial metric for assessing the stability of polymeric mixed micelles based on phospholipids is zeta potential. Strong repellent forces between particles and prevention of phospholipid-based polymeric mixed micelle aggregation in a buffer solution can result from a high absolute value of zeta potential, which signifies a high electric charge on the surface of the micelles. It was discovered that the zeta potential of docetaxel-loaded and blank phospholipid-based polymeric mixed micelles was −49.1±1.52 mV. According to Freitas C et al. (1998), a minimum zeta potential of more than −30 mV is generally regarded as acceptable [27] and suggestive of a good physical stability (see Figure 2).



(A)



(B)

Figure 2: Particle size distribution (A) and Zeta potential (B) of docetaxel-loaded phospholipid-based polymeric mixed micelles

2.3.2 Entrapment efficiency

The drug entrapment efficiency is an important parameter for drug delivery systems. This is especially true for expensive drugs. The entrapment efficiency of optimized docetaxel-loaded phospholipid based polymeric mixed micelles was found to be 95%.

2.3.3 Drug content

The drug content for optimized docetaxel-loaded phospholipid-based polymeric mixed micelles was found to be 96.45 ± 0.72.

2.3.4 Scanning Electron Microscopy (SEM)

The docetaxel-loaded phospholipid based polymeric mixed micelles were analyzed by SEM for surface morphology. The electron micrographs at different magnifications at 100x, 700x and 5000x revealed the formation of cubical as well as some spherical shape docetaxel-loaded phospholipid based polymeric mixed micelles formation as shown in Figure 3A, and 3B respectively. The initial morphological characterization confirms the formation of phospholipid based polymeric mixed micelles.

2.4 *In-vitro* docetaxel release from DTX-Ph-PmM

The release pattern of docetaxel from the docetaxel-loaded phospholipid based polymeric mixed micelles as evaluated using the Franz diffusion cell as shown in figure 4. The docetaxel-loaded phospholipid-based polymeric mixed micelles exhibited an initial fast release within 1 h [28]. This was followed by a controlled release of docetaxel from the phospholipid based polymeric mixed micelles over a period of 12 h. At the end of 12 h, over 98.20% of docetaxel was released from the phospholipid based polymeric mixed micelles whereas solution of docetaxel releases more than 98.91% docetaxel in only 4h. The results indicated the potential of phospholipid based polymeric mixed micelles to be utilized in the controlled drug delivery systems.

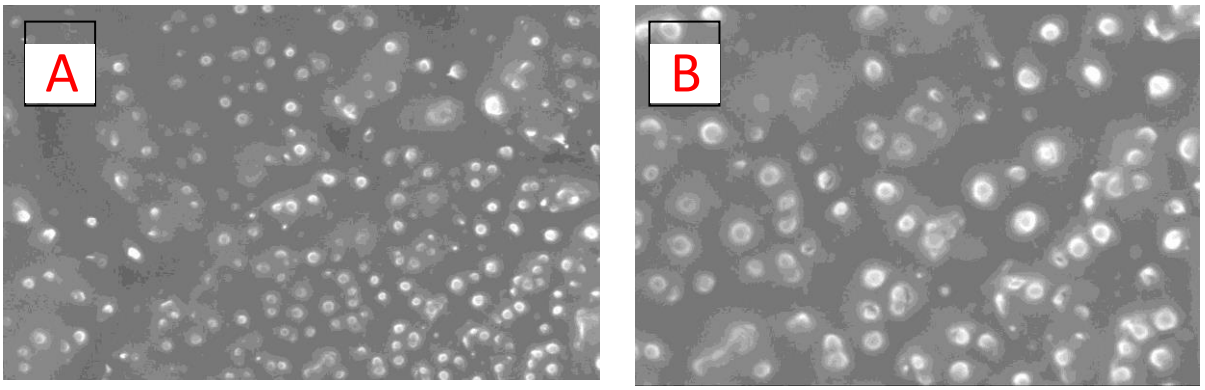


Figure 3: Scanning Electron Microscopic images of docetaxel-loaded phospholipid based polymeric mixed micelles

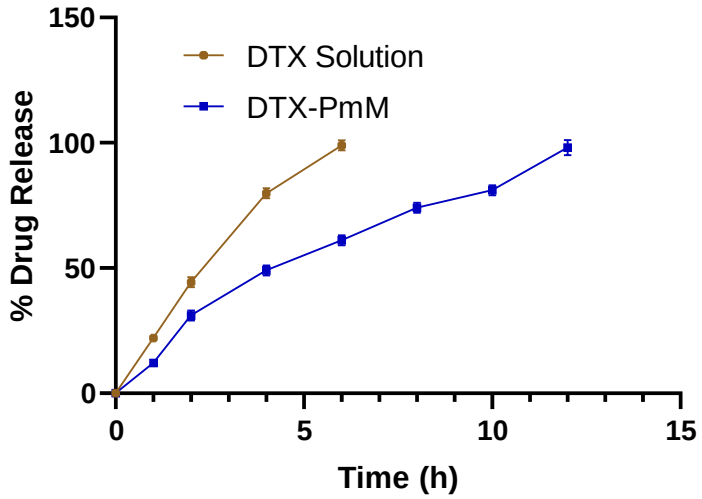


Figure 4: % drug release from docetaxel-loaded phospholipid based polymeric mixed micelles and docetaxel suspension

3. Conclusion

The preparation and optimization of the docetaxel-loaded polymeric mixed micelles were carried out through the utilization of Quality by Design based Box-Behnken design of experiment. Next, the formula that was optimized was described for various in vitro conditions. According to the study's overall findings, created DTX-Ph-PmM exhibits superior physicochemical qualities than the medication alone, which might increase the drug's bioavailability. Therefore, the DTX-Ph-PmM system may be the best option for docetaxel delivery that is regulated.

Declaration of interest

Authors declared no conflict of interest.

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