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DEVELOPMENT AND EVALUATION OF PRONIOSOMAL GEL CONTAINING DULOXETINE HYDROCHLORIDE FOR TOPICAL DRUG DELIVERY SYSTEM

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ABSTRACT

Duloxetine HCl, also known as (S)-N-methyl-3-(1-naphthalenyloxy)-2-thiophene propanamine hydrochloride, is an antidepressant and a selective serotonin and norepinephrine reuptake inhibitor used to treat major depression (MDD). Duloxetine HCl (DXT) is effectively absorbed following oral administration, but it takes 2 hours to begin absorption and reaches its tmax 6 hours after dosage. Due to substantial hepatic metabolism, duloxetine HCl (DXT) has limited and variable bioavailability, and it is also prone to breakdown in the acidic stomach media, resulting in subtherapeutic levels. There have been several attempts to address the disadvantages of limited oral bioavailability. Proniosomes offer excellent potential for improved drug delivery, through versatile routes by overcoming the permeation barriers faced by several drugs. A dermal therapeutic formulation like the proniosomal gel of Duloxetine HCl was developed and evaluated for the effective treatment of depression. The study aimed to develop a proniosomal gel containing duloxetine hydrochloride for topical delivery, enhance drug permeation through the barriers of the skin, and maintain the controlled plasma concentration. Duloxetine hydrochloride-loaded proniosomal gel was optimized through Design Expert 8 and Statgraphics Centurion 16 software, prepared by the Coacervation phase separation method, and then characterized for in vitro parameters and drug release order kinetics. The formulation (G14), out of all the trials, fulfilled the maximum requisites of the highest entrapment efficiency (93.58±0.12%) and vesicle size (241.02). After 24 hours, the in vitro drug release of the optimized formulation (G14) was 93.2700.647 vs 14.7680.237% from the control gel. The Higuchi model has a higher regression coefficient (0.9419) than other pharmacological models. The results suggest that the incorporation of Duloxetine HCl in proniosomal gel can significantly improve the release of the drug, increase bioavailability, and improve patient compliance. Thus, gel formulation could be considered a promising approach for efficient transdermal drug delivery of duloxetine HCl.

Keywords: Duloxetine hydrochloride, Span, Proniosomes, Improved bioavailability, Topical drug delivery.

INTRODUCTION

Depression is a common mental condition characterized by persistent sorrow, low self-esteem, decreased appetite, suicidal thoughts, insomnia, and loss of interest [1]. Depression is induced by a variety of factors, including pathogenic effects, social behaviours such as drug and alcohol misuse, and biological variables [2]. Pathological causes of depression include a chemical imbalance in the brain, a reduction in energy metabolism, and hormonal changes [3]. Depression, according to the serotonin hypothesis, is caused by dysfunctional serotonergic activity, which results in lower serotonin levels in the brain. Antidepressant medications include selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (duloxetine, venlafaxine), and monoamine oxidase inhibitors. SSRIs such as paroxetine, vilazodone, and fluvoxamine are first-line therapeutic options for individuals with depression, albeit with many contraindications. The current medicine has the following negative effects: delayed therapeutic onset, low bioavailability, erectile dysfunction, weight gain, dry mouth, anxiety, and insomnia. Some currently approved antidepressants undergo extensive first-pass metabolism, resulting in decreased oral bioavailability [4]. The time it takes the medicine to reach saturation is frequently extended, resulting in delayed therapeutic onset and lower therapeutic effectiveness. Furthermore, because the bioavailability is low, higher doses are required, increasing the likelihood of side effects. Because of the existence of the blood-brain barrier (BBB) and the blood-cerebrospinal fluid barrier (BCSFB), the therapeutic impact is also restricted. Traditional medications have a limited ability to cross the BBB and BCSFB [5]. According to studies, nanotechnology-based delivery systems can be used to overcome the above restrictions. The creation of novel nanocarriers as controlled drug delivery systems has advanced significantly in the field of nanotechnology research. New dosage forms are frequently developed using nanotechnology. One of the most advanced nanotechnology applications is the vesicular drug delivery system [6].

Vesicular drug delivery

Vesicular drug delivery is one of the approaches that encapsulate the drug e.g.: Niosomes, liposomes, pharmacosomes, transferosomes & provesicles such as proliposomes & proniosomes. The fact that liposomes and niosomes are particulate, acting as drug reservoirs, gives them an edge over other traditional dosage forms. A few alterations can also be made to modify the pattern and medication release. Additionally, it was discovered that the modified vesicles have the qualities necessary for drug delivery into the deeper layers of the skin. Proniosomes have drawn a lot of attention from researchers for their potential use as drug carriers and targeting agents since they have a number of benefits while avoiding some of the negative aspects of traditional medication formulations. The water-soluble carrier particles known as niosomes are dried to create niosomal dispersion after a brief agitation in a heated aqueous medium. Thus, proniosomes is the name given to this dehydrated result. The generated niosomes are more consistent in size and closely resemble traditional niosomes. The problems associated with dry, free-flowing products are diminished by the proniosomal technique, which is more stable during storage and sterilization. Proniosomes are a flexible delivery technique since they are simple to distribute, measure, transfer, and store. Additionally, they reduce issues with physical stability such as leakage, fusion, sedimentation, and aggregation during storage. Proniosomes increase a drug's therapeutic effects, lessen or eliminate its side effects, and increase its efficacy. Proniosomes are used to prevent first-pass hepatic metabolism, oral delivery-related side effects, and incompatibility with the gastrointestinal tract (GIT). Additionally, proniosomes prolong the duration of drug therapeutic levels, reduce the frequency of administration, and boost patient compliance. They also offer the potential for drug delivery through the topical and transdermal routes [7].

Topical drug delivery

The term "topical drug delivery system" refers to the application of a drug-containing formulation to the skin or mucous membrane in order to treat particular cutaneous disorders or cutaneous manifestations of a generalized disease to limit the drug's pharmacological effects on the skin's surface or deeper layers. The skin, vagina, eye, and nose are the principal routes for topical delivery that have been extensively researched. The section that follows provides a brief overview of the physiology of various routes, their associated defensive barriers, and the most recent patents filed for topically given neoteric formulations [8].

Gels may be a useful vehicle for topical medication delivery or localized drug action on the skin, as in the case of sprains or acute musculoskeletal problems. A gel is a semisolid formulation that contains an exterior solvent

phase, is hydrophobic or hydrophilic, and is immobilized inside the spaces available in a three-dimensional network structure. Gels provide for higher drug solubility and easier drug migration through the vesicle when compared to lotions and ointments because of their high water content. Recent research has described the use of other gel forms, including proniosomal gels, emulgels, bigels, and aerogels, for cutaneous medication administration [9].

Proniosomal gel

Proniosomal gel preparations are semisolid liquid crystal solutions created by dissolving non-ionic surfactants in water and a tiny amount of an organic solvent (like ethanol). These hybrids of liquid crystalline compact niosomes can become niosomes right away after being hydrated. Proniosomal gel for topical or dermal distribution doesn't need to be hydrated before use; instead, it can be administered directly or put onto an emulsion, gel, ointment, or other base material. The base material aids in the dilution of the active ingredient and the application of the formulation to the skin[9]. Proniosomal gel has the potential to significantly improve therapeutic efficacy and decrease medication side effects. Both hydrophilic and hydrophobic medicines can be captured by proniosomes. Typically, these have a transparent, translucent, or white semisolid gel texture, which keeps them physically stable throughout storage and transportation. Proniosomal gels may be used as transdermal medication delivery systems, according to research. Proniosomes are also referred to as "dry niosomes" because they need to be moistened to develop niosomal capillaries, which are necessary for drug release and skin permeation. Proniosomal gels are additionally thought to be more successful than niosomal gels because they can resolve a number of niosome-related physical stability issues (such as aggregation, sedimentation, destruction by hydrolysis, and fusion). Proniosomal gels may also be more efficient for transdermal drug delivery because they improve drug absorption through the skin barrier [10].

Herein, we report the development and evaluation of duloxetine HCl-loaded proniosomal gel for topical drug delivery. The duloxetine HCl-loaded proniosomal gel was developed to enhance drug permeation through the barriers of skin and to maintain the controlled plasma level concentration.

MATERIAL AND METHODS

Duloxetine was obtained as a gift sample from Ariheet Pharma, Mumbai. Cholesterol, Span 60 and Sodium hydroxide were procured from Qualikems Fine Chem Pvt. Ltd. All other solvents and chemicals used were of analytical grade.

Pre-formulation studies

All the preformulation studies like melting point, solubility study, and partition coefficient were carried out effectively [11][12].

Estimation of Duloxetine Hydrochloride

Determination of absorption maxima of Duloxetine Hydrochloride

A 10 µg/ml solution of Duloxetine Hydrochloride in methanol was scanned in the range of 200-400 nm using the UV spectrophotometer.

Preparation of Standard curve of Duloxetine Hydrochloride in methanol

The standard stock solution of Duloxetine HCl was prepared in methanol. From the Stock solution aliquots of accurately measured volume 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8 and 2ml were withdrawn and transferred to the 10ml volumetric flask separately and individually made up to 10 ml with methanol. The absorbance values were determined at 290nm using a UV spectrophotometer and a standard curve was plotted against concentration. From the calibration curve intercept, slope, straight-line equation and correlation coefficient were obtained [13].

FTIR Analysis

FTIR spectra of the pure drug and optimized proniosome formulation were analyzed by FTIR spectroscopy. The FTIR analysis was performed with KBr pellets and recorded in the range of 400–4000 cm^{-1}. The various modes of vibrations were identified and assigned to determine the different functional groups present in the samples [14].

Preparation of Duloxetine Hydrochloride loaded proniosomal gel

Accurately weighed amounts of soya lecithin, Cholesterol, span and Duloxetine HCl were put in a clean and dry glass container of 5ml capacity and 2.5ml ethyl alcohol (95%) was added to them. The glass container was covered with a lid and the mixture was warmed over a water bath at 60–70°C for about 15 minutes until the components were completely dissolved. Then the aqueous phase 1.6ml (water) was added and the mixture was warmed in the water bath at the same temperature for (2–5 minutes) till it became a clear solution which was left to cool at room temperature and the proniosomal gel was formed [15][16].

Optimization of the Duloxetine Hydrochloride-loaded proniosomal gel using the 3^2 Level Factorial Designs

A 3^2-randomized full factorial design was performed, and the amount of lecithin (A) and amount of span 60 (B) were taken as independent variables, while entrapment efficiency (Y1) was taken as dependent variables. The statistical optimization procedure was performed with the help of optimization software such as Design Expert 8 and Statgraphics Centurion 16. The software performs response surface methodology (RSM) which includes multiple regression analysis (MRA), ANOVA and statistical optimization.

Based upon this, 13 different runs were designed by the software applying the central composite design (CCD), The results were interpreted to find optimized formulation using numeric optimization in design expert.

Table 1: Independent variables with high and low levels

Factor	Name	Units	Low Actual	High Actual	Low Coded	High Coded	Mean
A	Amount of Lecithin	mg	90	240	-1	1	165
B	Amount Span 60	mg	90	180	-1	1	135
Response	Name						
Y1	Percentage drug entrapment						

Table 2: Composition of all 13 formulations prepared in central composite design

Formulation code	Factor 1 A: Amount of Lecithin (mg)	Factor 2 B: Amount Span 60 (mg)	Response 1 Percentage drug entrapment (%)
G1	165	180.0	
G2	240.0	135.0	
G3	90.0	135.0	
G4	240.0	180.0	
G5	240.0	90.0	
G6	90.0	90.0	
G7	165.0	90.0	
G8	165.0	135.0	
G9	165.0	135.0	
G10	90.0	180.0	
G11	165.0	135.0	
G12	165.0	135.0	
G13	165	135.0	

In vitro characterization parameters

Physical appearance

The physical properties and color of the Duloxetine HCl-loaded proniosomal gel were visually assessed.

pH determination of proniosomal gel:

A pH meter was used to determine the pH of the proniosomal gel. Results were tested in triplicates using a precisely determined 10% w/w water dispersion of optimized proniosomal formulations [17].

Percentage drug entrapment

The proniosomal gel (equal to 40 mg of Duloxetine HCl) is transferred to the 10ml glass tube and adds 10 ml of pH 7.4 phosphate buffer. The resulting fluid suspension was then sonicated in a bath sonicator. To separate the unentrapped drug from the mixture's duloxetine HCl-containing niosomes, the mixture was centrifuged at 20000 rpm for 30 minutes at 20°C. Methanol was then used to dilute the supernatant. The concentration of Duloxetine HCl in the subsequent solution was tested by UC visible spectrophotometers. The percentage of drug encapsulation was calculated by the following mathematical statement: [18]

$$Percentage\ drug\ entrapment = \frac{Total\ amount\ of\ drug - Free\ drug}{Total\ amount\ of\ drug} \times 100$$

Particle size measurement

Accurately measure 0.1 g of freshly optimized proniosomal gel was hydrated with the 100ml of water. Then it was subjected to a 30-minute sonication process in a 37°C water bath. Following dilution to 1 ml with distilled water and a 2-minute vortex, 10 l of the hydrated proniosomes were used. Dynamic light scattering was used to measure the particle size and PDI of the samples [17].

Zeta potential measurement

Zeta potential is a physical characteristic that is determined by the net surface charge of the vesicles. Freshly prepared proniosomal gel (0.1 g) was hydrated using 10 ml PB 7.4. It was then sonicated for 30 minutes in a water bath at 37°C. 10 µl of the hydrated proniosomes were taken and diluted to 1 ml with distilled water and vortexed for 2 minutes [17].

Transmission electron microscopy

The morphology of the vesicles was studied by taking one drop of niosomal scattering and diluting 10 times to load further into a carbon-covered grid for 1 min. The grid was then observed by transmission electron microscopy utilizing imaging viewer programming [16].

In vitro drug release studies

Using a Franz (vertical) diffusion cell, a semi-permeable dialysis membrane was positioned between the donor and receptor compartments to observe the in vitro drug release of Duloxetine HCl from the optimized proniosomal formulation. The diffusion cell's top was covered with paraffin paper. The proniosomal formulation was placed into the donor compartment. The receptor medium, a 20 ml aliquot of phosphate buffer pH 7.4, was kept at 37°C and swirled by a magnetic bar at 50 rpm. The cell's available diffusion area was 1.25 cm^2. At regular intervals (0.25, 0.5, 1, 2, 4, 8, 10, 12 and 24 h), a 2 ml portion of the receptor medium was removed and concurrently replaced by an equivalent volume of new receptor solution. The samples were filtered through 0.45 mm membrane filter before the estimation of the drug content by UV visible spectroscopy at 290 nm. The cumulative amount of the drug released through the dialysis membrane was then calculated to determine the average percentage release and flux values [19].

Drug release kinetics

- Zero order kinetics
- First order kinetics
- Higuchi model

RESULT AND DISCUSSION

Pre-Formulation

The selected drug Duloxetine HCl was subjected to the investigation of physical characterization parameters such as organoleptic properties, melting point, solubility, and partition coefficient and were found within the acceptance criteria as per IP.

Determination of absorption maxima of Duloxetine Hydrochloride

On scanning of the know concentration of 10µg/ml of duloxetine HCl in methanol in a range between 200-400nm using the UV spectrophotometry, the absorption maxima of the duloxetine HCl was observed to be 290nm.

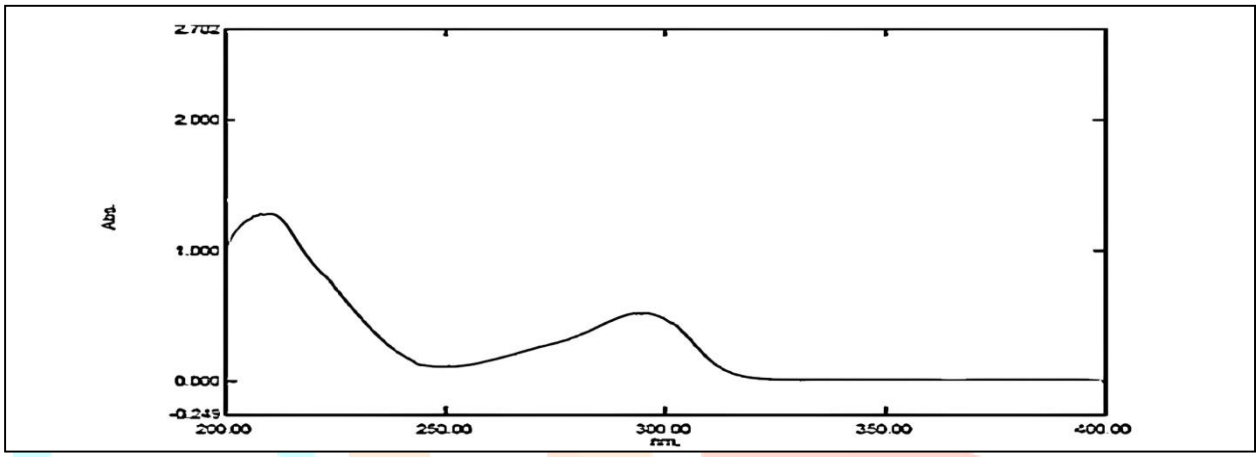

Figure 1: Absorption maxima of Duloxetine hydrochloride

Standard calibration curve of Duloxetine Hydrochloride in methanol

Table 3: Calibration curve of Duloxetine HCl in methanol

Concentration (µg/ml)	Absorbance at 290nm
0	0±0
2	0.076±0.002
4	0.171±0.003
6	0.276±0.002
8	0.371±0.003
10	0.469±0.003
12	0.577±0.003
14	0.666±0.002
16	0.758±0.004
18	0.866±0.004
20	0.960±0.004

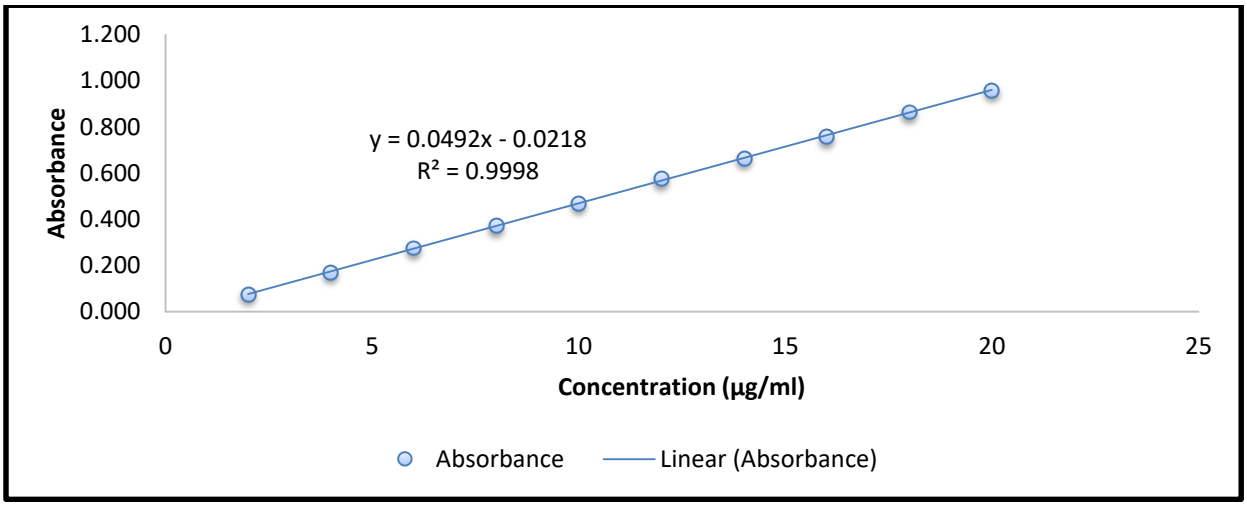

Figure 2: Standard calibration curve of Duloxetine HCl in methanol

FTIR Analysis

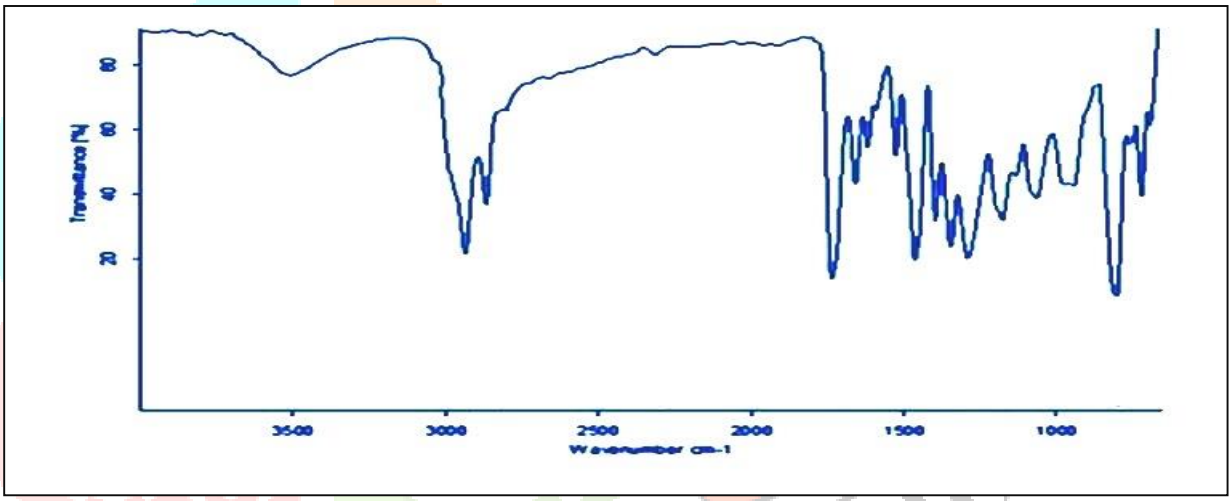

Figure 3: Graph of FTIR spectrum of duloxetine HCl

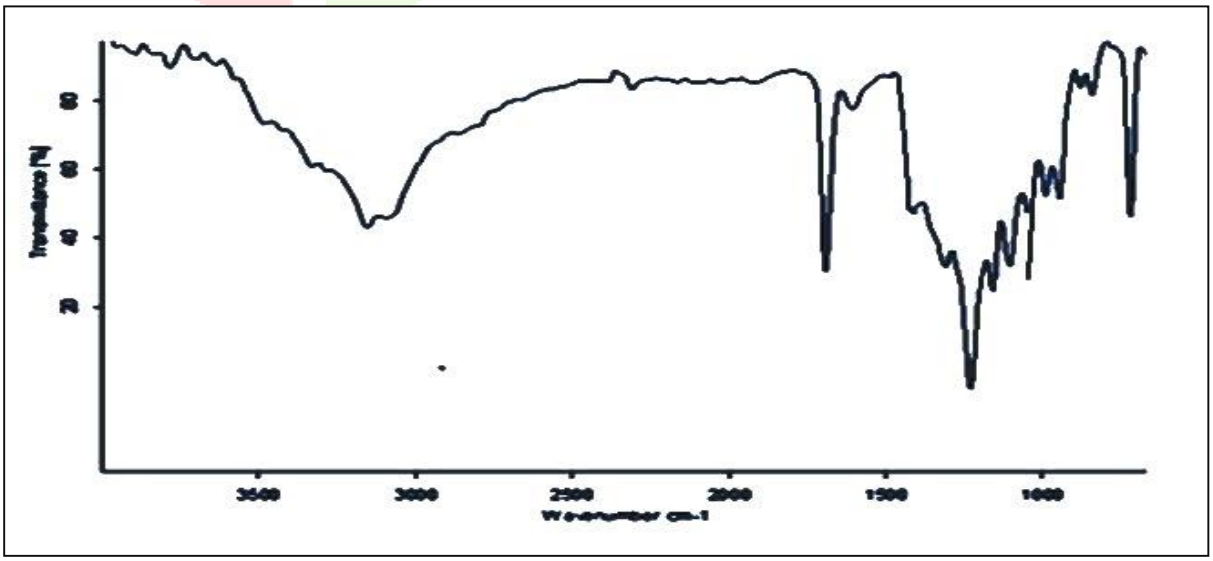

Figure 4: Graph of FT-IR Spectra of optimized formulation

FITR spectrum of pure drug demonstrated the characteristic peaks at 1579.05 (aromatic alkene), 1463.34 (thiophene ring), and 1233.53 (C–O bond stretching).
Optimized formulation FTIR spectrum displayed a very less no. of the characteristic peaks of the Duloxetine HCl with reduced intensity indicating the encapsulation of the drug in the niosomal vesicles.

Optimization of the Duloxetine Hydrochloride loaded proniosomal gel

3^2 Level Factorial design for the optimization of the Duloxetine Hydrochloride loaded proniosomal gel

The information obtained was modelled mathematically using a variety of methods, and the design program selected a fit model based on a number of variables, including the p-value, and adjusted determination coefficient (adj. R^2, and predicted determination coefficient (pred. R^2). The results of the experimental design demonstrated that the levels of lecithin and span60 significantly affected this system, resulting in high drug EE for the production of proniosomal gel containing Duloxetine HCl. The quadratic model showed the highest R2 values for all of the responses compared to the linear model and the two-factor model, making it the best match for the responses Y1 (%EE). A quadratic model with interactional and quadratic terms was used to reflect the effects of the variables. In order to represent the impacts of the variables, a quadratic model with interactional and quadratic terms was chosen. In order to evaluate the significance of the quadratic models on the responses and their quantitative effects, an analysis of variance (ANOVA) was carried out.

Table 4: Composition of the proniosomal gel as per the 3^2-level factorial designs

Formulation code	Factor A: Amount of Lecithin (mg)	Factor B:Amount Span 60 (mg)	Response Y1 Percentage drug entrapment
G1	165	180	84.61
G2	240	135	88.91
G3	90	135	75.77
G4	240	180	81.83
G5	240	90	66.52
G6	90	90	55.30
G7	16	90	71.29
G8	165	135	92.40
G9	165	135	91.31
G10	90	180	65.54
G11	165	135	93.35
G12	165	135	92.30
G13	165	135	93.48

The percentage of Duloxetine HCl drug entrapment varied between 55.30% and 93.48% for the 13 formulations due to the different factor combinations. The quadratic equation is as follows:

Percentage drug entrapment = 92.63+6.77A+6.48B+1.27AB-10.43A^2-14.82B^2.

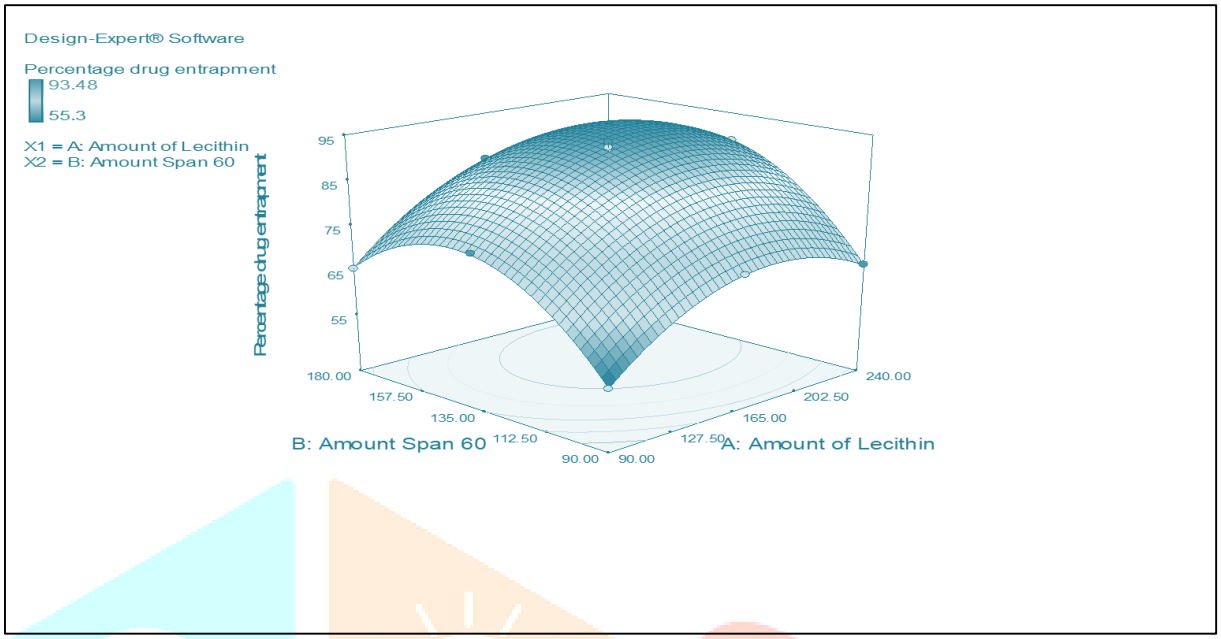

Figure 5: 3D graph indicating an effect of the variables over the percentage drug entrapment.

Optimization and validation

A further optimization and validation process was carried out using design expert software that had desirable properties to investigate the best formula solution of Duloxetine HCl loaded proniosomal gel, which was dependent on the prescriptive criteria of maximum% drug entrapment, after analyzing the polynomial equations that represented the dependent and independent variables.

Table 5: Composition, Predicted and observed values of the optimized formulation

Formulation code	Amount of Lecithin (mg)	Amount Span 60 (mg)	Predicted Percentage drug entrapment (%)	Observed percentage drug entrapment (%)
G14	193.86	138.73	94.16	93.58

The observed optimized formulation had EE of (93.58±0.12%), which was in good agreement with the predicted values.

In vitro characterization parameters
Physical appearance

Table 6: Physical appearance of all prepared Duloxetine HCl-loaded proniosomal gel formulations

S. No.	Formulation code	Appearance
1	G1	Homogenous, uniform gel
2	G2	Homogenous, uniform gel
3	G3	Homogenous, uniform gel
4	G4	Homogenous, uniform gel
5	G5	Homogenous, uniform gel
6	G6	Homogenous, uniform gel
7	G7	Homogenous, uniform gel
8	G8	Homogenous, uniform gel
9	G9	Homogenous, uniform gel
10	G10	Homogenous, uniform gel
11	G11	Homogenous, uniform gel
12	G12	Homogenous, uniform gel
13	G13	Homogenous, uniform gel

Every produced gel composition had a uniform and homogenous physical appearance upon visual inspection. Duloxetine HCl did not undergo phase separation or drug precipitation, as shown in Table 6.

Percentage drug entrapment
Percentage drug entrapment in all prepared formulations was shown in Table 7.

Table 7: Value and states of percentage drug entrapment of all prepared Duloxetine HCl loaded proniosomal gel formulations

Formulation code	Percentage (%) Drug entrapment
G1	84.61±0.85
G2	88.91±0.82
G3	75.77±0.48
G4	81.83±0.63
G5	66.52±0.33
G6	55.30±0.81
G7	71.29±0.59
G8	92.40±0.51
G9	91.31±1.11
G10	65.54±0.69
G11	93.35±0.26
G12	92.09±0.10
G13	93.48±0.21

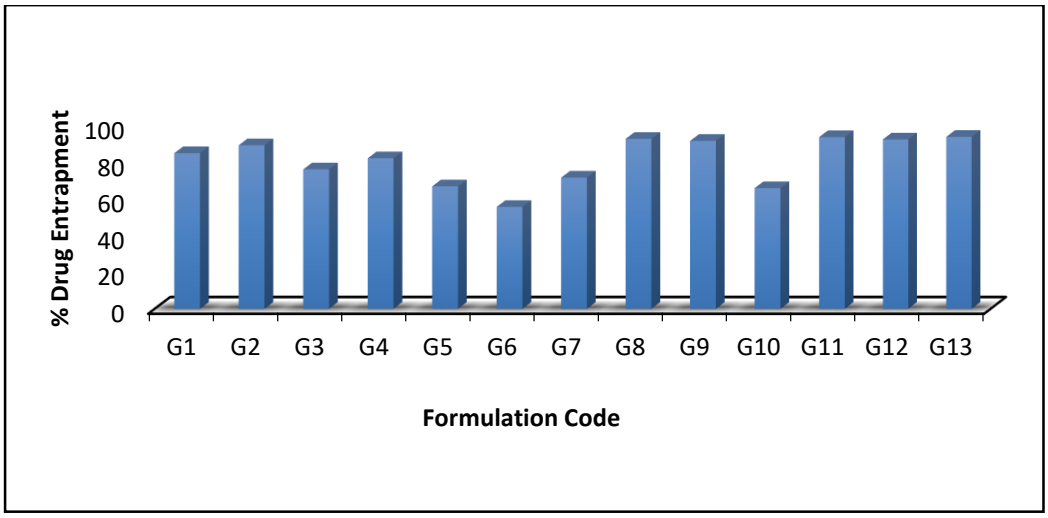

Figure 6: Percentage drug entrapment of all prepared Duloxetine HCl-loaded proniosomal gel formulation

The range of 55.30±0.81% to 93.58±0.12% was found to be the percentage of drugs entrapped in all produced formulations.

pH

pH of all prepared formulation was shown in Table 8.

Table 8: pH of all prepared formulations

Formulation code	pH
G1	6.690±0.026
G2	6.507±0.038
G3	6.217±0.057
G4	6.370±0.062
G5	6.200±0.026
G6	6.303±0.075
G7	6.647±0.051
G8	6.717±0.029
G9	6.417±0.078
G10	6.470±0.061
G11	6.313±0.059
G12	6.317±0.047
G13	6.270±0.085

The pH of all of the developed formulations was found to range from 6.200±0.026 to 6.717±0.029.

Evaluation of optimized formulation G14

Visual appearance Percentage drug entrapment and pH

The optimized Duloxetine HCl-loaded proniosomal gel appeared as a homogenous, uniform semisolid gel. Percentage drug entrapment of Duloxetine HCl in optimized formulation G14 was found to be 93.58±0.12%. The Ph value of the optimized formulation was found to be 6.173±0.065

Particle Size and Zeta Potential

Table 9: Particle size, PDI and Zeta Potential of optimized formulation G14

S. No.	Formulation code	Particle size (nm)	PDI	Zeta Potential (mv)
1	**G14**	241.02	0.184	-24.65

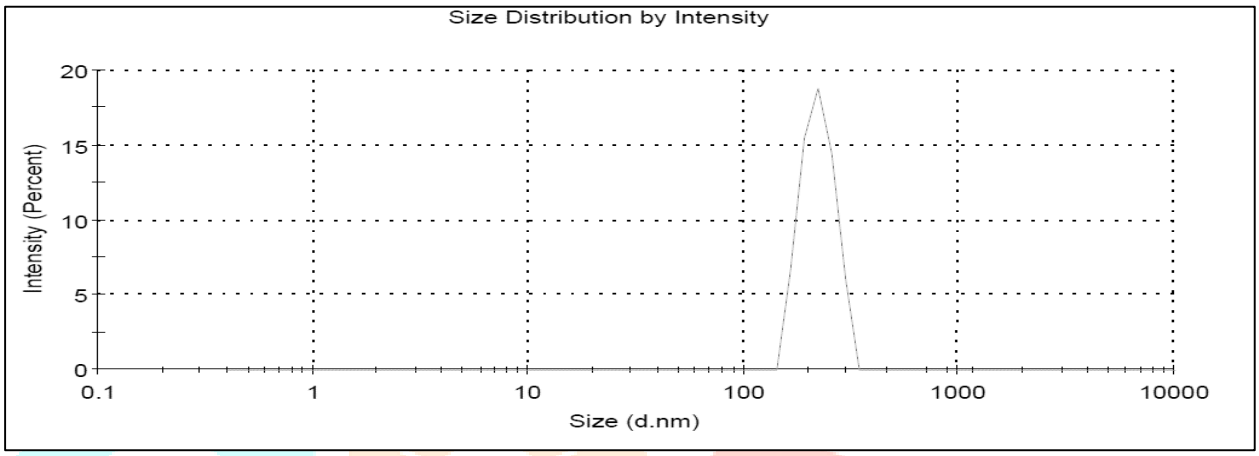

Figure 7: Vesicle size distribution graph of optimized formulation

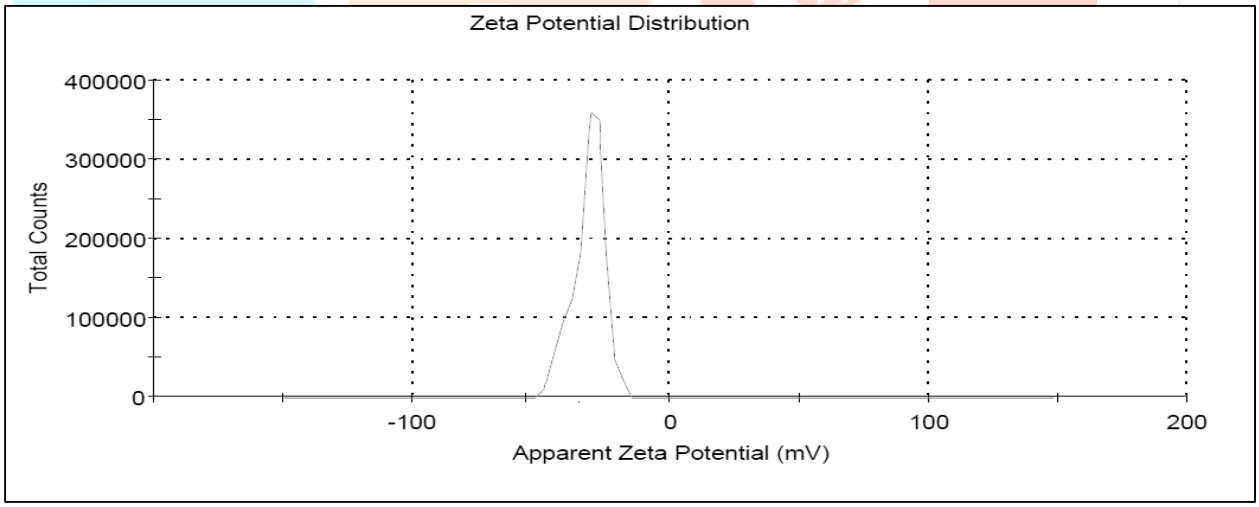

Figure 8: Zeta Potential distribution graph of optimized Duloxetine HCl loaded proniosomal gel formulation G14

Fig. 7 shows that the particle size and PDI value were respectively 241.02 nm and 0.184 also, as seen in Figure 8, the zeta potential showed that the produced formulation was stable, measuring at -24.65 mv.

Transmission electron microscopy (TEM)

TEM micrograph indicated a homogeneous distribution of small, spherical nano vesicles as shown in Figure 9.

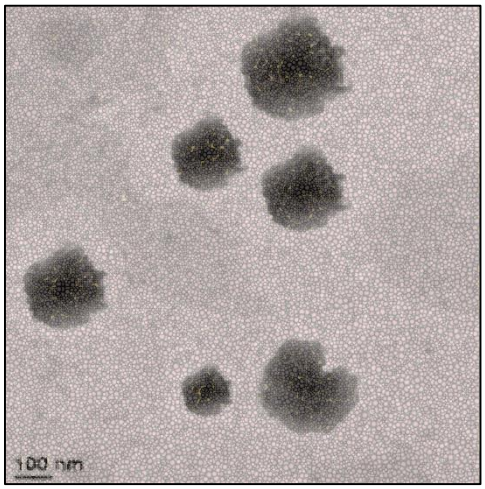

Figure 9: TEM micrograph of optimized formulation G14

In vitro, Percentage drug release study of Control gel of Duloxetine Hydrochloride and Duloxetine Hydrochloride loaded proniosomal gel formulations G14

Table 10: Percentage drug study of Control gel of Duloxetine HCl and Duloxetine HCl loaded proniosomal gel formulations G14

Time(hr.)	% Drug release of Control gel	% Drug release of formulation G14
0	0±0	0±0
0.25	2.566±0.032	16.890±1.078
0.5	4.745±0.205	21.921±0.647
1	6.849±0.075	32.591±0.862
2	8.892±0.140	41.890±1.078
4	9.753±0.216	52.027±0.323
8	11.407±0.463	71.540±0.995
10	12.817±0.410	81.230±1.509
12	13.777±1.250	93.338±0.755
24	14.768±0.237	93.270±0.647

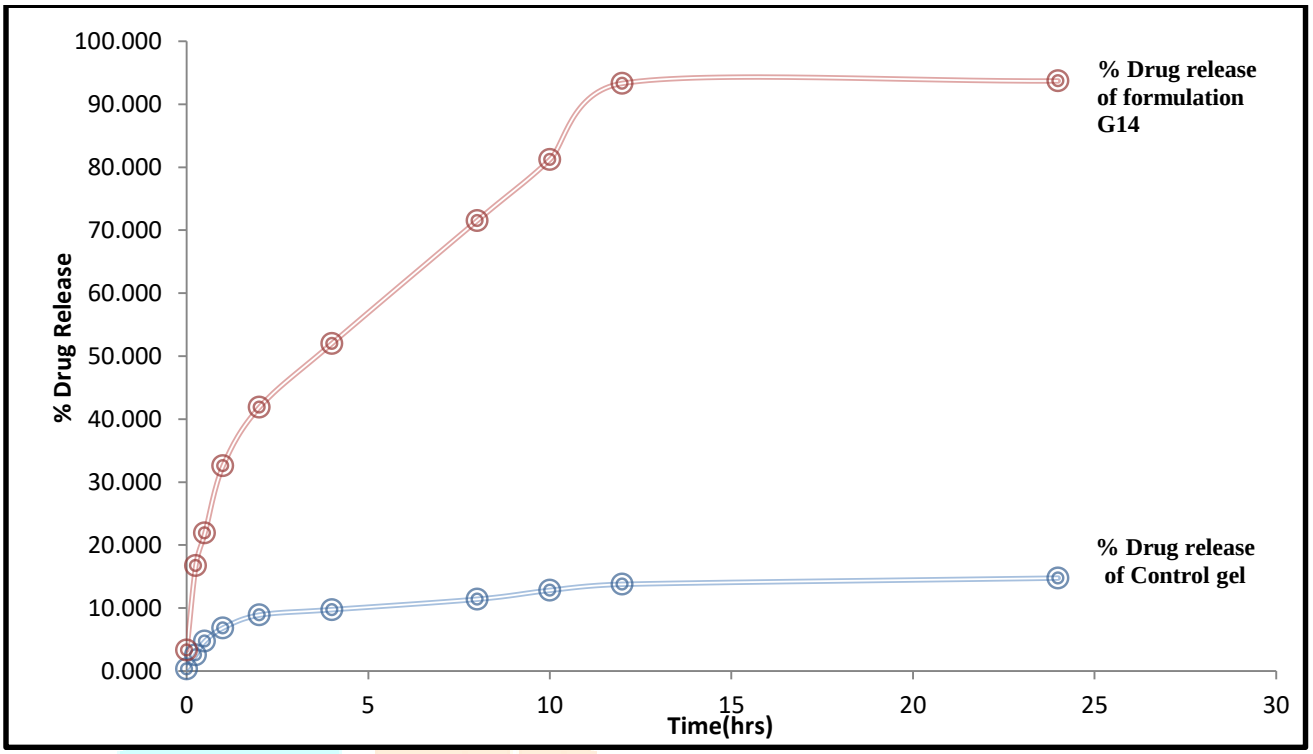

Figure 10: In-vitro drug release of control gel and proniosomal gel formulations G14

The Duloxetine HCl release profile from the selected proniosomal gel formulations (G14) with the Duloxetine HCl release profile from the equivalent Carbopol gels. It was observed that the drug was released from formulations in two phases: a rapid initial burst phase, followed by a steady and persistent release for the duration of the trial's 24 hours. The drug may have been integrated between fatty acid chains in the bilayers of niosomal vesicles, which led to an initial rapid release when niosomes were dispersed in the release medium. After that, a steady way followed the drug liberation. The proniosomal gel formulation demonstrated drug release of 93.270±0.647 vs 14.768±0.237% release of drug from the control gel after 24 hours.

In-vitro drug release kinetic Study

In-vitro drug release kinetic data of formulation G14 proniosomal gel was as given below.

Zero order

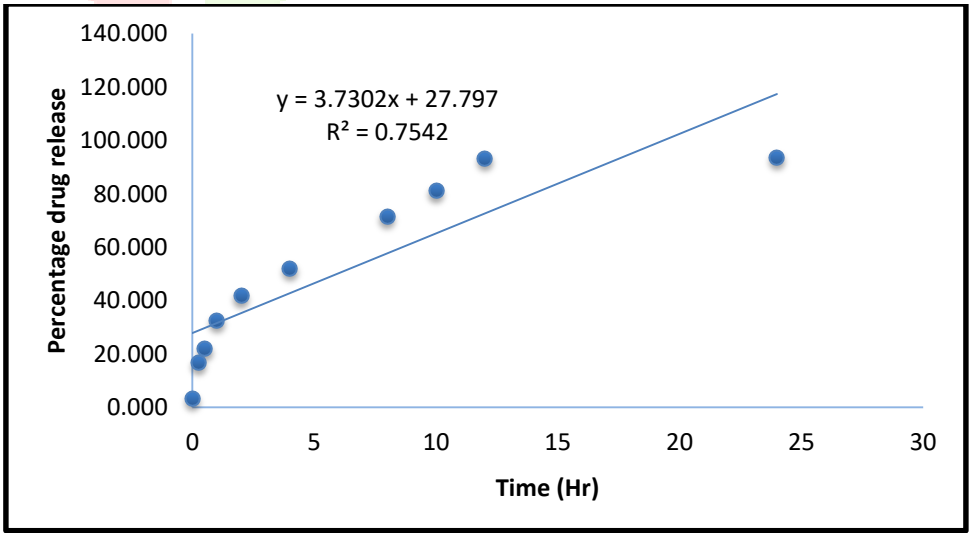

Figure 11: Graph of Zero order kinetics

First order

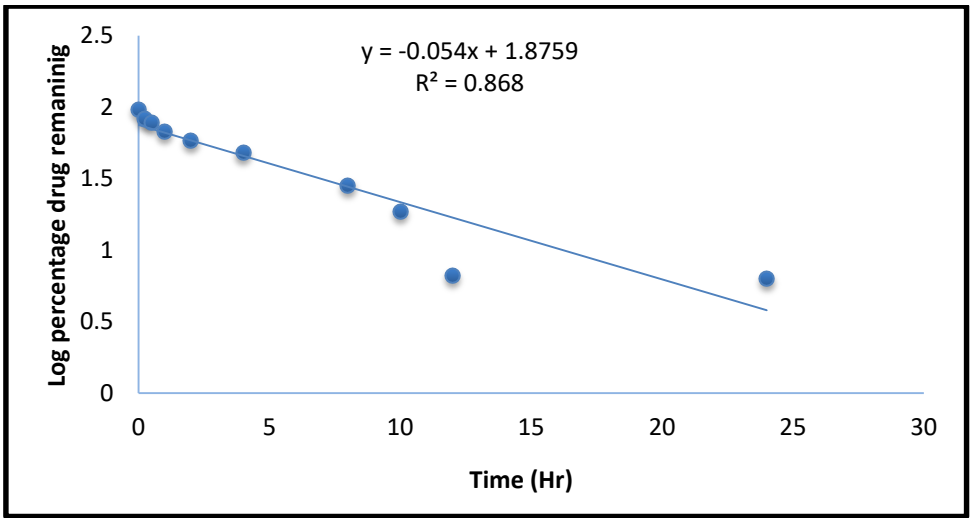

Figure 12: Graph of First order kinetic

Higuchi Model

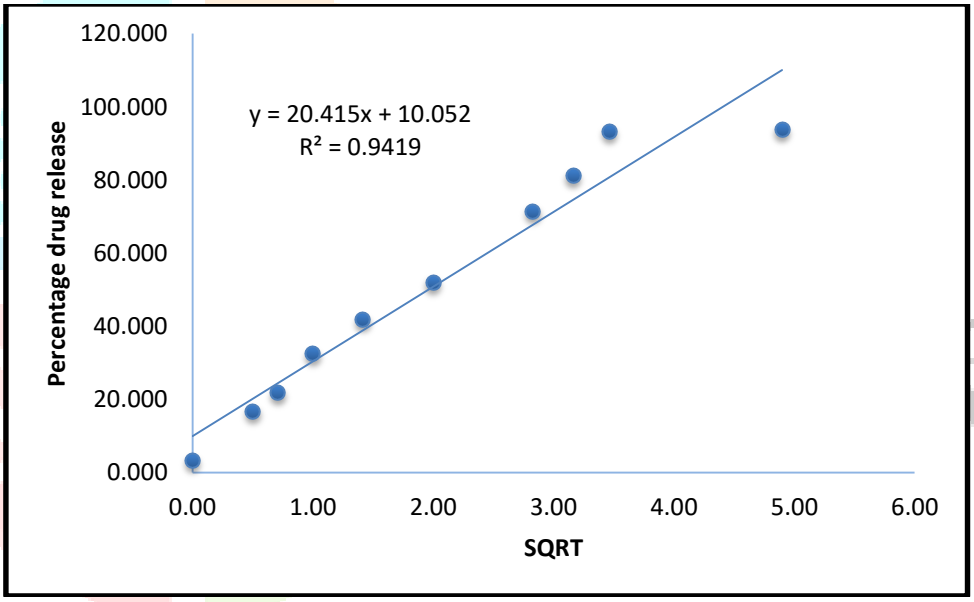

Figure 13: Graph of Higuchi model kinetic

Fig. 11-13 displays the regression coefficients that were calculated for the zero order, first order, and Higuchi models. Because the Higuchi model has a greater value of the regression coefficient (0.9419) than other models of drug release, the release of Duloxetine HCl-loaded proniosomal gel formulations G14 follows it.

CONCLUSION

The optimised proniosomal gel with a vesicle size small enough to permit topical distribution of Duloxetine HCl and excellent encapsulation efficiency was successfully created. Through topical administration, the G14 demonstrated significantly enhanced permeability enhancement and stability, as well as superior control over drug release for a longer period of time. As a result, topical use of duloxetine-loaded proniosomal gel enhances bioavailability. The results of the investigation demonstrated that proniosomes offer alternative colloidal carrier approaches in topical drug delivery. The results revealed that Duloxetine hydrochloride proniosomal gel prepared by the Coacervation phase separation method was capable of controlling and releasing the drug for an extended period of time. It was concluded that duloxetine hydrochloride Proniosomal gel could be of therapeutic significance in antidepressant therapy.

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