

Formulation and Evaluation of Bedaquiline Fumarate-Loaded Nanoemulsion**Divanshu Bansal¹, Sunil Sain², Megha Singh³**¹Research Scholar, Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur, Rajasthan, India²Associate Professor, Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur, Rajasthan, India³HOD, UVR Group of Labs, Greater Noida (U.P.), India

Received: 01-07-2026 / Revised: 15-08-2026 / Accepted: 21-09-2026

Corresponding author: Divanshu Bansal

Conflict of interest: Nil

Abstract

Bedaquiline fumarate is described in the thesis as a poorly water-soluble drug, creating a formulation challenge for oral delivery. The study aimed to formulate and evaluate a bedaquiline-loaded nanoemulsion using poly(δ -decalactone) (PDL) as the polymeric oil phase and Pluronic F-68 as surfactant. Pre-formulation investigations included organoleptic assessment, melting point determination, FTIR, X-ray diffraction, differential scanning calorimetry, UV analysis, partition coefficient determination, calibration curves and solubility studies. Nanoemulsions were prepared by a nanoprecipitation approach, followed by evaluation of particle size, polydispersity index (PDI), zeta potential, drug content/entrapment, in-vitro release, release kinetics, stability and in-vitro antibacterial activity. The thesis reports poor solubility of the drug in water compared with acetone and methanol. The calibration curves showed reported R^2 values of 0.9969 and 0.9999 for the specified solvent systems. In-vitro release data in PBS pH 6.8 showed greater cumulative release from the drug-loaded nanoemulsion than from free bedaquiline at the reported time points. The zero-order model had the highest reported correlation coefficient ($R^2 = 0.9777$). The thesis reports a zone of inhibition of 2.8 ± 0.52 mm for bedaquiline-loaded nanoemulsion and 1.56 ± 0.06 mm for bedaquiline suspension. Storage observations indicated better stability under refrigerated conditions than under the stated accelerated condition. Some formulation identifiers and values differ across thesis sections; this article preserves the values and terminology as presented rather than attempting to reconcile them.

Keywords: Bedaquiline fumarate; nanoemulsion; poly(δ -decalactone); Pluronic F-68; nanoprecipitation; drug release; antibacterial activity.

DOI: 10.25258/ijcpr.18.10.85

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Nanoemulsions are dispersions of nanosized droplets of one immiscible liquid in another, commonly oil and water, stabilized by surfactants or emulsifiers. The thesis describes their pharmaceutical interest in improving aqueous solubility, bioavailability and delivery of drugs. Their small droplet size provides a large interfacial area and may support improved dispersion and drug delivery. Nanoemulsions can be developed in several dosage forms and may be administered through different routes, although the present work focuses on oral delivery.

Nanoemulsions are kinetically stable rather than thermodynamically stable systems. Their physical stability can be affected by Ostwald ripening, flocculation, coalescence, creaming and sedimentation. Composition, surfactant

concentration, temperature, pH and preparation conditions are therefore important formulation considerations. High-energy techniques include high-pressure homogenization and ultrasonication, while low-energy approaches use system properties or phase behavior to form small droplets.

Poor aqueous solubility and bedaquiline: The thesis identifies poor aqueous solubility as a limitation in oral drug delivery because dissolution can affect drug absorption and bioavailability. Bedaquiline fumarate is described as a diarylquinoline drug used in multidrug-resistant tuberculosis treatment. The thesis emphasizes its lipophilic character and low water solubility as the rationale for investigating a nanoemulsion delivery system.

The study explores a polymeric nanoemulsion containing bedaquiline fumarate, using poly(δ -decalactone) as the polymeric oil/carrier component and Pluronic F-68 as surfactant. The work combines pre-formulation assessment, formulation development, physicochemical characterization, in-vitro release and antibacterial evaluation. The article below follows the study structure and reports the experimental observations available in the thesis without introducing outside experimental data.

Aim and Objectives: The stated aim was to formulate an oral-delivery nanoemulsion of bedaquiline and to evaluate its potential advantages over conventional delivery.

The objectives listed in the thesis were:

- Preparation and optimization of bedaquiline-loaded nanoemulsion.
- Characterization and evaluation of the bedaquiline-loaded nanoemulsion.
- Evaluation of in-vitro antibacterial activity and maximization of drug solubility.
- Design of a nanoemulsion-based delivery system to encapsulate the drug and improve drug stability, with lipid nanoemulsions considered as candidates for oral administration.
- Assessment of the antibacterial potential against bacterial strains including *Mycobacterium tuberculosis*.
- Evaluation of mean particle size, polydispersity index, zeta potential, zone of inhibition and minimum inhibitory concentration.

Study workflow: The plan of work comprised pre-formulation studies; compatibility studies between the drug, polymer and surfactant; formulation of PDL nanoemulsion by nanoprecipitation; optimization of formulation and process variables; and characterization of the drug-loaded nanoemulsions.

The listed pre-formulation procedures included organoleptic evaluation, melting point, FTIR, XRD, DSC, UV spectral analysis and calibration curve preparation, partition coefficient and solubility studies. The planned evaluation included droplet-size analysis, PDI, zeta potential, pH, in-vitro release and release-kinetics analysis. The thesis also reports stability studies and in-vitro antibacterial activity.

Materials and Methods

Drug and formulation components: Bedaquiline fumarate was the active drug. The thesis identifies poly(δ -decalactone) (PDL) as the polymeric carrier/oil component and Pluronic F-68 as the surfactant.

Solubility screening also included acetone, methanol, phosphate-buffered saline (PBS) and water. The drug-polymer-surfactant mixture was assessed for possible interactions by FTIR.

Pre-formulation studies: Organoleptic properties were recorded for the drug sample. The melting point was determined by the capillary method. FTIR spectroscopy was used to examine characteristic functional-group bands, X-ray diffraction was used to assess crystalline characteristics, and differential scanning calorimetry was included for thermal characterization. UV-visible spectroscopy was used to identify the wavelength maximum and prepare calibration curves.

The partition coefficient was determined by the shake-flask method using n-octanol and water. Solubility was assessed in selected solvents and aqueous media. Calibration curves were prepared in the solvent systems described in the thesis, and absorbance was measured using a UV-visible spectrophotometer.

Preparation and optimization: The thesis states that bedaquiline-loaded nanoemulsions were prepared using a nanoprecipitation/spontaneous preparation approach with PDL and Pluronic F-68. Formulation and process variables included the drug: polymer:surfactant ratio, stirring speed and stirring time. Six batches, RNE1 to RNE6, were compared in the optimization table. The recorded conditions ranged from 800 to 1300 rpm and from 1 to 6 hours, with different component ratios.

Because the thesis contains differing descriptions of the best-performing batch in different sections, this article does not silently assign a single reconciled batch identity. Batch-specific observations are reported in the results with their corresponding thesis context.

Characterization of nanoemulsions: Particle size and PDI were measured using a zeta sizer (Malvern, UK), according to the thesis. Zeta potential was also determined. Formulation pH was measured using a digital pH meter.

Drug content was determined using a UV-visible spectrophotometric method after diluting 10 μ L of bedaquiline nanoemulsion 1000-fold with methanol; the thesis gives drug content as dissolved drug divided by added drug, multiplied by 100.

FTIR compatibility and formulation analysis: FTIR spectra of bedaquiline, PDL, Pluronic F-68 and their physical mixture were examined to identify characteristic peaks and assess possible drug-excipient interaction. The prepared placebo and drug-loaded nanoemulsions were also compared by FTIR.

In-vitro drug release: In-vitro release was assessed using a dialysis bag in PBS pH 6.8. The method section specifies stirring at $37 \pm 0.5^\circ\text{C}$ and 100 rpm, with a dialysis membrane molecular-weight cut-off reported as 12,000–14,000 Da. Samples were evaluated over time and cumulative drug release was calculated. The thesis compares free bedaquiline with bedaquiline-loaded nanoemulsion.

Release-kinetics models: Release data were fitted to zero-order, first-order, Higuchi, Hixson–Crowell and Korsmeyer–Peppas models. The correlation coefficients reported for these models were used to compare the fit of the release data.

Stability and morphology: Stability was assessed under refrigerated conditions reported as approximately $3 \pm 5^\circ\text{C}$ and under $25 \pm 2^\circ\text{C}/60 \pm 5\%$ relative humidity. Samples were examined at intervals for particle size, PDI and zeta potential. The thesis also describes centrifugation stress testing and transmission electron microscopy (TEM) for morphology.

In-vitro antibacterial activity Antibacterial activity was evaluated by the agar-well diffusion method,

with the thesis describing testing against *Mycobacterium tuberculosis*. The zone of inhibition was reported for bedaquiline-loaded nanoemulsion, blank nanoemulsion, bedaquiline suspension and normal control. Minimum inhibitory concentration (MIC) values were also reported.

Results

Organoleptic and physicochemical characterization: The drug sample was described as a whitish crystalline powder, odorless and bitter. The capillary-method melting point was reported as $175 \pm 2^\circ\text{C}$ in the pre-formulation results.

The drug profile elsewhere in the thesis lists a melting-point range of $158\text{--}163^\circ\text{C}$; these values are retained as separately reported in the source.

Spectral and solid-state studies: The FTIR description identifies bands attributed to O–H stretching at $3350\text{--}3200\text{ cm}^{-1}$, aromatic C–H stretching at $3050\text{--}3010\text{ cm}^{-1}$, aliphatic C–H stretching at $2950\text{--}2850\text{ cm}^{-1}$, and a fumarate carbonyl band near $1725\text{--}1700\text{ cm}^{-1}$. Bands were also described for aromatic C=C, C–N, C–O and aromatic C–H bending.

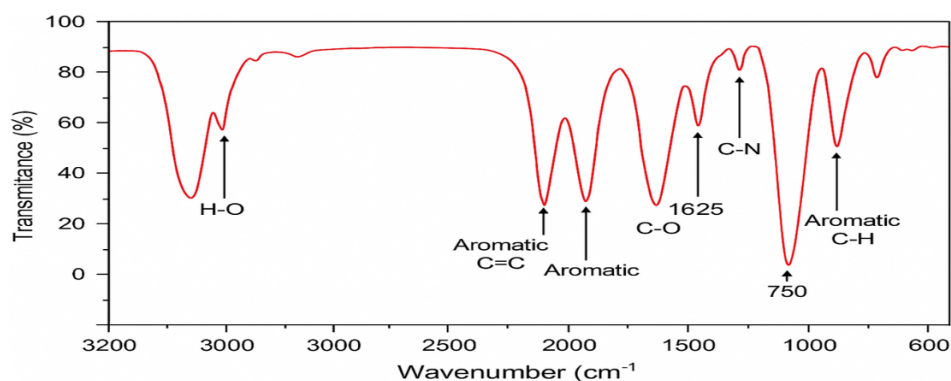


Figure 1:

The XRD description reports distinct peaks around 2θ values of $13\text{--}14^\circ$, $16\text{--}20^\circ$, $23\text{--}24^\circ$ and $27\text{--}29^\circ$, interpreted in the thesis as confirming crystalline character. The DSC discussion describes a melting endotherm near 160°C , alongside other thermal features described in the thesis.

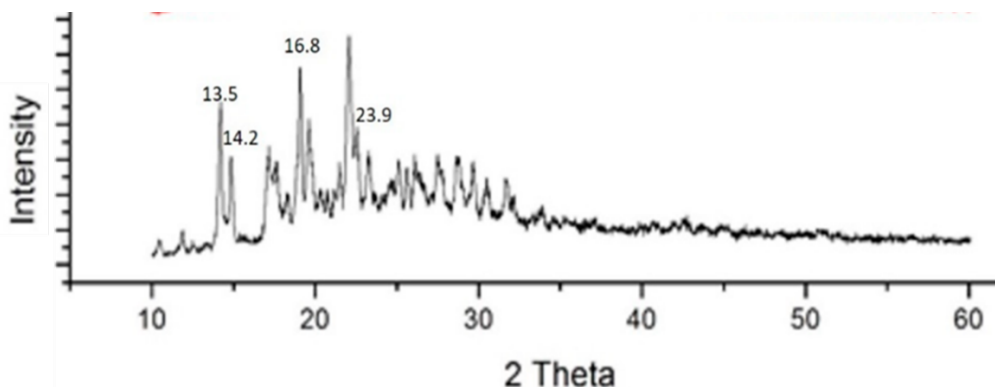


Figure 2:

UV analysis and partition coefficient: The UV maximum for bedaquiline in acetone was reported at 324 nm. The shake-flask determination gave a partition coefficient/log P value of 7.3 ± 0.02 for n-octanol/water, which the thesis interpreted as evidence of the drug's lipophilic nature.

Calibration curves: For bedaquiline in PBS pH 6.8 and water (70:30), the thesis reports an R^2 value of 0.9969. For PBS pH 6.8 and methanol (70:30), the reported R^2 value was 0.9999. The tables identify measurements at the stated wavelengths and report mean $\pm$ SD for $n = 3$.

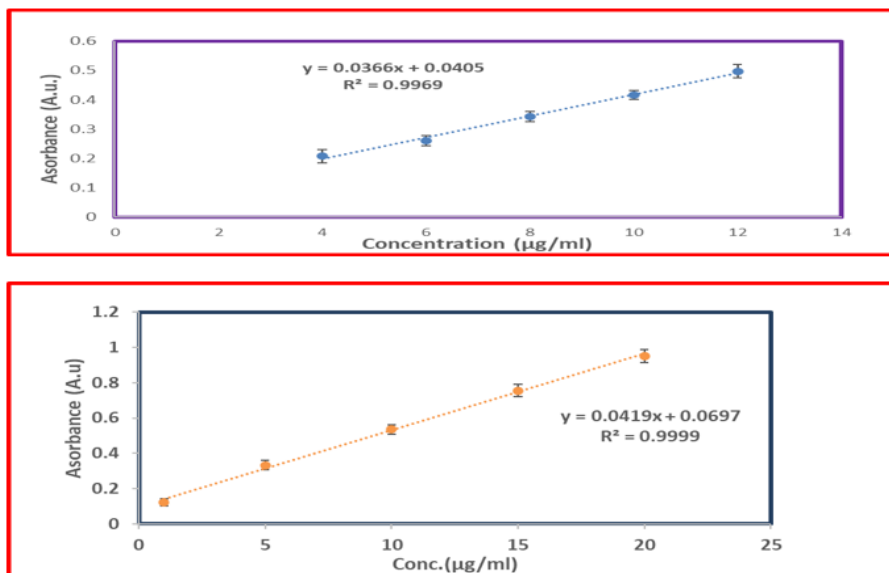


Figure 3:

Solubility: The reported solubility values were 100 ± 5 mg/mL in acetone, 30 ± 2.52 mg/mL in methanol, 9 ± 2 mg/mL in PBS pH 7.4, and 0.8 ± 0.0025 mg/mL in water. These results show the lowest reported solubility in water among the listed media and form the basis for selecting a formulation approach intended to address the drug's aqueous-solubility limitation.

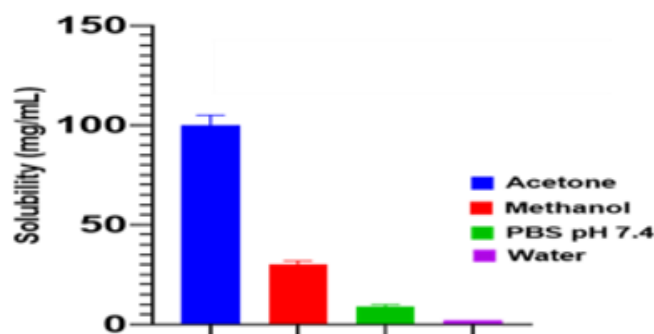


Figure 4:

Excipient solubility and compatibility: The thesis reports bedaquiline solubility in selected formulation excipients as 100 ± 1.21 mg/mL in poly(δ -decalactone), 89.84 ± 1.84 mg/mL in Pluronic F-68 and 85.73 ± 3.01 mg/mL in Tween.

The thesis notes that surfactant concentration needs consideration because high amounts may cause irritation. FTIR analysis of the drug, polymer, surfactant and physical mixture was used to assess compatibility. The presence of characteristic drug peaks in the physical-mixture spectra was

interpreted in the thesis as indicating no chemical interaction between the drug, surfactant and polymer. Comparison of placebo and drug-loaded nanoemulsion FTIR spectra showed no significant differences, which the thesis interpreted as consistent with drug incorporation in the formulation.

Formulation batches: The optimization table lists six batches. The table reports the following drug: polymer:surfactant ratios, stirring speeds, times and batch values:

Table 1:

Batch	Ratio	Speed (rpm)	Time (h)	Globule size (nm)	PDI	Zeta potential (mV)	Entrapment (%)
RNE1	1:1:10	800	1	140.5	0.233	-4.11	71.32
RNE2	1:3:20	900	2	130.1	0.148	-4.00	79.4
RNE3	1:5:30	1000	3	101.5	0.124	-3.96	99.95
RNE4	1:7:40	1100	4	170.8	0.178	-4.02	92.15
RNE5	1:9:50	1200	5	189.5	0.232	-4.15	76.2
RNE6	1:11:60	1300	6	210.8	0.255	-4.08	70.03

The thesis text elsewhere identifies RNE3 as optimized based on a combination of particle size, PDI and zeta potential, while the batch table reports the highest entrapment value for RNE1. The summary also reports RNE3 particle size of 116.6 ± 6.35 nm, PDI of 0.347 ± 0.05 , pH of 7.1 ± 0.03 and entrapment of $99.95 \pm 1.35\%$. These discrepancies are preserved rather than resolved by adding assumptions.

Particle size, PDI and zeta potential: The thesis reports average globule sizes for selected nanoemulsion formulations in the range of 78.00 to 166.1 nm in one characterization section. It

describes the drug-loaded formulation as having a PDI of 0.347 ± 0.05 in the summary, and reports a PDI of 0.242 for the blank formulation and 0.347 for the drug-loaded system in the results discussion. The thesis interprets the PDI values as indicating a relatively narrow size distribution.

The zeta-potential values listed in the formulation table were between -3.96 and -4.15 mV.

In the stability table, initial values are reported as -5.61 ± 0.1 mV for blank nanoemulsion and -11.1 ± 0.21 mV for bedaquiline-loaded nanoemulsion. The thesis discusses zeta potential as a parameter relevant to resistance against droplet aggregation.

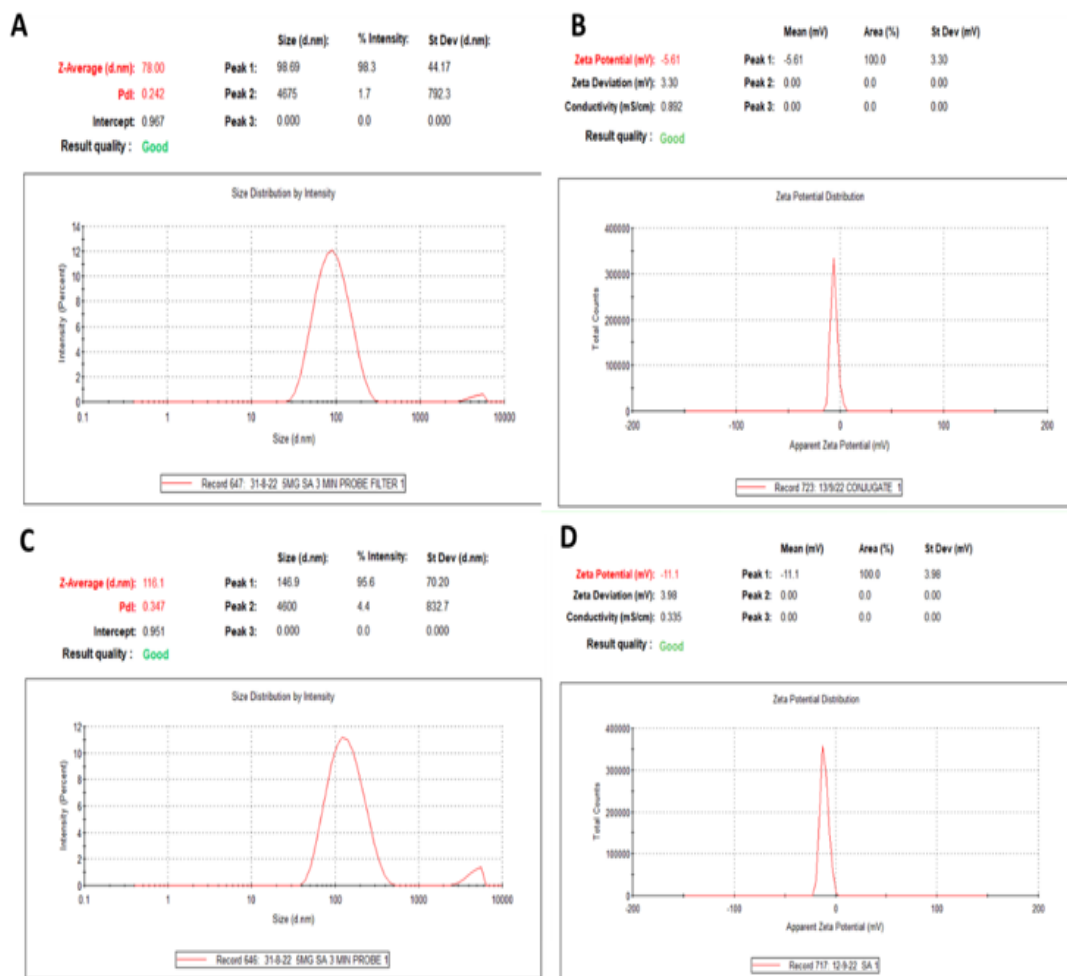


Figure 5:

In-vitro drug release: The cumulative drug-release data in PBS pH 6.8 are summarized below. At 2 hours, free bedaquiline release was 13.66% and bedaquiline-NE release was 18.97%. At 4 hours, the respective values were 22.64% and 37.23%. At 6 hours, values were 31.02% and 51.37%; at 8 hours, 39.36% and 58.76%. The thesis additionally reports bedaquiline-NE release of 68.071% at 10 hours, 81.67% at 12 hours and

90.11% at 14 hours. The thesis states that free bedaquiline reached 39.36% cumulative release at the reported 8-hour table point, while the narrative describes 39.36% at 14 hours.

This internal difference is not reconciled here. Across the tabulated common time points, the reported cumulative release for bedaquiline-NE was higher than for free bedaquiline.

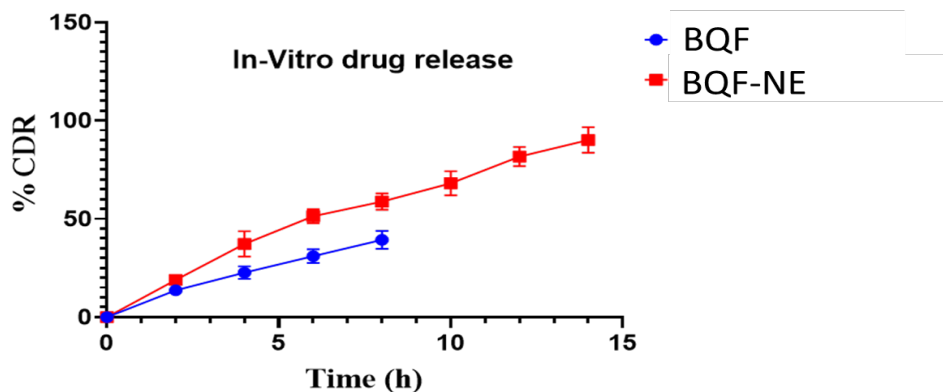


Figure 6:

Release kinetics: The reported correlation coefficients (R^2) were 0.6410 for first-order, 0.9777 for zero-order, 0.9685 for Higuchi, 0.7094 for Hixson–Crowell and 0.8369 for Korsmeyer–Peppas. Zero-order had the highest R^2 among the models listed in the thesis, and the thesis describes the result as indicating a controlled-release pattern.

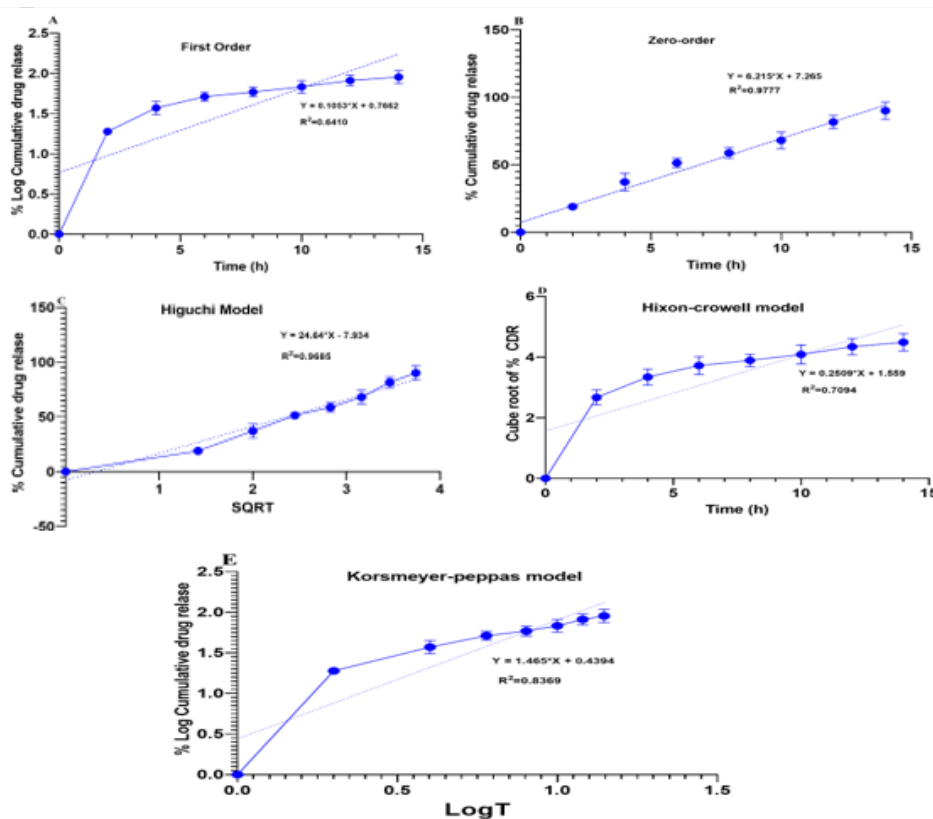


Figure 7:

Stability studies: The thesis reports no visible phase separation, creaming or sedimentation after centrifugation for samples stored under refrigerated conditions, while such signs were reported under $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH after centrifugation. During three months of storage, particle size, PDI and zeta potential were monitored. At the end of three months under the stated refrigerated condition, the table reports blank nanoemulsion size of 150.1 ± 9.1 nm and drug-loaded nanoemulsion size of 163.2 ± 7.56 nm. Under $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH, the corresponding three-month values were $280.1 \pm$

9.13 nm and 310.2 ± 6.2 nm. The PDI values at three months under the latter condition were reported as 0.48 ± 0.025 for blank nanoemulsion and 0.592 ± 0.016 for drug-loaded nanoemulsion.

The thesis concludes from these observations that the formulations were more stable under refrigerated conditions than under the stated accelerated condition. It also notes an increase in size and PDI under the warmer condition, which it discusses in relation to coalescence and aggregation.

Table 2:

Storage Condition	Storage Time (Month)	B-NE			BQF-NE		
		Size (nm) (Mean $\pm$ SD)	PDI (Mean $\pm$ SD)	Zeta Potential	Size (nm) (Mean $\pm$ SD)	PDI (Mean $\pm$ SD)	Zeta Potential (Mean $\pm$ SD)
$3\pm 5^\circ\text{C}$	0	78.00 ± 9.1	0.242 ± 0.014	-5.61 ± 0.1	116.1 ± 8.16	0.347 ± 0.011	-11.1 ± 0.2
	1	140.2 ± 9.1	0.26 ± 0.013	-3.98 ± 0.13	152.2 ± 8.1	0.17 ± 0.02	-3.78 ± 0.2
	2	146.4 ± 9.1	0.28 ± 0.012	-5.18 ± 0.14	159.1 ± 7.1	0.19 ± 0.02	-4.28 ± 0.25
	3	150.1 ± 9.1	0.28 ± 0.018	-6.22 ± 0.21	163.2 ± 7.56	0.192 ± 0.012	-5.81 ± 0.22
$25\pm 2^\circ\text{C}$ $60\pm 5\%$ RH	0	78.00 ± 9.1	0.242 ± 0.014	-5.61 ± 0.1	116.1 ± 8.16	0.347 ± 0.011	-11.1 ± 0.21
	1	160.2 ± 6.13	0.3 ± 0.013	-6.98 ± 0.13	170.2 ± 8.13	0.27 ± 0.021	-7.78 ± 0.28
	2	185.4 ± 8.1	0.42 ± 0.012	-8.18 ± 0.58	210.1 ± 9.15	0.49 ± 0.025	-8.28 ± 0.25
	3	280.1 ± 9.13	0.48 ± 0.025	-10.22 ± 0.25	310.2 ± 6.2	0.592 ± 0.016	-11.81 ± 0.21

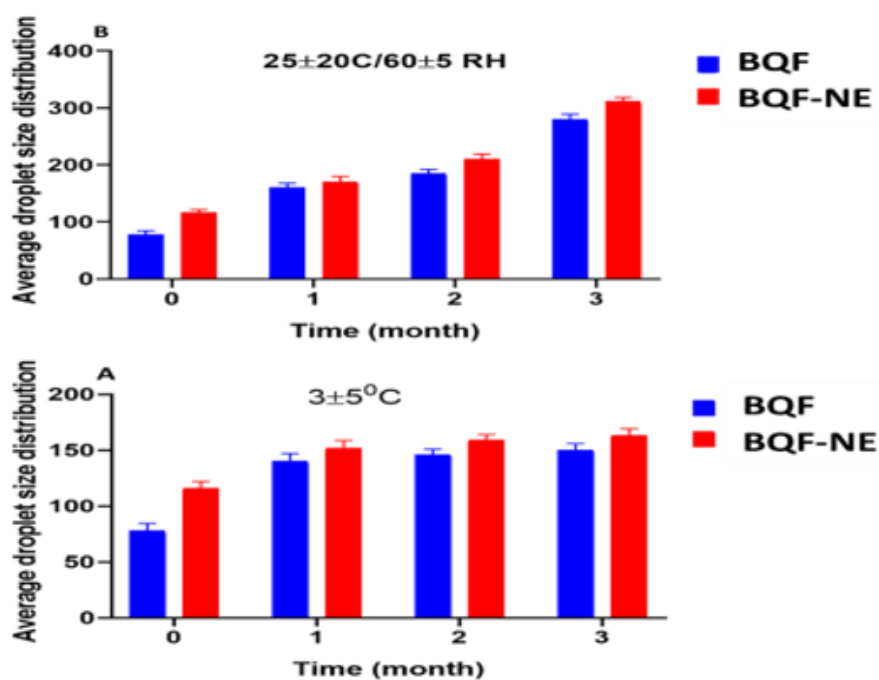


Figure 8:

Morphology: Transmission electron microscopy was described as showing spherical morphology and a uniform size distribution for B-NE and bedaquiline-loaded nanoemulsion. The thesis reports no visible aggregation or Ostwald ripening in the images and interprets this as supporting physical integrity of the observed formulation.

In-vitro antibacterial activity: The zone-of-inhibition table reports 2.8 ± 0.52 mm for bedaquiline-loaded nanoemulsion, 0.81 ± 0.68 mm for blank nanoemulsion, 1.56 ± 0.06 mm for

bedaquiline suspension and 0.0089 ± 0.0059 mm for normal control. The accompanying narrative describes the drug-loaded nanoemulsion as showing the greatest zone among the listed preparations. The MIC table reports $50.4 \mu\text{g}$ for pure bedaquiline, $20.34 \mu\text{g}$ for bedaquiline-NE and 1 mg for B-NE. The paragraph in the thesis mentions four values while the displayed table lists three formulations; this article reports the tabulated values and notes the source inconsistency rather than inferring the missing category.

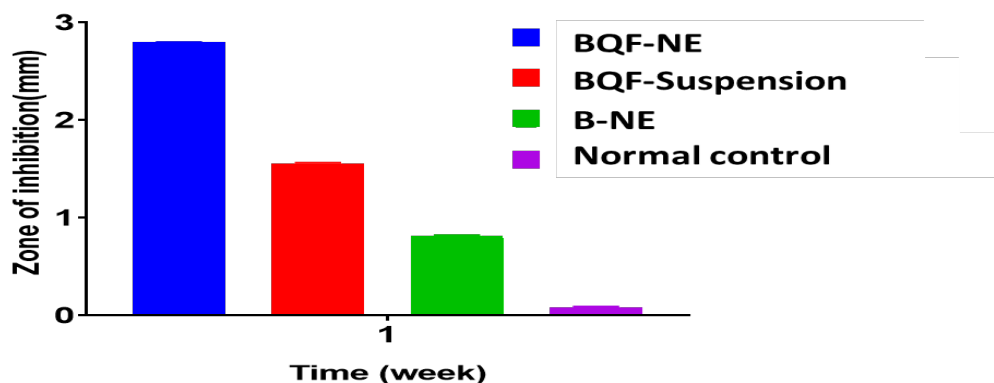


Figure 9:

Discussion

Taken together, the thesis results indicate that the investigated polymeric nanoemulsion was developed to address the poor aqueous solubility of bedaquiline fumarate. The reported solvent-solubility results support the formulation rationale. The FTIR discussion did not identify a major drug–excipient interaction, and the in-vitro release table shows higher cumulative release from the nanoemulsion than from free drug at the shared reported time points.

The release-kinetics analysis gave the highest R^2 for the zero-order model among those compared. Antibacterial testing reported a larger zone of inhibition for bedaquiline-loaded nanoemulsion than for the bedaquiline suspension and blank nanoemulsion. Stability observations favored refrigerated storage over the stated accelerated condition. However, batch identity and some numerical descriptions differ between the optimization table, results narrative and summary. These discrepancies limit the ability to state a single unambiguous optimized-batch profile from the thesis alone.

Conclusion

The thesis describes the preparation and evaluation of a bedaquiline fumarate-loaded polymeric nanoemulsion using PDL and Pluronic F-68. Pre-formulation studies characterized the drug and documented low solubility in water relative to the

other tested media. The formulation was evaluated for physicochemical properties, drug–excipient compatibility, particle size, PDI, zeta potential, drug release, release kinetics, stability, morphology and in-vitro antibacterial activity. The reported in-vitro release results show higher cumulative release for bedaquiline-loaded nanoemulsion than for free bedaquiline at the common time points presented. Zero-order kinetics had the highest reported correlation coefficient among the evaluated models. The bedaquiline-loaded nanoemulsion showed the highest reported zone of inhibition among the listed test preparations, and the tabulated MIC was lower for bedaquiline-NE than for pure bedaquiline. Stability results favored refrigerated storage compared with the stated $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$ condition. These findings are limited to the experiments and reporting contained in the supplied thesis. They do not establish clinical efficacy or safety. Several internal inconsistencies are present in the source, including different descriptions of the optimized batch, particle-size and entrapment values, and the time associated with one cumulative-release value. No attempt has been made to invent missing values or reconcile these differences.

Declarations: Funding, conflicts of interest, author contributions, ethics approval and data-availability statements were not independently added because the thesis material provided for this article did not establish those declarations.

References

- Alqahtani, M. S., Kazi, M., Alsenaidy, M. A., & Ahmad, M. Z. (2021). Advances in Oral Drug Delivery. *Frontiers in Pharmacology*, 12. <https://doi.org/10.3389/fphar.2021.618411>
- Marhamati, M., Ranjbar, G., & Rezaie, M. (2021). Effects of emulsifiers on the physicochemical stability of Oil-in-water Nanoemulsions: A critical review. *Journal of Molecular Liquids*, 340, 117218. <https://doi.org/10.1016/j.molliq.2021.117218>
- McClements, D. J. (2012). Nanoemulsions versus microemulsions: terminology, differences, and similarities. *Soft Matter*, 8(6), 1719–1729. <https://doi.org/10.1039/C2SM06903B>
- Singh, Y., Meher, J. G., Raval, K., Khan, F. A., Chaurasia, M., Jain, N. K., & Chourasia, M. K. (2017). Nanoemulsion: Concepts, development and applications in drug delivery. *Journal of Controlled Release*, 252, 28–49. <https://doi.org/10.1016/j.jconrel.2017.03.008>
- Savjani, K. T., Gajjar, A. K., & Savjani, J. K. (2012a). Drug Solubility: Importance and Enhancement Techniques. *ISRN Pharmaceutics*, 2012, 1–10. <https://doi.org/10.5402/2012/195727>
- Serajuddin, A. T. M. (2007). Salt formation to improve drug solubility. *Advanced Drug Delivery Reviews*, 59(7), 603–616. <https://doi.org/10.1016/j.addr.2007.05.010>
- Tadros, T., Izquierdo, P., Esquena, J., & Solans, C. (2004). Formation and stability of nano-emulsions. *Advances in Colloid and Interface Science*, 108–109, 303–318. <https://doi.org/10.1016/j.cis.2003.10.023>
- Strickley, R. G. (2004). Solubilizing Excipients in Oral and Injectable Formulations. *Pharmaceutical Research*, 21(2), 201–230. <https://doi.org/10.1023/B:PHAM.000016235.32639.23>
- Chaurasia, G. (2016). A review on pharmaceutical preformulation studies in formulation. *International Journal of Pharmaceutical Sciences and Research*, 7(6), 2313–2320. [https://doi.org/10.13040/IJPSR.0975-8232.7\(6\).2313-20](https://doi.org/10.13040/IJPSR.0975-8232.7(6).2313-20)
- Verma, G., & Mishra, M. K. (2016). Pharmaceutical preformulation studies in formulation and development of new dosage form: a review. *International Journal of Pharma Research & Review*, 5(10), 12–20.
- Bharate, S. S., & Vishwakarma, R. A. (2013). Impact of preformulation on drug development. *Expert Opinion on Drug Delivery*, 10(9), 1239–1257. <https://doi.org/10.1517/17425247.2013.783563>
- Dave, V. S., Haware, R. V., Sangave, N. A., Sayles, M., & Popielarczyk, M. (2015). Drug-excipient compatibility studies in formulation development: current trends and techniques. *American Association of Pharmaceutical Scientists*.
- Gurpreet, K., & Singh, S. K. (2018). Review of nanoemulsion formulation and characterization techniques. *Indian Journal of Pharmaceutical Sciences*, 80(5), 781–789. <https://doi.org/10.4172/pharmaceutical-sciences.1000422>
- Jaiswal, M., Dudhe, R., & Sharma, P. K. (2015). Nanoemulsion: An advanced mode of drug delivery system. *3 Biotech*, 5(2), 123–127. <https://doi.org/10.1007/s13205-014-0214-0>
- Solans, C., Izquierdo, P., Nolla, J., Azemar, N., & Garcia-Celma, M. J. (2005). Nano-Emulsions. *Current Opinion in Colloid & Interface Science*, 10(3–4), 102–110. <https://doi.org/10.1016/j.cocis.2005.06.004>
- Kumar, M., Bishnoi, R. S., Shukla, A. K., & Jain, C. P. (2019). Techniques for formulation of nanoemulsion drug delivery system: a review. *Preventive Nutrition and Food Science*, 24(3), 225–234. <https://doi.org/10.3746/pnf.2019.24.3.225>
- Kesisoglou, F., Panmai, S., & Wu, Y. (2007). Nanosizing—Oral formulation development and biopharmaceutical evaluation. *Advanced Drug Delivery Reviews*, 59(7), 631–644. <https://doi.org/10.1016/j.addr.2007.05.003>
- Leuner, C. (2000). Improving drug solubility for oral delivery using solid dispersions. *European Journal of Pharmaceutics and Biopharmaceutics*, 50(1), 47–60. [https://doi.org/10.1016/S0939-6411\(00\)00076-X](https://doi.org/10.1016/S0939-6411(00)00076-X)
- Merisko-Liversidge, E., Liversidge, G. G., & Cooper, E. R. (2003). Nanosizing: a formulation approach for poorly-water-soluble compounds. *European Journal of Pharmaceutical Sciences*, 18(2), 113–120. [https://doi.org/10.1016/S0928-0987\(02\)00251-8](https://doi.org/10.1016/S0928-0987(02)00251-8)
- Pouton, C. W. (2000). Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and ‘self-microemulsifying’ drug delivery systems. *European Journal of Pharmaceutical Sciences*, 11, S93–S98. [https://doi.org/10.1016/S0928-0987\(00\)00167-6](https://doi.org/10.1016/S0928-0987(00)00167-6)
- Qian, C., Decker, E. A., Xiao, H., & McClements, D. J. (2012). Physical and chemical stability of β -carotene-enriched nanoemulsions: Influence of pH, ionic strength, temperature, and emulsifier type. *Food Chemistry*, 132(3), 1221–1229. <https://doi.org/10.1016/j.foodchem.2011.11.091>
- Silva, H. D., Cerqueira, M. Â., & Vicente, A. A. (2012). Nanoemulsions for Food Applications: Development and Characterization. *Food and Bioprocess*

- Technology, 5(3), 854–867. <https://doi.org/10.1007/s11947-011-0683-7>
23. Teixeira, M. C., Severino, P., Andreani, T., Boonme, P., Santini, A., Silva, A. M., & Souto, E. B. (2017). d- α -tocopherol nanoemulsions: Size properties, rheological behavior, surface tension, osmolarity and cytotoxicity. *Saudi Pharmaceutical Journal*, 25(2), 231–235. <https://doi.org/10.1016/j.jsps.2016.06.004>
24. Zielińska, A., Carreiró, F., Oliveira, A. M., Neves, A., Pires, B., Venkatesh, D. N., Durazzo, A., Lucarini, M., Eder, P., Silva, A. M., Santini, A., & Souto, E. B. (2020). Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology. *Molecules*, 25(16), 3731. <https://doi.org/10.3390/molecules25163731>
25. Ajayi, T. O., Poka, M. S., & Witika, B. A. (2024). Development of bedaquiline nanoemulsions intended for paediatric multidrug-resistant tuberculosis: excipient selection and preformulation studies. *Frontiers in Medical Technology*, 6, 1388113. <https://doi.org/10.3389/fmedt.2024.1388113>
26. Ajayi, T. O., Poka, M. S., & Witika, B. A. (2024). Formulation and optimisation of bedaquiline nanoemulsions for the potential treatment of multi drug resistant tuberculosis in paediatrics using quality by design. *Scientific Reports*, 14, 31891. <https://doi.org/10.1038/s41598-024-83408-1>