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# DEVELOPMENT, CHARACTERIZATION AND EVALUATION OF NIOSOMAL DRUG DELIVERY SYSTEM FOR ORAL DRUG DEVLIVERY

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**ABSTRACT:**

**Background:** Ticagrelor is an effective antiplatelet agent widely used in the prevention of thrombotic cardiovascular events; however, its limited aqueous solubility and moderate oral bioavailability restrict its therapeutic performance.

**Objective:** The present investigation aimed to formulate and evaluate a Ticagrelor-loaded niosomal system to improve drug entrapment, permeability, and oral delivery characteristics.

**Methods:** Preformulation studies were conducted to determine the physicochemical properties of Ticagrelor, including solubility, melting point, and spectroscopic characteristics. Drug-loaded niosomes were prepared by the ether injection technique using non-ionic surfactants and cholesterol. A $3^2$ factorial design was employed to optimize the formulation variables. The developed vesicles were evaluated for particle size, zeta potential, entrapment efficiency, morphology, thermal behavior, crystallinity, drug release, and permeability. The optimized niosomal dispersion was further incorporated into tablet dosage form and subjected to standard quality control tests.

**Results:** Ticagrelor exhibited high solubility in organic solvents such as ethanol and methanol, while showing poor solubility in aqueous media. FTIR studies confirmed the compatibility of the drug with selected excipients. Among the prepared formulations, formulation A9 demonstrated superior performance with an entrapment efficiency of 89.7%, particle size of 280.5 nm, and zeta potential of −26.8 mV. Scanning electron microscopy revealed the formation of discrete spherical vesicles. Differential scanning calorimetry and X-ray diffraction studies indicated a reduction in drug crystallinity following niosomal encapsulation. In vitro release studies showed prolonged drug release with cumulative release reaching 91.13%. Ex vivo permeation experiments demonstrated significantly improved permeability compared with the pure drug. The niosomal tablets complied with pharmacopeial requirements and exhibited satisfactory hardness, friability, and drug content uniformity.

**Conclusion:** The developed niosomal formulation effectively enhanced the physicochemical and biopharmaceutical properties of Ticagrelor. Improved drug entrapment, sustained release behavior, and enhanced permeability suggest that niosomal delivery may serve as a promising strategy for improving the oral performance and therapeutic effectiveness of Ticagrelor.

***Keywords:*** Ticagrelor, Niosomes, Oral Drug Delivery, Entrapment Efficiency, Nanocarrier System, Sustained Release, Permeability Enhancement, Factorial Design.

## INTRODUCTION:

Cardiovascular diseases remain one of the leading causes of morbidity and mortality worldwide, accounting for a substantial healthcare burden. Antiplatelet therapy plays a critical role in the prevention of thrombotic complications associated with acute coronary syndrome (ACS), myocardial infarction (MI), and percutaneous coronary intervention (PCI). Ticagrelor is a direct-acting and reversible P2Y12 receptor antagonist that has gained considerable clinical importance due to its rapid onset of action and potent inhibition of platelet aggregation. Unlike thienopyridine derivatives such as clopidogrel, Ticagrelor does not require metabolic activation, resulting in more predictable pharmacological activity and improved therapeutic response.[1]

Despite its clinical advantages, the oral delivery of Ticagrelor is challenged by its poor aqueous solubility and moderate bioavailability. The drug exhibits limited dissolution in gastrointestinal fluids, which may restrict its absorption following oral administration. Furthermore, extensive first-pass metabolism contributes to reduced systemic availability. These limitations can affect therapeutic outcomes and necessitate the development of advanced drug delivery approaches capable of enhancing drug solubility, permeability, and overall bioavailability.[2-3]

Ticagrelor exerts its antiplatelet effect by selectively inhibiting adenosine diphosphate (ADP)-mediated activation of P2Y12 receptors on platelets, thereby preventing platelet aggregation and thrombus formation. The drug is rapidly absorbed after oral administration and undergoes extensive plasma protein binding. Metabolism occurs predominantly through cytochrome P450 3A enzymes, and elimination takes place mainly through fecal excretion. Although generally well tolerated, Ticagrelor therapy may be associated with adverse reactions such as dyspnea, bleeding episodes, and gastrointestinal discomfort, emphasizing the need for optimized formulations that can improve therapeutic efficiency while minimizing potential side effects.[4-5]

Nanotechnology-based drug delivery systems have emerged as effective platforms for overcoming the limitations of poorly soluble drugs. Among these systems, niosomes have attracted significant attention because of their ability to encapsulate both hydrophilic and lipophilic compounds within vesicular structures formed from non-ionic surfactants. Niosomes offer several advantages, including enhanced drug stability, controlled release characteristics, improved membrane permeation, reduced toxicity, and cost-effective manufacturing. Compared with conventional liposomes, niosomes exhibit superior physical stability and longer shelf life, making them attractive carriers for oral drug delivery

applications.

Considering these advantages, the present study focuses on the development of Ticagrelor-loaded niosomes using suitable surfactants and cholesterol as vesicle-forming components. The formulation was optimized using a factorial design approach to achieve desirable vesicle characteristics and maximize drug entrapment. Comprehensive characterization was performed through particle size analysis, zeta potential measurement, scanning electron microscopy, thermal and crystallographic studies, drug release evaluation, and permeation assessment.[6-9]

The objective of this research was to enhance the oral delivery of Ticagrelor through niosomal encapsulation, thereby improving its solubility, permeability, and bioavailability. The successful development of such a delivery system may contribute to improved therapeutic efficacy, reduced dosing frequency, and better patient compliance in the long-term management of cardiovascular disorders.

## MATERIALS AND METHODS:

### Materials:

Ticagrelor was kindly supplied by Zydus Pharmaceuticals Ltd. as a gift sample and was used as the active pharmaceutical ingredient throughout the study. Cholesterol and Span 60 were procured from Research Lab, Mumbai, India. Ethanol, diethyl ether, talc, magnesium stearate, and microcrystalline cellulose (MCC) were obtained from Research Lab Fine Industries, Mumbai, India. All chemicals and reagents employed in the investigation were of analytical grade and were used without further purification. The selected materials were utilized for the preparation, optimization, and evaluation of the niosomal drug delivery system.

## METHODS:

### Preformulation Studies

Preformulation investigations were performed to assess the physicochemical characteristics of Ticagrelor and to generate essential information for formulation development. The drug was initially examined for its physical appearance, color, and odor. The melting point was determined using a digital melting point apparatus to verify its purity and identity.[10-11]

Solubility studies were conducted according to the procedures outlined in the Indian Pharmacopoeia to evaluate the solubility behavior of Ticagrelor in different solvents. The amount of solvent required to achieve complete dissolution of the drug was recorded. The ultraviolet absorption characteristics of Ticagrelor were studied in ethanol and phosphate buffer (pH 6.8). For this purpose, a primary stock solution containing 1000 µg/mL of

Ticagrelor was prepared and subsequently diluted to obtain a working concentration of 10 µg/mL. The resulting solution was scanned within the wavelength range of 200–400 nm using a UV–Visible spectrophotometer to determine the wavelength corresponding to maximum absorbance (λmax).[12-14]

**Drug–Excipient Compatibility Study**

Compatibility between Ticagrelor and the selected formulation excipients was evaluated using Fourier Transform Infrared (FTIR) spectroscopy. Infrared spectra of the pure drug, individual excipients, and their physical mixtures were recorded using a Bruker ALPHA FTIR spectrophotometer over the spectral range of 4000–400 $cm^{-1}$ with a resolution of 4 $cm^{-1}$.[15]

For compatibility assessment, physical mixtures containing equal proportions of Ticagrelor and excipients were prepared and stored under ambient conditions in sealed glass containers. Samples were analyzed periodically to identify any changes in characteristic absorption peaks that could indicate chemical interactions or instability. The obtained spectra were compared to confirm the compatibility of the drug with the excipients selected for niosome preparation.

**Optimization of Niosomal Formulation Using a $3^2$ Full Factorial Design**

A systematic optimization approach was adopted to obtain a niosomal formulation with desirable physicochemical properties. A $3^2$ full factorial design was employed to investigate the influence of formulation variables on critical quality attributes. This experimental design enables the simultaneous evaluation of multiple factors while minimizing the number of experimental runs required.[16-20]

Two independent formulation variables were selected for optimization: the concentration of surfactant ($X_1$) and the concentration of cholesterol ($X_2$). Each variable was studied at three different levels. The effects of these variables on entrapment efficiency ($Y_1$) and particle size ($Y_2$) were assessed as dependent responses. Statistical analysis of the generated data was performed to establish the relationship between formulation variables and response parameters. Based on the optimization results, the formulation exhibiting maximum drug entrapment and an appropriate particle size distribution was selected as the optimized niosomal formulation.

**Table 1: Optimization of process variables by using $3^2$ factorial design**

| Independent Variables | | |
|---|---|---|
| **Factors** | **Coded Values** | **Actual Values** |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cholesterol Mg (X1) | -1 | 0 | +1 | 50 | 100 | 150 |
| Span 60 Mg (X2) | -1 | 0 | +1 | 100 | 150 | 200 |
| **Responses (Dependent Variables)** | | | | | | |
| Y1= %Entrapment efficiency | | | | | | |
| Y2= Particle Size (nm) | | | | | | |

**Preparation of Ticagrelor-Loaded Niosomes**

Ticagrelor-loaded niosomes were prepared using the ether injection method. Briefly, Span 60 and cholesterol were dissolved in diethyl ether to obtain the organic phase, while Ticagrelor was dissolved in ethanol. The drug solution was mixed with the surfactant-containing organic phase and slowly injected into phosphate buffer (pH 6.8) at a controlled rate of approximately 1 mL/min under continuous stirring. The aqueous phase was maintained at 60–65°C to facilitate rapid evaporation of the organic solvent. The temperature gradient between the organic and aqueous phases resulted in instantaneous vaporization of ether, leading to the spontaneous formation of vesicular structures. The obtained niosomal dispersion was subsequently frozen and subjected to lyophilization using a freeze dryer for 24 h. The dried niosomal powder was collected and stored under refrigerated conditions until further characterization.[21-23]

**Evaluation of Niosomes:**

**Entrapment Efficiency**

The percentage entrapment efficiency of Ticagrelor within the niosomal vesicles was determined by centrifugation. The niosomal dispersion was centrifuged at 5000 rpm for 30 min to separate the entrapped drug from the free drug present in the aqueous phase. The supernatant was collected, suitably diluted with phosphate buffer (pH 6.8), and analyzed spectrophotometrically at 256.2 nm. The entrapment efficiency was calculated using the amount of drug encapsulated within the vesicles relative to the total drug content.[24]

**Particle Size Analysis**

The mean particle size and size distribution of the prepared niosomes were determined by dynamic light scattering (DLS) using a Horiba Zetasizer. Measurements were performed under appropriate dilution conditions to ensure accurate characterization of the vesicular

system.[25]

**Zeta Potential Measurement**

The surface charge of the niosomal vesicles was assessed by measuring the zeta potential using a Horiba Zetasizer. Electrophoretic mobility measurements were carried out based on laser Doppler electrophoresis to evaluate the physical stability of the colloidal dispersion.[26]

***In Vitro* Drug Release Study**

The release behavior of Ticagrelor from the niosomal formulation was evaluated using the dialysis membrane diffusion technique. A known quantity of the formulation was placed in a dialysis membrane and immersed in 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.2°C under continuous stirring. At predetermined intervals, aliquots of the dissolution medium were withdrawn and replaced with fresh buffer to maintain sink conditions. The samples were analyzed spectrophotometrically at 256.2 nm to determine the cumulative drug release.[27]

**Saturation Solubility Study**

The saturation solubility of the optimized formulation was determined by adding an excess amount of the sample to phosphate buffer (pH 6.8). The suspension was agitated continuously for 24 h at 37 ± 0.5°C to achieve equilibrium. After filtration, the concentration of dissolved drug in the filtrate was quantified using UV–Visible spectrophotometry.[28]

**Scanning Electron Microscopy**

The surface morphology and structural characteristics of the optimized niosomal formulation were examined using scanning electron microscopy (SEM). Samples were mounted on suitable stubs, coated with a conductive material, and observed at different magnifications to evaluate vesicle shape and surface characteristics.[29-32]

**X-Ray Diffraction Analysis**

X-ray diffraction (XRD) studies were performed to investigate the crystalline nature of the pure drug and the optimized niosomal formulation. Diffraction patterns were recorded over a scanning range of 4°–50° (2θ) under operating conditions of 40 kV and 40 mA. Comparative analysis of diffraction peaks was used to assess changes in crystallinity following niosomal encapsulation.[33]

**Differential Scanning Calorimetry**

Differential scanning calorimetry (DSC) was employed to evaluate the thermal behavior of the drug and formulation components. Samples were heated from 40°C to 300°C at a constant heating rate of 10°C/min under a nitrogen atmosphere. Thermograms were analyzed to identify possible changes in melting behavior and physical state after formulation.[34]

**Precompression Evaluation of Niosomal Tablet Blend**

Precompression studies were performed to assess the flow and compression characteristics of the powder blend intended for tablet formulation. Parameters including bulk density, tapped density, angle of repose, Hausner's ratio, and compressibility index were evaluated to determine the suitability of the blend for direct compression.

Bulk density was calculated as the ratio of powder mass to its untapped volume, whereas tapped density was determined after mechanically tapping the powder-filled cylinder until a constant volume was obtained. The angle of repose was measured using the fixed funnel method to assess flowability. Hausner's ratio was calculated from the relationship between tapped and bulk densities, while Carr's compressibility index was determined to evaluate powder compressibility and interparticle interactions.[35-36]

**Preparation of Niosomal Tablets**

Niosomal tablets were prepared by the direct compression technique. The optimized niosomal formulation equivalent to 60 mg of Ticagrelor was blended with accurately weighed quantities of microcrystalline cellulose, magnesium stearate, and talc. The powder mixture was thoroughly mixed to ensure homogeneity and uniform distribution of all components. The final blend was compressed into tablets using a Fluidpack Accura ten-station rotary tablet compression machine. The prepared tablets were subsequently evaluated for their physical and pharmaceutical quality attributes.[37-38]

**Table 2: Tablet formulation of Ticagrelor Niosomes**

| Sr. No. | Ingredients | Quantity(mg) |
|---|---|---|
| 1. | Niosomes of Batch A9 | 242 |
| 2. | MCC | 50 |
| 3. | Magnesium Stearate | 6 |
| 4. | Talc | 2 |

**Evaluation of Niosomal Tablets**

The prepared niosomal tablets were evaluated for various quality control parameters to ensure their suitability for oral administration. Tablet hardness was determined using a hardness tester to assess the mechanical strength required to withstand handling, packaging, and transportation. Five tablets were randomly selected, and the average hardness value was recorded. Friability testing was performed using a Roche friabilator to evaluate the resistance of tablets to abrasion and mechanical shock. A pre-weighed sample of tablets was subjected to 100 revolutions, after which the tablets were dedusted and reweighed. The percentage

weight loss was calculated, and a friability value below 1% was considered acceptable.

Weight variation testing was carried out by individually weighing ten randomly selected tablets and comparing their weights with the average tablet weight. The results were evaluated according to pharmacopeial specifications to ensure uniformity in tablet mass. Drug content uniformity was assessed by finely powdering a selected number of tablets, followed by dissolution of an accurately weighed quantity equivalent to the required drug dose in ethanol with the aid of sonication. The resulting solution was filtered, suitably diluted, and analyzed using a UV–Visible spectrophotometer at 255 nm to determine the drug content and ensure uniform distribution of Ticagrelor within the tablets.

The in vitro drug release profile of the niosomal tablets was investigated using a USP dissolution apparatus II (paddle method). The dissolution study was conducted in phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C, with the paddle speed adjusted to 50 rpm. At predetermined time intervals over a period of 9 h, samples were withdrawn and replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The collected samples were analyzed spectrophotometrically at 256.2 nm, and the cumulative percentage drug release was calculated.

To understand the mechanism of drug release from the developed tablets, dissolution data were fitted to different kinetic models, including zero-order, first-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas models. These mathematical models were used to evaluate the release pattern and identify the predominant mechanism governing drug release from the niosomal matrix system.

The stability of the optimized niosomal tablet formulation was evaluated under accelerated storage conditions according to ICH guidelines. The formulation was stored at 40 ± 2°C and 75 ± 5% relative humidity in a stability chamber for one month. Samples were withdrawn at predetermined intervals and analyzed for drug content and in vitro drug release characteristics to assess any changes in formulation performance during storage.[39-41]

**RESULTS AND DISCUSSION:**

**Preformulation study:**

Ticagrelor appears as a white or off-white crystalline powder. Its melting point was determined to be 138±2°C, consistent with the reported range of 138-140°C, confirming its purity. The solubility study revealed that Ticagrelor is freely soluble in ethanol and methanol but sparingly soluble in phosphate buffer (pH 6.8) and distilled water.

**Excipient Characterization and Compatibility Study:**

**FTIR spectrum of Ticagrelor**

The FTIR spectrum of Ticagrelor was analyzed, and its characteristic peaks were identified and compared with standard IR spectra. All essential functional group peaks were present, confirming the authenticity of the drug sample. Key vibrations observed included O-H stretching (3371.30 $cm^{-1}$) for alcohol, N-H stretching (3285.74 $cm^{-1}$) for amide, C=C stretching (1616.86 $cm^{-1}$) for alkynes, C=N stretching (1512.47 $cm^{-1}$) for imines and oximes, and C-F stretching (1272.26 $cm^{-1}$) for fluoro compounds.

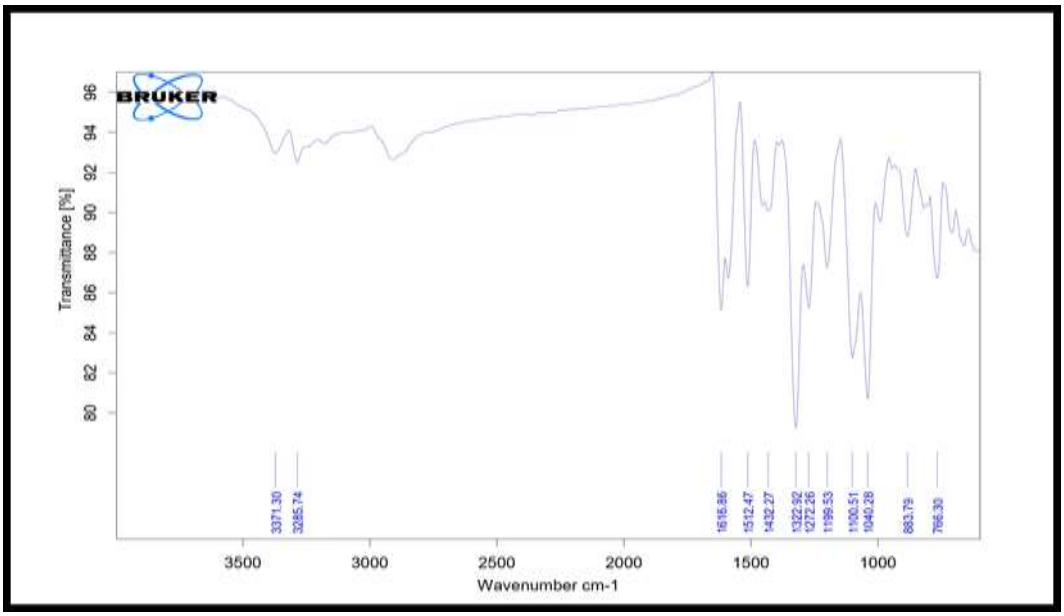



**Figure 1: FTIR Spectrum of Ticagrelor**

**Drug excipient compatibility**

Following Figures 3, 4 and 5 shows compatibility study of drug, physical mixture and formulation. With FTIR spectroscopy, the potential interaction between the medication and excipients was investigated. When comparing the IR peaks of pure Carvedilol to that of the medication blended with excipients, the findings showed no appreciable differences. So, the results of the FTIR spectroscopy indicate that the medicine and the specified excipients were compatible.

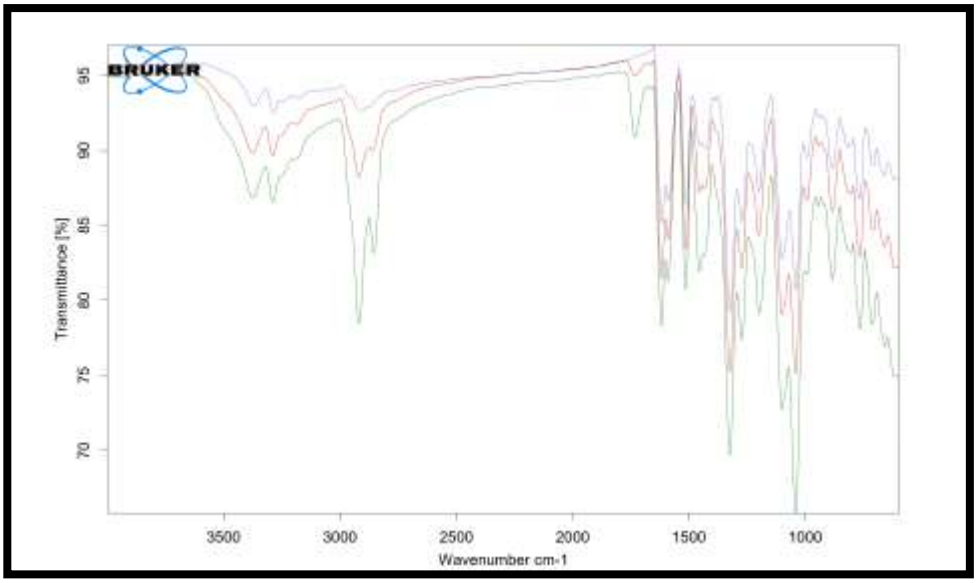



**Figure 2: Initial compatibility study of Drug-Blue, Physical mixture-Green, Formulation-Red**

## EVALUATION OF NIOSOMES:

### Entrapment efficiency and Drug content:

Nine different formulations of Ticagrelor-loaded niosomes were created using different quantities of cholesterol and surfactant; the % entrapment efficiency was determined to be between 75.5 and 89.7. The capacity of vesicles to load medicinal agents is represented by the and EE of niosomes.

**Table 3: Entrapment efficiency of Niosomes formulation**

| Sr. No. | Formulation code | %Entrapment efficiency |
|---|---|---|
| 1. | A1 | 75.5 |
| 2. | A2 | 80.08 |
| 3. | A3 | 82.81 |
| 4. | A4 | 80 |
| 5. | A5 | 79.32 |
| 6. | A6 | 84.55 |
| 7. | A7 | 79.03 |
| 8. | A8 | 86 |
| 9. | A9 | 89.7 |

**Particle Size:**

Particle size and polydispersity index of nine formulations of ticagrelor loaded noisome was analysed.

**Table 4: Particle size and Polydispersity index of Niosomes formulation**

| Sr. No. | Formulation code | Particle size (nm) | Polydispersity Index |
|---|---|---|---|
| 1. | A1 | 360.2 | 0.628 |
| 2. | A2 | 447.5 | 0.638 |
| 3. | A3 | 675 | 0.564 |
| 4. | A4 | 210.2 | 0.542 |
| 5. | A5 | 270.6 | 0.467 |
| 6. | A6 | 370 | 0.687 |
| 7. | A7 | 180 | 0.458 |
| 8. | A8 | 205.8 | 0.501 |
| 9. | A9 | 280.5 | 0.689 |

**Zeta potential:**

-26.8mV was ZP value of optimized niosomal formulation of Batch A9. It indicates prepared optimized formulation have sufficient surface charge to prevent aggregation of vesicles.

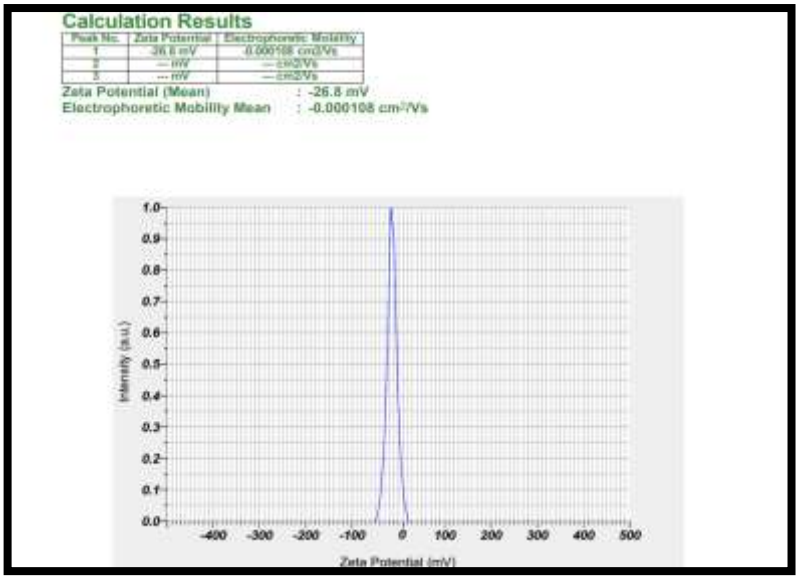



**Figure 3: Zeta potential of Optimized batch A9**

***In-Vitro* Drug Release:**

The drug release rate from the Optimized Niosomal formulation Batch (A9) was found to in range 20.09% to 91.13%. The release rate was found to be in sustained manner.

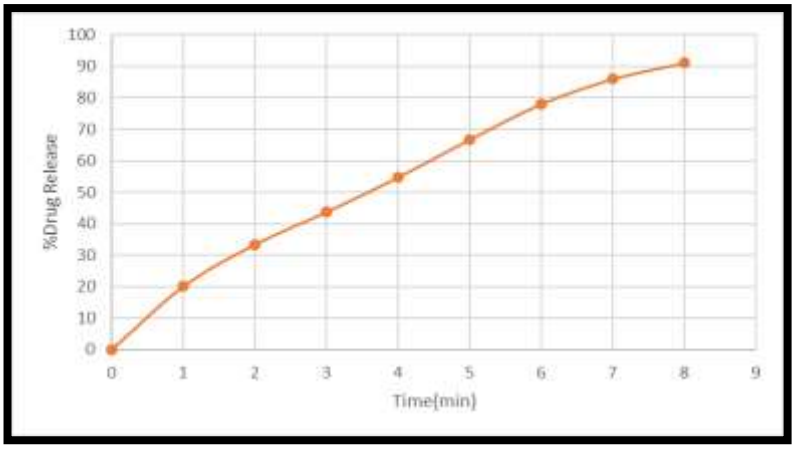



**Figure 4: %Drug Release of Optimized Niosomal formulation Batch (A9)**

**Saturation solubility study:**

Saturation solubility study of optimized niosomal formulation can be examined:

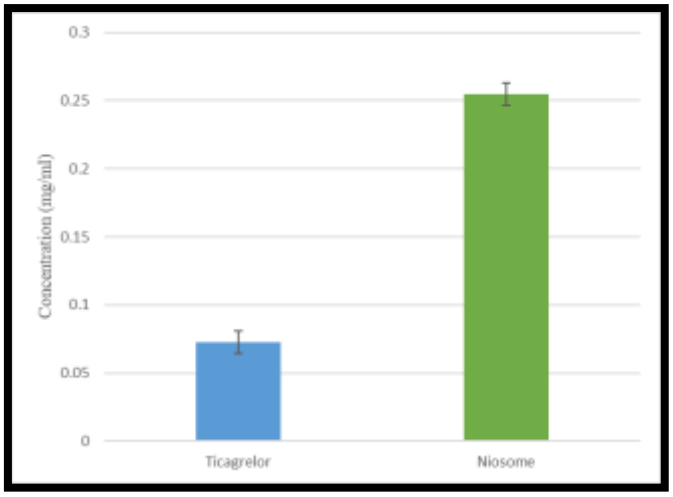



**Figure 5: Saturation Solubility**

**Scanning Electron microscopy (SEM):**

SEM was used to observe the optimized Niosomal formulation Batch (A9) size, shape, and surface morphology.

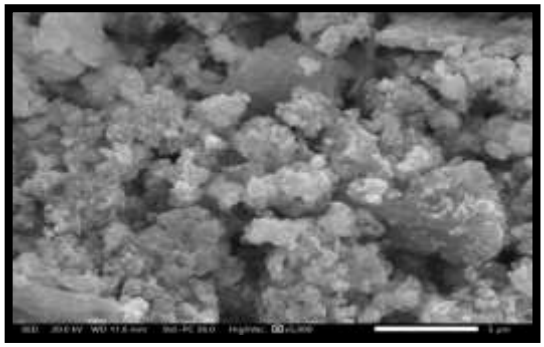


**Figure 6: SEM images of optimized formulation of Niosomes batch A9**

**XRD:**

The phase composition, crystal structure, and powder orientation are examples of physical attributes that may be examined using the X-ray diffraction method. Sharp peaks such as 10.381°, 13.253°, 17.864°, 22.354°, 23.992°, and 24.012° were seen in ticagrelor powder at the diffraction angle (2Θ), showing a characteristic crystalline structure. On the other hand, the Niosomal formulation exhibit less intense peaks, suggesting that crystalline structure of drug can be modified.

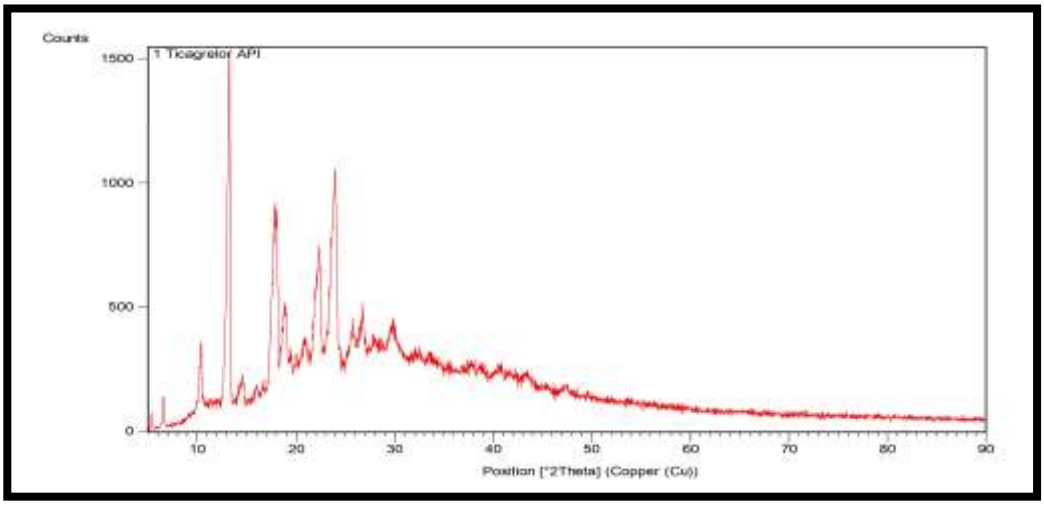



**Figure 7: XRD Image of Ticagrelor**

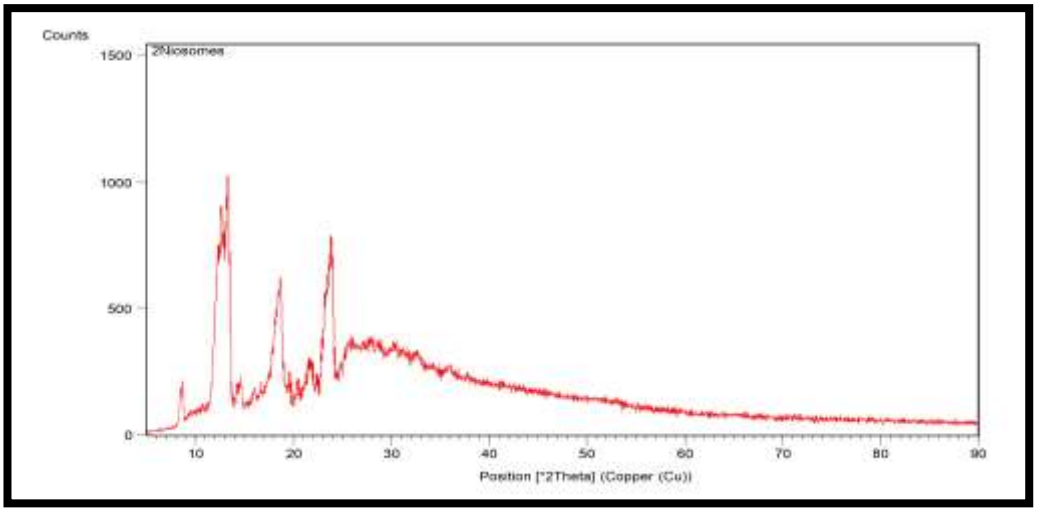



**Figure 8: XRD Image of Optimized Niosomal Formulation (Batch A9)**

**DSC:**

DSC is technique which based on thermal analysis. It enables measurements such as glass transition, melting point and crystallization. The DSC thermogram of Ticagrelor showed the sharp peak at 142.80℃ corresponding to its melting point, indicating its crystallinity and the

Optimized Niosomal formulation (Batch A9) shows peak at 109.23°C which confirming it is in amorphous state.

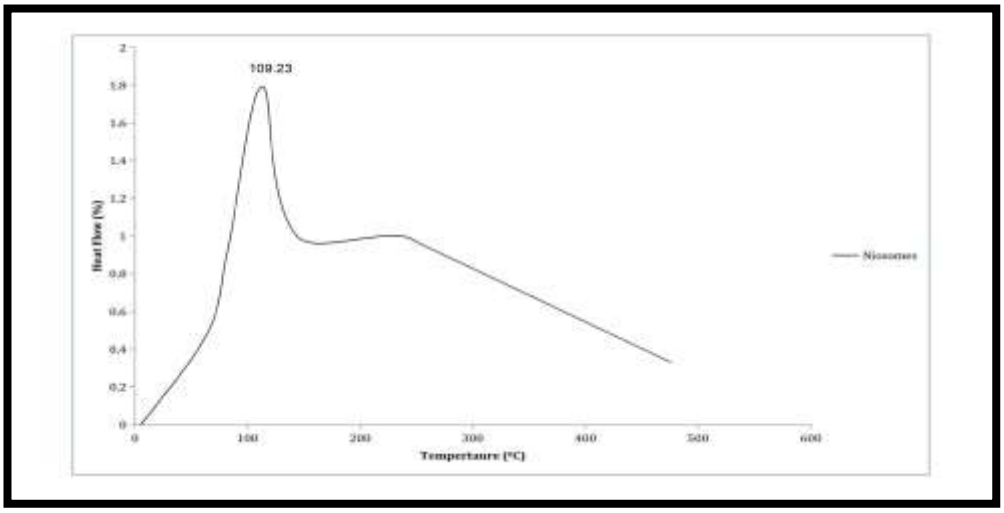



**Figure 9: DSC Thermogram of Optimized Niosomal Formulation (Batch A9)**

**Full Factorial Design:**

A $3^2$ full factorial design was used to formulate the dosage form, evaluating two factors (cholesterol $X_1$ and surfactant $X_2$) at three levels. Nine experimental trials were conducted, and % Entrapment Efficiency ($Y_1$) and Particle Size ($Y_2$) were analyzed as dependent variables. A predictive equation was generated based on the independent variables ($X_1$ and $X_2$).

**Table 5: Actual & Coded Value for $3^2$Factorial Design**

| Coded Values | Actual value | |
|---|---|---|
| | X1 (Amount of Cholesterol) | X2 (Amount of Surfactant) |
| -1 | 50 | 100 |
| 0 | 100 | 150 |
| +1 | 150 | 200 |

**Optimization of Process variables using $3^2$ Factorial Design:**

**A. Response 1: Entrapment efficiency (Y1)**

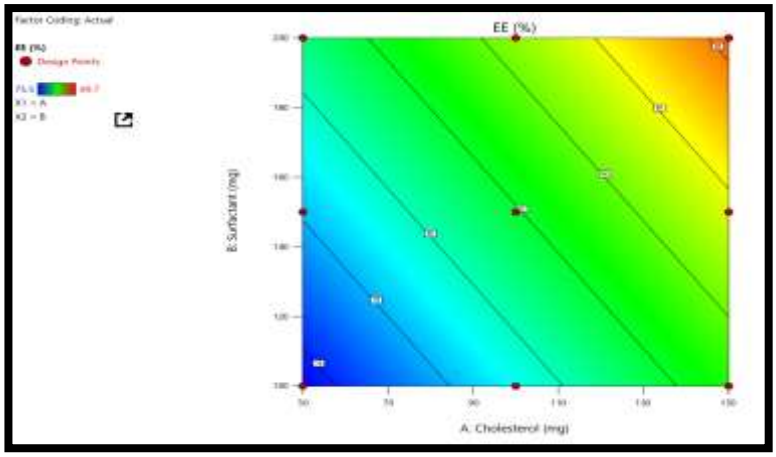



**Figure 10: Contour Plot for Response 1: %Entrapment efficiency**

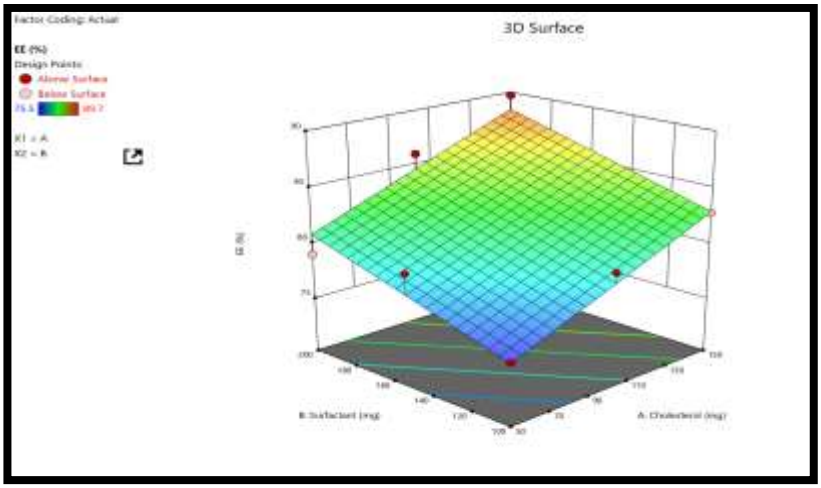



**Figure 11: 3D structure for response 1: %Entrapment efficiency**

**Effect of experimental variables on the %Entrapment efficiency:**

EE of Niosomes shows all values are in limit, indicating given model were fitted for optimizing % Entrapment efficiency. ANOVA indicated the impact of the independent variables, cholesterol(X1) and surfactant(X2) concentration on entrapment efficiency. Entrapment efficiency increases with an increase in cholesterol and surfactant concentration.

**B. Response 2: Particle Size (Y2)**

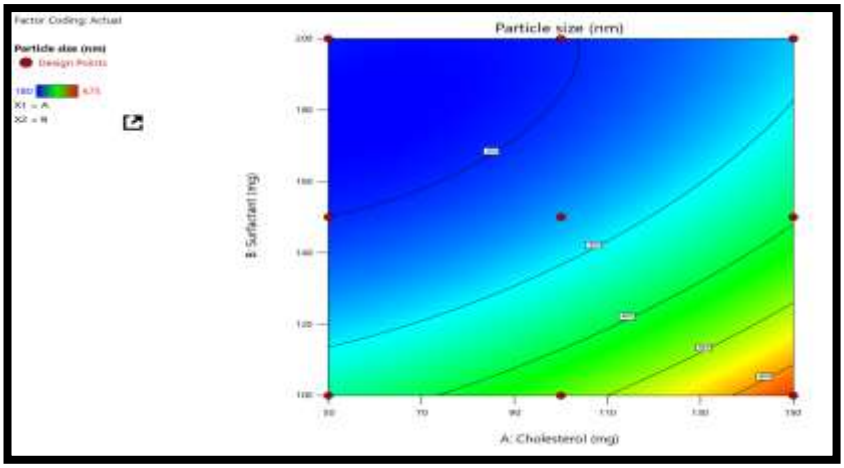



**Figure 12: Contour Plot for Response 2: Particle Size**

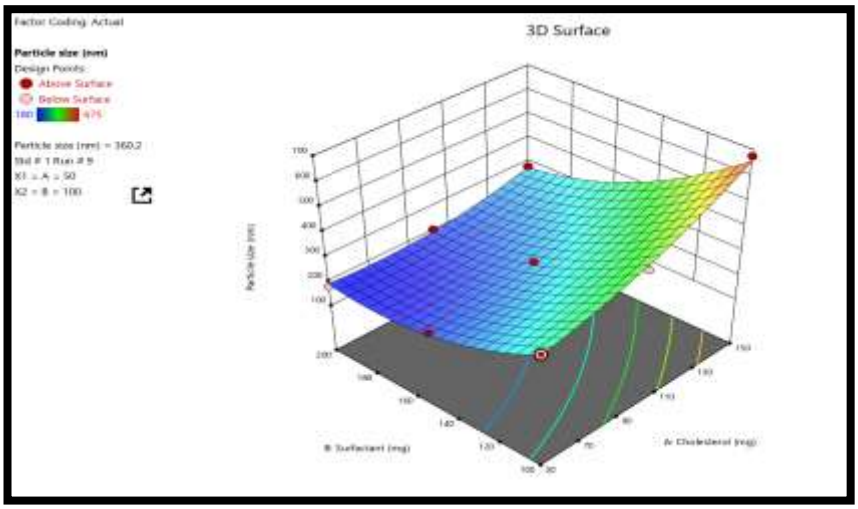



**Figure 13: 3D structure for response 2: Particle Size**

**Effect of experimental variables on the particle size:**

The particle size of Niosomes shows all values are in limit, indicating given model were fitted for optimizing particle size. ANOVA indicated impact of independent variables such as cholesterol($X_1$) and surfactant ($X_2$) concentration on particle size. Concentration of surfactant increases particle size get decreases and as the concentration of cholesterol increases particle size get increases.

**Graphical and numerical optimization with selection of an optimised batch (niosomes):**

After analysis of independent variables at distinctive levels and dependent variables batch A9 was reported to optimized batch. In this Batch A9, the Amount of Cholesterol was 150 mg and Amount of Surfactant 200 mg.

**Table 6: Parameters of Optimised Batch**

| Batch | Amount of Cholesterol | Amount of Surfactant | Entrapment Efficiency (%) | Particle Size (nm) | Desirability |
|---|---|---|---|---|---|
| A9 | 150 | 200 | 89.70 | 280.5 | 0.853 |

**PRECOMPRESSIONAL STUDIES OF NIOSOMAL TABLET:**

Good flow property was observed of all the parameters i.e. Bulk density, Tapped density, % Compressibility Index, Hausner's ratio and angle of repose. Hence, the physical mixture of the tablet formulation was suitable for tablet compression.

**Table 7: Preformulation parameters for tablet compression of Optimized Niosomes**

| Formulation code | Bulk density | Tapped density | Angle of Repose | Hausner's Ratio | Carr's Compressibility index(%) |
|---|---|---|---|---|---|
| A9 | 0.358±0.02 | 0.418±0.05 | 33.6° | 1.16 | 14.35% |

**Mean±SD, (n=3)*

**EVALUATION OF NIOSOMAL TABLET FORMULATION:**

**Hardness test:**

The developed tablets hardness of 5.2kg/cm$^2$ was discovered, showing a sufficient strength.

**Friability test:**

It was discovered that the friability was 0.652%, which was less than 1% and in compliance with the pharmacopoeial criteria.

**Weight Variation Test:**

The weight variation test was computed utilizing the formula for percentage deviation. It was discovered that the percentage deviation was1.8%, which meets the weight variation test's acceptance requirements.

**Content Uniformity:**

The content uniformity of tablets was determined to be 90.7 % which was found to be in between the range 85% to 115% complying with the pharmacopoeial specifications.

**Table 8: Evaluation of Niosomal tablet formulation**

| Formulation code | Weight Variation test (%) | Content Uniformity (%) | Friability test (%) | Hardness test (kg/cm$^2$) |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| A9 | 1.8%±0.08 | 90.7%±0.37 | 0.652%±0.05 | 5.2kg/cm²±0.042 |

*Mean±SD, (n=3)

***In-vitro* Drug Release**:

The drug release rate from the Niosomal tablet formulation was found to in range 17.83% to 89.94% from 1st to 9th hours. Niosomal tablet formuation showed sustained drug release compared to marketed formulation of ticagrelor tablet.

**Table 9: *In-vitro* Drug Release of Marketed Formulation**

| Sr.No. | Time(min) | Marketed formulation |
|---|---|---|
| 1. | 0 | 0 |
| 2. | 15 | 26.03±0.26 |
| 3. | 30 | 45.90±0.34 |
| 4. | 45 | 73.58±0.27 |
| 5. | 60 | 91.13±0.45 |

*Mean±SD, (n=3)

**Table 10: *In-vitro* Drug Release of Niosomal Tablet**

| Sr.No. | Time (min) | Niosomal Tablet formulation |
|---|---|---|
| 1. | 0 | 0 |
| 2. | 60 | 17.83±0.36 |
| 3. | 120 | 31.01±0.29 |
| 4. | 180 | 43.18±0.26 |
| 5. | 240 | 52.58±0.22 |
| 6. | 300 | 63.39±0.43 |
| 7. | 360 | 72.45±0.38 |
| 8. | 420 | 84.90±0.33 |
| 9. | 480 | 88.86±0.25 |

*Mean±SD, (n=3)

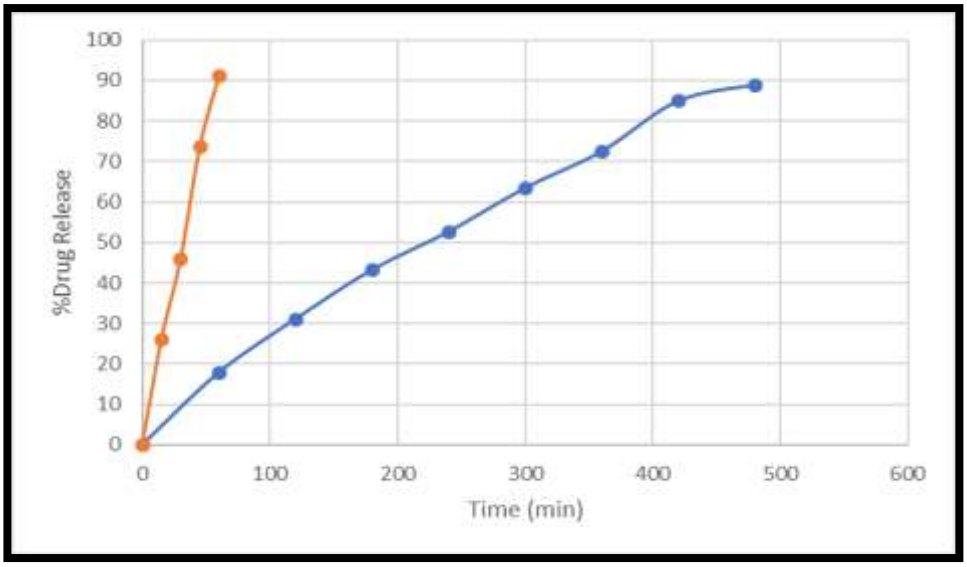
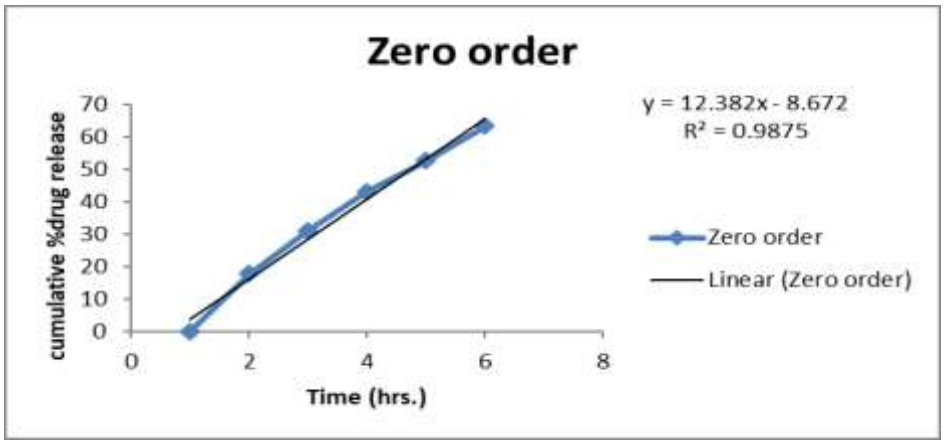
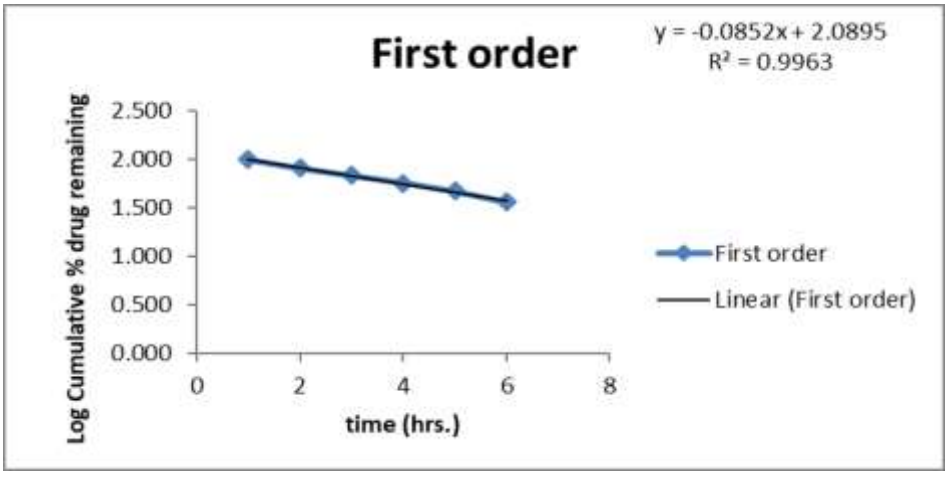


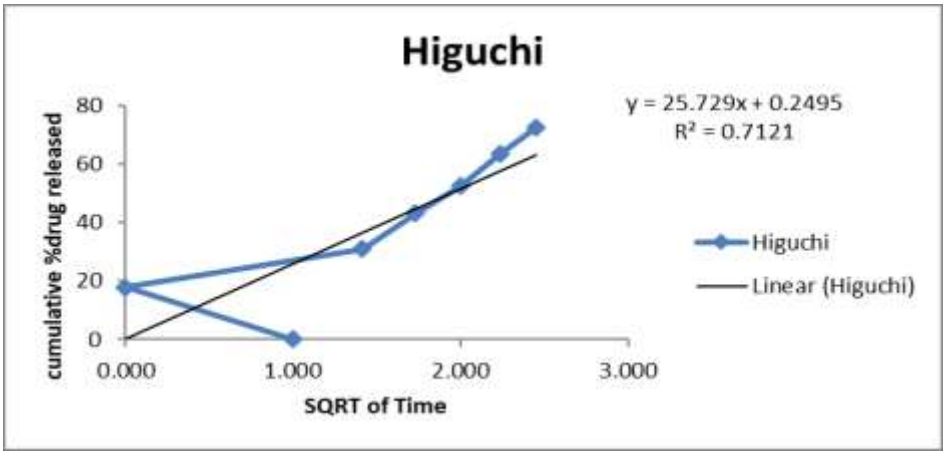

**Figure 14: Comparison of In Vitro Drug Release of Marketed Formulation and Niosomal Tablet**

**Drug release kinetics:**

To determine the mechanism of drug release for niosomal tablet, the in-vitro drug release data was used for various kinetic models.





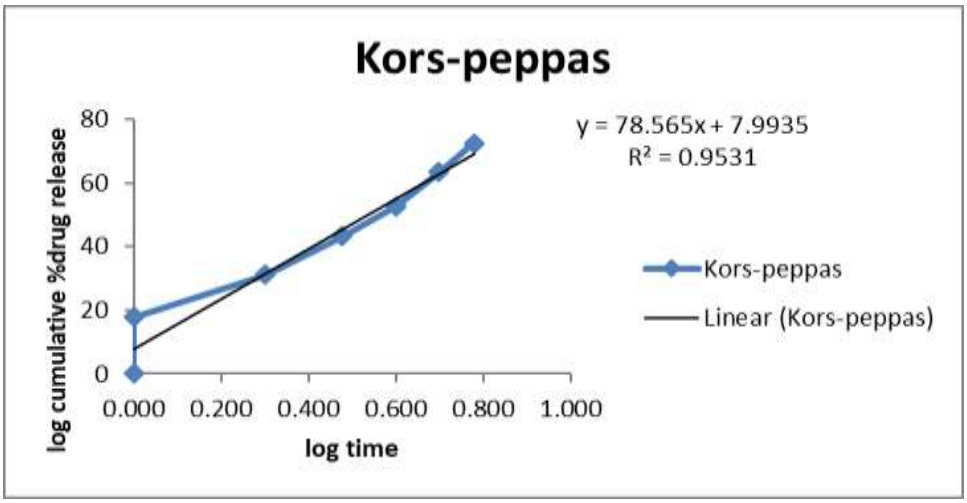




**Figure 15: Graphs of different kinetic models for drug release**

**Stability Study:**

Effect of ageing on hardness, drug content and dissolution profile of Niosomes was also analyzed. Tablets of A9 were kept at 25℃/75% RH for 1 month. Then the hardness, drug content and dissolution rate were measured for aged tablets. The outcome demonstrated that the chemical and physical characteristics of tested niosomal tablets were not altered significantly and all tested niosomal tablet were found to be stable.

**CONCLUSIONS:**

The present investigation successfully developed and optimized a Ticagrelor-loaded niosomal drug delivery system using the ether injection technique combined with a $3^2$ full factorial design approach. The optimized formulation exhibited desirable physicochemical characteristics, including high drug entrapment efficiency, nanosized vesicles, and satisfactory stability. Compatibility studies confirmed the absence of significant interactions between Ticagrelor and the selected excipients, indicating the suitability of the formulation components. Characterization studies demonstrated successful encapsulation of Ticagrelor within the niosomal vesicles, accompanied by improved solubility and modified drug release

behavior. The optimized formulation provided a sustained release profile and exhibited superior permeation across the biological membrane compared with the pure drug, suggesting enhanced absorption potential. Furthermore, the lyophilized niosomal powder displayed acceptable flow properties and was successfully compressed into tablets that complied with pharmacopeial quality requirements. Overall, the developed niosomal tablet formulation offers a promising strategy for improving the oral delivery of Ticagrelor by enhancing its solubility, permeability, and potential bioavailability. These findings support the application of niosomal nanocarriers as an effective platform for the delivery of poorly water-soluble drugs and may contribute to improved therapeutic outcomes in the management of cardiovascular disorders.

**CONFLICT OF INTEREST:**

Authors declare that there is no Conflict of interest.

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