RESEARCH PAPER

Formulation, Characterization & In-Vitro Study of Self Micro Emulsifying Drug Delivery System of Rivaroxaban

Sujit Ubale[1], Dr. R. P. Singh[2*]
[1]Ph.D. scholar, Nims Institute of Pharmacy, Nims University Rajasthan, Jaipur, India.
Email: sujitubale707@gmail.com
[2*]Professor, Nims Institute of Pharmacy, Nims University Rajasthan, Jaipur, India.
Email: ravindraceutics@gmail.com (Corresponding Author)
***Corresponding author: Dr. R. P. Singh, Professor, Nims Institute of Pharmacy, Nims University Rajasthan, Jaipur, India**
Email: ravindraceutics@gmail.com
Received: 28th May, 2026; **Revised:** 9th June, 2026; **Accepted:** 13th June, 2026; **Available Online:** 14th June, 2026

ABSTRACT

Background

Poor aqueous solubility limits the oral delivery of many BCS class II drugs, contributing to low and variable bioavailability; rivaroxaban, an anticoagulant with reported oral bioavailability of ~66%, was therefore formulated as a self-microemulsifying drug delivery system (SMEDDS) to enhance solubilization and in vitro performance.

Materials and Methods

Apparent solubility screening by UV spectrophotometry (250 nm) identified cinnamon oil as the preferred oil (19.7 ± 0.5 mg/mL; higher than Capryol 90, oleic acid, castor oil, Capmul and Captex), Cremophor EL as surfactant (12.5 ± 0.50 mg/mL), and Transcutol HP as co-surfactant (15.3 ± 0.35 mg/mL). Pseudo-ternary phase diagrams constructed by water titration at room temperature (oil:Smix 9:1 to 1:9) delineated microemulsion regions and supported selection of cinnamon oil/Cremophor EL/Transcutol HP systems. Liquid SMEDDS containing 20 mg rivaroxaban were prepared by cyclomixing and mild heating (40 °C) to obtain clear, stable preconcentrates and were evaluated for self-emulsification, dispersibility, transmittance, drug loading, compatibility, robustness, thermodynamic stability, and droplet characteristics.

Results

Formulations emulsified rapidly (≈20–30 s; <1 min) and showed Grade I dispersibility in water, 0.1 N HCl, and pH 6.8 phosphate buffer, with no precipitation or phase separation over 24 h and robustness upon 1:100–1:1000 dilution. High clarity was confirmed by >95% transmittance (e.g., 98.3 ± 0.71% in water) and drug loading was high (e.g., 98.14 ± 0.78%). FT-IR peaks of the formulation matched pure rivaroxaban, indicating no detectable drug–excipient interaction, and samples passed centrifugation (3500 rpm, 30 min) and freeze–thaw cycling (−20 to +25 °C). Droplet sizes across oil:Smix ratios were in the ~198–257 nm range with negative zeta potential, while the optimized F1 1:9 system showed ~257 nm droplets, PDI ~0.63, and zeta potential around −17.2 mV. In 0.1 N HCl, the SMEDDS markedly accelerated dissolution versus a marketed tablet supporting SMEDDS as a promising approach to improve rivaroxaban delivery and, more broadly, oral performance of poorly water-soluble drugs.

Conclusion

The developed SMEDDS formulation of rivaroxaban demonstrated excellent self-emulsification properties, rapid drug release, and enhanced dissolution compared to conventional marketed tablets. This approach offers a promising strategy for improving the oral bioavailability of BCS class II drugs like rivaroxaban.

Keywords: Self-microemulsifying drug delivery systems (SMEDDS), Rivaroxaban, Solubility, Pseudo-ternary phase diagrams.

How to cite this article: Ubale S, Singh RP. Formulation, Characterization & In-Vitro Study of Self Micro Emulsifying Drug Delivery System of Rivaroxaban. Int J Drug Deliv Technol. 2026;16(60s):363-370. DOI: 10.25258/ijddt.16.60s.41

Source of support: Nil.

Conflict of interest: None

1. INTRODUCTION: Oral administration is the most common method for drug delivery. Nevertheless, approximately 40% of new drug candidates exhibit poor water solubility, which complicates their oral delivery. This is due to their low bioavailability, significant intra- and inter-subject variability, and the absence of dose proportionality (1). Various formulation strategies are employed to enhance the bioavailability of class II drugs by either increasing their dissolution rate or maintaining the drug in solution within the intestinal lumen. To achieve

effective oral delivery of these poorly water-soluble drugs, it is essential to enhance their solubility (2). Several technological approaches have been developed to improve the solubility of such drugs, including particle size reduction, salt formation, hydrotropy, solid dispersions, pH adjustment, the use of surfactants, complexation, supercritical fluid processes, and co-solvency. Each of these strategies presents limitations due to the development of alternative formulation strategies, such as lipid-based formulations. (2,3,4)

2.MATERIALS AND METHODS:

2.1 Materials: Rivaroxaban was a generous gift from Alkem laboratory, Mumbai. Capryol 90, Capmul, Captex, Cinnamon oil, Castor oil, Oleic acid, Labrasol, Tween 20, Cremaphor EL, Labrafil M2125, Ethanol, Trascutol HP etc.

2.2 Solubility Analysis: The apparent solubility of rivaroxaban was assessed in various oils, surfactants, and co-surfactants at ambient temperature to identify the most suitable oil and surfactant. Approximately 1 g of each vehicle was placed in separate cap tubes, and an excess amount of rivaroxaban was introduced into each vehicle. The mixtures were sealed and heated at 50 °C in a water bath shaker to enhance solubilization. Subsequently, the mixtures were agitated using a shaker at room temperature for 48 hours. Upon reaching equilibrium, the samples were collected and centrifuged at 10,000 rpm for 15 minutes. A 100 µL aliquot of the supernatant was collected, appropriately diluted with acetonitrile, and the concentration of rivaroxaban was determined using UV spectrophotometry at 250 nm. (5,6)

2.3 Construction of Pseudo-Ternary Phase Diagrams: Pseudo-ternary phase diagrams were developed for selected oils, surfactants, and co-surfactants with water at room temperature using the water titration method (7). The surfactant was combined with the co-surfactant in ratios of 1:1, 1:2, and 2:1, respectively (8). Aliquots of the surfactant/co-surfactant mixture were then combined with oil in ratios of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, and 1:9 in separate vials and titrated with water at room temperature. The samples were equilibrated for 30 seconds and visually assessed after each addition (9). Based on these visual observations, the systems were categorized as nanoemulsions, microemulsions, coarse dispersions, and gel phases. Subsequently, pseudo-ternary phase diagrams were constructed using Triplot software (10). Samples that appeared bluish-white were identified as microemulsions (11).

3. Characterization of SMEDDS:

3.1 Self-emulsification and Visual Assessment: The prepared emulsions were incrementally introduced into 250 mL of water. Self-emulsifying mixtures exhibit rapid dispersion in water with gentle agitation (12).

3.2 Dispersibility Test: The self-emulsification properties of the SMEDDS formulations were evaluated through visual assessment. The time required for microemulsion formation was determined by the gradual addition of the formulation into 250 mL of distilled water, simulated gastric fluid, and phosphate buffer at pH 6.8, each in separate glass beakers maintained at 37 °C (13). The contents were gently stirred using a magnetic stirrer set at 100 rpm. The emulsification tendency was classified as "good" if emulsification occurred rapidly, within less than 1 minute, resulting in a clear or transparent appearance (14). Conversely, the emulsification tendency was deemed "poor" if the emulsion formed was less clear (15). Based on visual appearance and the time required for self-emulsification, formulations were graded accordingly.

Grade I: Rapidly forming (within 1 min) micro-emulsion with a clear (or) bluish appearance.
Grade II: Rapidly forming, slightly less clear emulsion with a bluish-white appearance.
Grade III: Fine milky emulsion that formed within 2 minutes.
Grade IV: Dull, greyish white emulsion with a slight oily appearance that is slow to emulsify (more than 2 minutes). (16)

3.3 Phase Separation and Stability Study of Emulsions: Each SMEDDS formulation (50 µL) was introduced into vials containing 5 mL of double-distilled water and simulated gastric fluid at room temperature, followed by cyclomixing for 1 minute. The mixtures were subsequently stored and monitored for phase separation and drug precipitation at intervals of 2, 4, 6, 8, 12, and 24 hours. (17)

3.4 Robustness to Dilution: The prepared SMEDDS formulations were diluted at ratios of 1:100 and 1:1000 using distilled water, 0.1 N HCl, and a phosphate buffer with a pH of 6.8. These diluted microemulsions were stored for 24 hours and subsequently examined visually for any indications of phase separation or drug precipitation. (18)

3.5 Percentage Transmittance: Each SMEDDS formulation (100 µL) was added to a vial containing 10 mL of double-distilled water, 0.1 N HCl, and a phosphate buffer with a pH of 6.8, all maintained at

room temperature (T °C). The mixture underwent cyclomixing for 1 minute. Subsequently, each sample was analyzed for percentage transmittance at 250 nm. (19)

3.6 Drug Loading Efficiency: The drug content within the formulation was quantified using UV-spectrophotometry. Precisely 50 mg of each formulation was weighed and subsequently diluted to 100 mL with acetonitrile. The resulting solutions were then analyzed spectroscopically after appropriate dilution. (20)

3.7 FT-IR Studies: FT-IR spectra of the pure drug and its combinations with excipients were acquired using a Bruker-Alpha FT-IR spectrophotometer. The spectra for the drug, excipients, and their combinations were recorded by accumulating 24 scans at a resolution of 4 cm^{-1} across the range of 400–4000 cm^{-1}. The spectra of the drug-excipient mixtures were then compared with that of the pure drug to identify any interactions. (21)

3.8 Thermodynamic Stability Studies: The SMEDDS formulations prepared were evaluated through thermodynamic stability studies to assess the impact of centrifugation and temperature on the stability of microemulsions. (22)

3.9 Centrifugation Study: The formulations were incorporated into deionized water at a 1:20 ratio and subjected to centrifugation at 3500 rpm for 30 minutes. Subsequently, they were examined for phase separation or precipitation. (23)

3.10 Freeze–Thaw Cycle: Formulations that demonstrated stability under centrifugation were further evaluated through freeze–thaw cycles. In this study, SMEDDS formulations were diluted with deionized water at a 1:20 ratio and subjected to two freeze–thaw cycles, alternating between -20 °C and +25 °C. Each temperature was maintained for 48 hours, after which samples were examined for phase separation or precipitation. (24)

3.11 In vitro Drug Release Study: An in vitro drug release study was conducted for both the pure drug and Rivaroxaban SMEDDS. The percentage and cumulative percentage of drug release were determined based on the absorbance and concentration derived from the standard graph of rivaroxaban. This in vitro drug release study was carried out over a period of 60 minutes in 0.1N HCl. (25)

3.12 Droplet Size and Zeta Potential Determination: The prepared SMEDDS formulations were introduced into distilled water at a 1:1000 ratio within a test tube and subsequently mixed for one minute using a cyclo mixer. The droplet size, polydispersity index (PDI), and zeta potential of the emulsions were measured at 25 °C employing the dynamic light scattering (DLS) technique at a 90° angle, utilizing a Zeta sizer Nano ZS90. (26)

3.13 Preparation of Liquid SMEDDS: Various ratios of oil, surfactant, and co-surfactant were selected for the formulation systems, with Rivaroxaban consistently maintained at 20 mg across all formulations. A surfactant/co-surfactant mixture (Smix) was prepared by combining appropriate proportions of surfactants and co-surfactants, followed by cyclomixing. Rivaroxaban was precisely weighed and dissolved in suitable proportions of oil and Smix. The formulations underwent cyclomixing for 1 minute to ensure uniform mixing and were subsequently heated in a thermostatic water bath at 40 °C to enhance drug solubilization. Cyclomixing continued until transparent preparations were achieved. The final liquid SMEDDS of Rivaroxaban were stored at room temperature for 48 hours and examined for signs of turbidity or phase separation. The formulation was then characterized for various parameters. (27)

4. RESULTS AND DISCUSSION:

4.1 Solubility of Rivaroxaban in Various Oils: The solubility of rivaroxaban in different oils was assessed using a UV spectrophotometer. Table 1 presents the saturation solubility of rivaroxaban in these oils. Cinnamon oil was chosen for the formulation due to its ability to form a stable emulsion.

TABLE1: Solubility of Rivaroxaban in Various Oils

Oils	Solubility(mg/mL)
Capryol 90	13.2 ± 0.10
Cinnamon oil	19.7 ± 0.5
Oleic acid	16.9 ± 0.15
Castor oil	1.6 ± 0.20
Capmul	0.78 ± 0.25
Captex	0.90 ± 0.51

All values are expressed as Mean, n = 3

4.2 Solubility of Rivaroxaban in Various Surfactants: The solubility of Rivaroxaban in different co-surfactants was assessed, leading to the selection of Cremaphor EL for the formulation. Table 3 provides a detailed listing of the solubilities of the various co-surfactants.

TABLE 2: Solubility of Rivaroxaban In Various Surfactants

Surfactants	Concentration(mg/mL)
Cremaphor EL	12.5± 0.50
Labrasol	9.8 ± 0.15
Tween 20	8 ± 0.10

All values are expressed as Mean, n = 3

4.3 Solubility of Rivaroxaban in Various Co-surfactants:

The solubility of Rivaroxaban in different co-surfactants was assessed, leading to the selection of Transcutol HP for the formulation. Table 3 provides a detailed listing of the solubilities of the various co-surfactants.

TABLE 3: Solubility of Rivaroxaban In Various Co-Surfactants

Co surfactants	Concentration(mg/mL)
Labrafil M2125	7.7 ± 0.35
Ethanol	6.8 ± 0.20
Transcutol HP	15.3 ± 0.35

All values are expressed as Mean n = 3

4.4 Selection of Excipients: Following solubility assessments of various oils, surfactants, and co-surfactants, excipients demonstrating superior solubility were chosen for formulation. The selected components include cinnamon oil as the oil, Cremaphor EL as the surfactant, and Transcutol HP as the co-surfactant. Pseudo-ternary phase diagrams were developed to delineate the microemulsion regions and determine appropriate compositions of oil, surfactant, and co-surfactant for the formulation of SMEDDS. These diagrams indicated that systems utilizing cinnamon oil as the oily phase, Cremaphor EL as the surfactant, and Transcutol HP as the co-surfactant exhibited effective micro-emulsifying properties.

4.5 Size and Zeta Potential Determination: The prepared formulations were subjected to analysis using a zeta sizer to ascertain their size and zeta potential values, as presented in the tables below.

TABLE 4: F1 Formulation

Oil: S_{mix}	Size of emulsion droplets (nm)	Zeta Potential (mV)	PDI
F1 1:9	257.1	-17.2	0.632
F1 2:8	244.2	-12.1	0.421
F1 3:7	230.3	-7.7	0.678
F1 4:6	224.2	-6.5	0.721
F1 5:5	212.2	-5.7	0.843
F1 6:4	209.4	-3.1	0.772
F1 7:3	203.2	-2.1	0.852
F1 8:2	201.4	-1.6	0.764
F1 9:1	198.1	-1.2	0.819

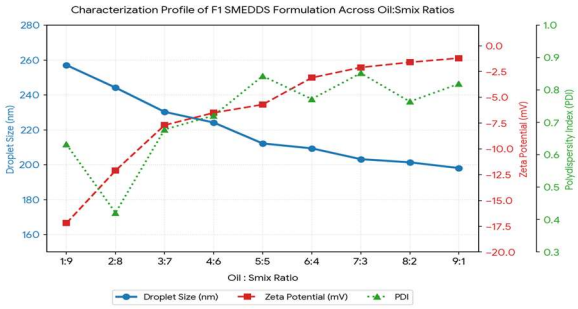

Figure.1- F1 (1:9) Droplet size, Zeta potential and PDI

4.6 Self-emulsification and visual assessment: The formulations were evaluated for self-emulsification time through visual assessment. Self-emulsifying mixtures are expected to disperse quickly in an aqueous medium with gentle agitation. The self-emulsification times for the prepared SMEDDS are presented in Table 6. The SMEDDS of Rivaroxaban achieved emulsification in under one minute (20-30 seconds). The efficiency of all the prepared emulsions was satisfactory.

TABLE 6: Self Emulsification Time (Sec)

S. no	Formulation	Emulsification time	Remark

1	F1 1:9	25 ± 1.2 sec	Good

4.7 Dispersibility Test: formulations exhibited grade 1 emulsions when tested in distilled water, 0.1N HCl, and phosphate buffer at pH 6.8.

TABLE 7: Dispersibility Test Results

Formulation name	Distilled water	0.1N HCL	Phosphate buffer of pH 6.8
F1 1:9	Grade 1	Grade 1	Grade1

4.8 Phase Separation and Stability Study of Emulsions: The SMEDDS formulations were monitored for drug precipitation and phase separation at 2, 4, 6, 8, 12, and 24-hour intervals. It was determined that none of the formulations exhibited either precipitation or phase separation of the drug. The findings are detailed in Table 8.

TABLE 8: Phase Separation and Precipitation of The Drug

S. no	Formulation	Precipitation	Phase separation
1	F1 1:9	No	No

4.9 Robustness to Dilution: Formulations were diluted using excess water, 0.1N HCl, and a phosphate buffer with a pH of 6.8. The diluted samples were stored for 24 hours and subsequently examined visually for any precipitation or phase separation of the drug. The absence of precipitation or phase separation indicates that all formulations were stable upon dilution (Table 9).

TABLE 9: Robustness to dilution

S. no	Formulation name	Distilled water	0.1N HCL	Phosphate buffer of pH 6.8
1	F1 1:9	No	No	No

No-indicates no phase separation and precipitation

4.10 Percentage Transmittance: The transmittance percentage at 250 nm was measured for each diluted sample. The findings, detailed in Table 10, reveal that all formulations exhibited transmittance exceeding 95%, thereby indicating the presence of clear emulsions.

TABLE 10: Percentage Transmittance

S. no	Formulation name	Distilled water	0.1N HCL	Phosphate buffer pH 6.8
1	F1 1:9	98.3±0.71	96.46±0.18	97.47±0.34

All values are expressed as Mean ± SD (n = 3)

4.11 Drug Loading Efficiency: Each SMEDDS formulation, weighing 50 mg, was diluted with 100 mL of acetonitrile. The resulting solutions underwent spectrophotometric analysis after appropriate dilution. Absorbance measurements were conducted at a wavelength of 250 nm. The findings are detailed in Table 11. Both formulations exhibited a drug loading efficiency exceeding 90%.

TABLE 11: Drug Loading Efficiency of Formulations

S. no	Formulation name	Drug loading efficiency
1	F1 1:9	98.14±0.78

All values are expressed as Mean ± SD (n = 3)

4.12 FT-IR Studies: The spectra of the drug-excipient mixtures and the formulations were analyzed in comparison to the spectrum of the pure drug to identify any potential interactions. Notable peaks were detected at 2979 cm^{-1}, 2938 cm^{-1}, 2138 cm^{-1}, 1738 cm^{-1}, 1666 cm^{-1}, 1546 cm^{-1}, and 1281 cm^{-1}, corresponding to CH stretching, OH stretching, CN stretching, C=C stretching, C-N stretching, C=O stretching, and C-Cl stretching, respectively. The FT-IR spectra of both the pure drug and the formulation exhibited significant similarity due to the presence of identical functional groups. This similarity suggests the absence of interactions between rivaroxaban and the excipients utilized in the formulation.

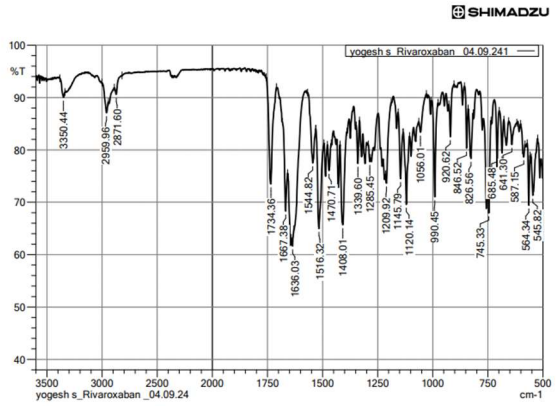

Figure.2 – FTIR spectra of Rivaroxaban loaded liquid SMEDDS optimized batch F1

4.13 Thermodynamic Stability Studies: Thermodynamic stability studies aim to identify meta-stable formulations. The SMEDDS underwent centrifugation and freeze-thaw cycles. The emulsions demonstrated stability during centrifugation at 3,500 rpm and temperature cycles ranging from -20 °C to +25 °C. No precipitation or phase separation was observed in the formulations. The results are detailed in Table 12.

TABLE 12: Thermodynamic Stability Studies

S. No	Formulation name	Centrifugation (3,500 rpm for 30min)	Freeze thaw cycle (-20 °C and +25 °C)
1	F1 1:9	Pass	Pass

4.14 In vitro Drug Release Study: Following a 60-minute drug release study conducted in 0.1 N HCl, the pure drug exhibited a release rate of 99.8%.

Time (minutes)	SMEDDS (% drug release)	Marketed tablet (% drug release)
0	0	0
10	45	12
20	78	35
30	92	52
40	98.5	78
50	99.8	88
60	100	94

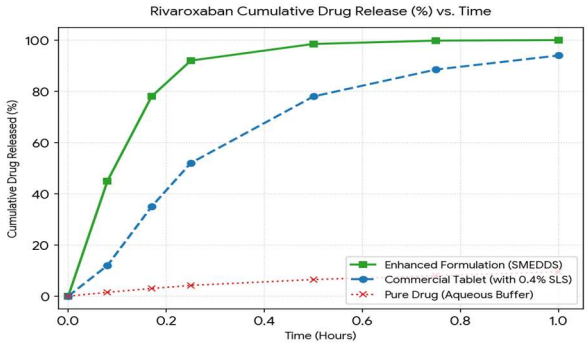

Figure.3- Comparison of % Drug Release

CONCLUSION:

The poorly soluble drug rivaroxaban was chosen for the formulation of a self-micro-emulsifying drug delivery system (SMEDDS) due to its limited aqueous solubility and an oral bioavailability of 66%. This system was developed to enhance the solubility and bioavailability of rivaroxaban. The solubility of rivaroxaban in various oils, surfactants, and co-surfactants was assessed using UV-spectrophotometry, leading to the selection of Transcutol HP as the co-surfactant for the formulation. SMEDDS were prepared by selecting oil: Smix ratios ranging from 1:9 to 9:1. Mixtures, specifically F1(1:9), were selected for the formulation of SMEDDS, maintaining a constant drug amount of 20 mg in all formulations. The prepared formulations underwent evaluation for self-emulsification and visual assessment, phase separation and drug precipitation, robustness to dilution, percentage transmittance, drug loading efficiency, FT-IR studies, thermodynamic stability studies, droplet size, polydispersity index (PDI), and zeta potential. All formulations emulsified within 25-30 seconds, i.e., in less than one minute. No formulation exhibited drug precipitation or phase separation, and all were robust to dilution. The formulations demonstrated a percentage transmittance exceeding more than 95%, indicating clear emulsions. Drug loading efficiency exceeded 90% in all formulations. Thermodynamic stability studies confirmed that all formulations remained stable after centrifugation and freeze-thaw cycles. The droplet sizes were between 198.1 nm and 257.1 nm, with PDI values between 0.42 and 0.85, indicating uniform particle size. The zeta potentials

were between -1.2 and -17.2 mV. The FT-IR spectrum revealed no interaction between the drug and excipients. Based on the evaluation tests and the dissolution study, formulation F1(1:9) exhibited greater drug release compared to marketed formulation and demonstrated superior self-emulsification properties with a droplet size of 257.1 nm and more uniform particles (PDI = 0.63). The present studies suggest that SMEDDS can be effectively utilized as a drug delivery system for rivaroxaban.

References

1. Bakrey H, Abdu A, Shivgotra R, Soni B, Sharma M, Bakrey A, et al. Innovative Strategies and Advances in Drug Delivery Systems to Address Poor Solubility: A Comprehensive Review. CDT. 2025 July 21;26(13):879–902.
2. Rathod VG, Deshmukh NB, Deshmukh SP. Advanced Formulation Strategies for Enhancing the Bioavailability of Poorly Soluble Drugs: A Comprehensive Review. AJPS. 2025 Oct 4;429–432.
3. Arbaz Ajaz S, Majaz Q, Kalam I, Shaikh A, Shaikh M, Ayyaj P. Solubility Enhancement of BCS Class 2 Drugs by Solid Dispersion Technique. RJPDFT. 2024 Aug 7;215–220.
4. Mahmood T, Sarfraz RM, Ismail A, Ali M, Khan AR. Pharmaceutical Methods for Enhancing the Dissolution of Poorly Water Soluble Drugs. ASSAY Drug Development Technologies. 2023 Mar 1;21(2):65–79.
5. Shah PJ, Patel MP, Shah J, Nair AB, Kotta S, Vyas B. Amalgamation of solid dispersion and melt adsorption techniques for augmentation of oral bioavailability of novel anticoagulant rivaroxaban. Drug Delivery and Translational Research. 2022 Apr 25;12(12):3029–3046.
6. Awatade PR, Veer VS, Kasabe AJ, Dhepe SD. Analytical method development and validation of rivaroxaban in bulk and pharmaceutical dosage forms using RP-HPLC. ijhs. 2022 June 13;14688–14702.
7. Hill RM, Li X, Davis HT. Ternary Phase Behavior of Mixtures of Siloxane Surfactants, Silicone Oils, and Water. In Routledge; 2019. p. 313–348.
8. Dhas N, Nishchaya K, Pardeshi C, Panzade P, Patel V, Kudarha R, et al. Role of Surfactants and Co-Surfactants in the Formulation of Microemulsions. In Apple Academic, 2025. p. 57–90.
9. Kumar S, Wadhwa K, Pahwa R, Ali J, Baboota S. Screening of surfactant mixture ratio for preparation of oil-in-water nanoemulsion: A technical note. J Appl Pharm Sci. 2024 Jan 1;
10. Hayuningtyas A, Jitphongsaikul P, Hamad A. Winsor Phase Diagram of a Colloidal System from the Mixture of Water, Eugenol, and Tween 20. RICE. 2022 Mar 25;1(1):22–17.
11. Angelico R. Special Issue "Micro/NNanoemulsions Smart Colloids for Multiple Applications." Nanomaterials. 2022 Oct 24;12(21):3734.
12. Iqbal S, Waqar MA, Riaz T, Qureshi A, Tabassam N, and Mehboob T. A Comprehensive Review of Self-Emulsifying Drug Delivery Systems (SEDDS) and Their Recently Developed Formulations. Ijpihs. 2023 Dec 21;5(1).
13. Hsieh CM, Yang TL, Putri AD, Chen CT. Application of Design of Experiments in the Development of Self-Microemulsifying Drug Delivery Systems. Pharmaceuticals. 2023 Feb 13;16(2):283.
14. Utomo A, Alderman NJ, Padron GA, Özcan-Taşkın NG. Comparative study on emulsification in the presence of a nanoclay (Pickering emulsion) or a surfactant using high-intensity mixing. Chemical Engineering Research and Design. 2023 Aug 6;197:617–627.
15. El Kinawy OS, Petersen S, Helmdach L, Ulrich J. Parameter Selection of Emulsification Processes: Conditions for Nano- and Macroemulsions. Chem Eng & Technol. 2012 July 5;35(9):1604–1608.
16. Gavrilov DI, Tishkov SV, Blynskaya EV, Alekseev KV, Minaev SV, Abramova DM, et al. Development of approaches for the creation of self-emulsifying drug delivery systems. Pharmacy and Pharmaceutical Technology. 2023 Feb 25;(1):34–41.
17. Sharvani K, Shripathy D, Shabaraya A. Self-Microemulsifying Drug Delivery Systems: Formulation Design and Characterization. Zenodo (CERN European Organization for Nuclear Research). 2022 June 7;
18. Djekic L, Primorac M. Formulation and characterization of self-microemulsifying drug delivery systems based on biocompatible nonionic surfactants. Hem Ind. 2014 Jan 1;68(5):565–573.
19. Yan B, Ma Y, Guo J, Wang Y. Self-microemulsifying delivery system for improving bioavailability of water-insoluble drugs. J Nanopart Res. 2020 Jan 1;22(1).
20. Jain R, Vinode P. Role of various spectroscopic techniques in method validation for quantitative determination of drug products. Adv Pharma J. 2023 Jan 1;8(6):148–154.
21. Bunaciu AA, Hoang VD, Aboul-Enein HY. Fourier transform infrared spectroscopy used in drug excipients compatibility studies. Applied Spectroscopy Reviews. 2024 Dec 5;60(5):385–403.
22. Midha K, Nagpal M, Singh G, Aggarwal G. Prospective of solid self-microemulsifying systems in novel drug delivery. CDD. 2017 Dec 13;14(8).
23. Szolláth R, Bárdos V, Stifter-Mursits M, Angi R, Mazák K. Effects of Different Centrifugation

Parameters on Equilibrium Solubility Measurements. MPs. 2025 Oct 2;8(5):116.
24. Prasad H. A Review on Formulation Design of Self Micro Emulsifying Drug Delivery System to Improve Solubility. Zenodo (CERN European Organization for Nuclear Research). 2023 June 12;
25. Mandake RG, Shinde SS, Belaskar VY, Jagtap AM, Vambhurkar GB, Nitalikar MM. Modification of the Dissolution Profile of Rivaroxaban by spray drying. Asian Journal of Pharmaceutical and Technology. 2018 Jan 1;8(4):203.
26. Vithani K, Jannin V, Pouton CW, and Boyd BJ. Colloidal aspects of dispersion and digestion of self-dispersing lipid-based formulations for poorly water-soluble drugs. Advanced Drug Delivery Reviews. 2019 Jan 21;142:16–34.
27. Madan JR, Patil K, Awasthi R, Dua K. Formulation and evaluation of solid self-microemulsifying drug delivery system for azilsartan medoxomil. International Journal of Polymeric Materials and Polymeric Biomaterials. 2019 Nov 26;70(2):100–116.