COREALIS Pharma

ENHANCING LUMEFANTRINE BIOAVAILABILITY THROUGH VERTICAL HOT MELT EXTRUSION

An Optimized Approach to Pediatric Malaria Treatment

WHITEPAPER JANUARY 2026
PRESENTED AT AAPS 2025

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INTRODUCTION

Executive Summary

Every minute, a child under five dies from malaria. While Lumefantrine remains a cornerstone in first-line treatment, its poor solubility and dependence on dietary fats severely limit therapeutic exposure in children—particularly in fasting or malnourished conditions.

Corealis Pharma, in collaboration with **Rondol Industrie** and **Institut Jean Lamour**, investigated the use of Vertical Hot Melt Extrusion (VHME) to produce amorphous solid dispersions (ASDs) of Lumefantrine. The study demonstrated a six-fold increase in dissolution, enhanced flowability, and robust stability under stress conditions, confirming VHME as a viable, scalable, and energy-efficient platform for developing child-friendly antimalarial formulations.

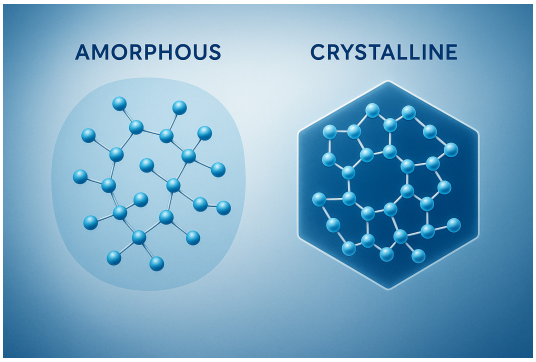
Introduction

Malaria continues to pose a significant global health challenge, particularly in pediatric populations. The World Health Organization (WHO) recommends artemether–lumefantrine combination therapies as the first-line treatment. However, Lumefantrine's low aqueous solubility and fed-state dependence complicate dose accuracy and therapeutic consistency in children. (1)

Corealis Pharma's research addresses two of the most persistent formulation challenges in modern drug development:

1. Enhancing bioavailability and solubility of poorly water-soluble APIs such as Lumefantrine.
2. Designing robust, child-friendly dosage forms that maintain efficacy and stability even in the absence of dietary fats or optimal intake conditions.

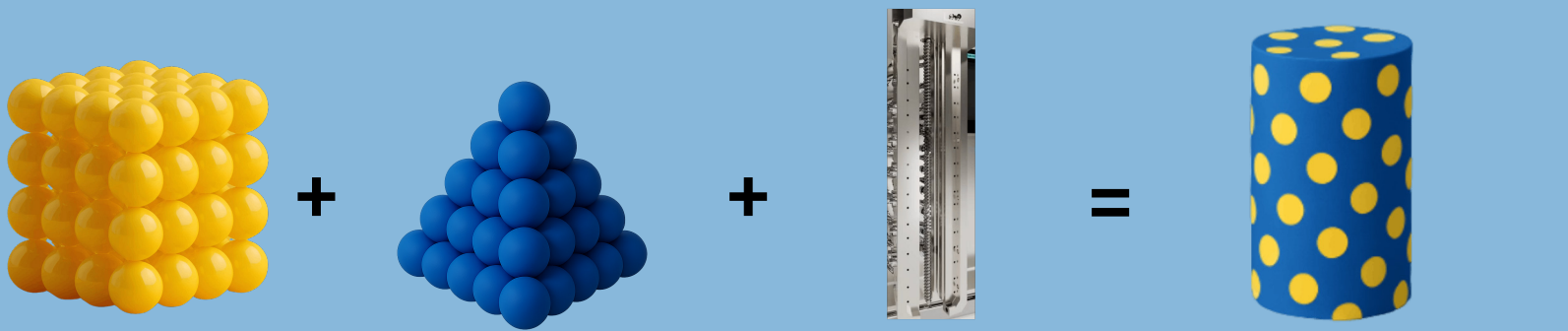
Developing amorphous solid dispersions (ASDs) represents a promising strategy to enhance solubility and bioavailability of poorly



water-soluble drugs. Vertical Hot Melt Extrusion (VHME), an emerging continuous manufacturing process, enables precise control of temperature and shear forces, resulting in homogeneous dispersions with improved process scalability and energy efficiency. (2)

Corealis Pharma leveraged its formulation development and process optimization expertise to evaluate the potential of VHME in producing stable Lumefantrine ASDs suitable for pediatric use.

METHODS



Pure Lumefantrine (cristalline)

Soluplus® (polyvinyl caprolactam–polyvinyl acetate–polyethylene glycol graft copolymer)

Vertical Hot Melt Extruder: Barrels + Liners + Twin Screw

Amorphous Solid Dispersion Lumefantrine + Soluplus®

Methods

Amorphous solid dispersions (ASDs) were prepared using a Rondol Vertical Twin-Screw Extruder (10.5 mm, 40:1 L/D). Two formulations were produced:

Ingredient	Formulation A (% w.w	Formulation B (% w.w)
Lumefantrine	25.0	50.0
Soluplus®	75.0	50.0

Key processing parameters—including temperature profile, screw design, and feed rate—were optimized to ensure homogeneous extrusion and drug stability. Comprehensive char`acterization included XRPD, DSC/TGA, SEM, powder flow properties, compactability, hygroscopicity, and solubility/dissolution testing.

Vertical All in One twin screw extruder 10.5mm 40:1 L:D

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RESULTS & DISCUSSION

Amorphous Conversion and Stability:

XRPD confirmed complete transformation of crystalline Lumefantrine into amorphous form for both ASDs, with no recrystallization observed after thermal and mechanical stress testing.

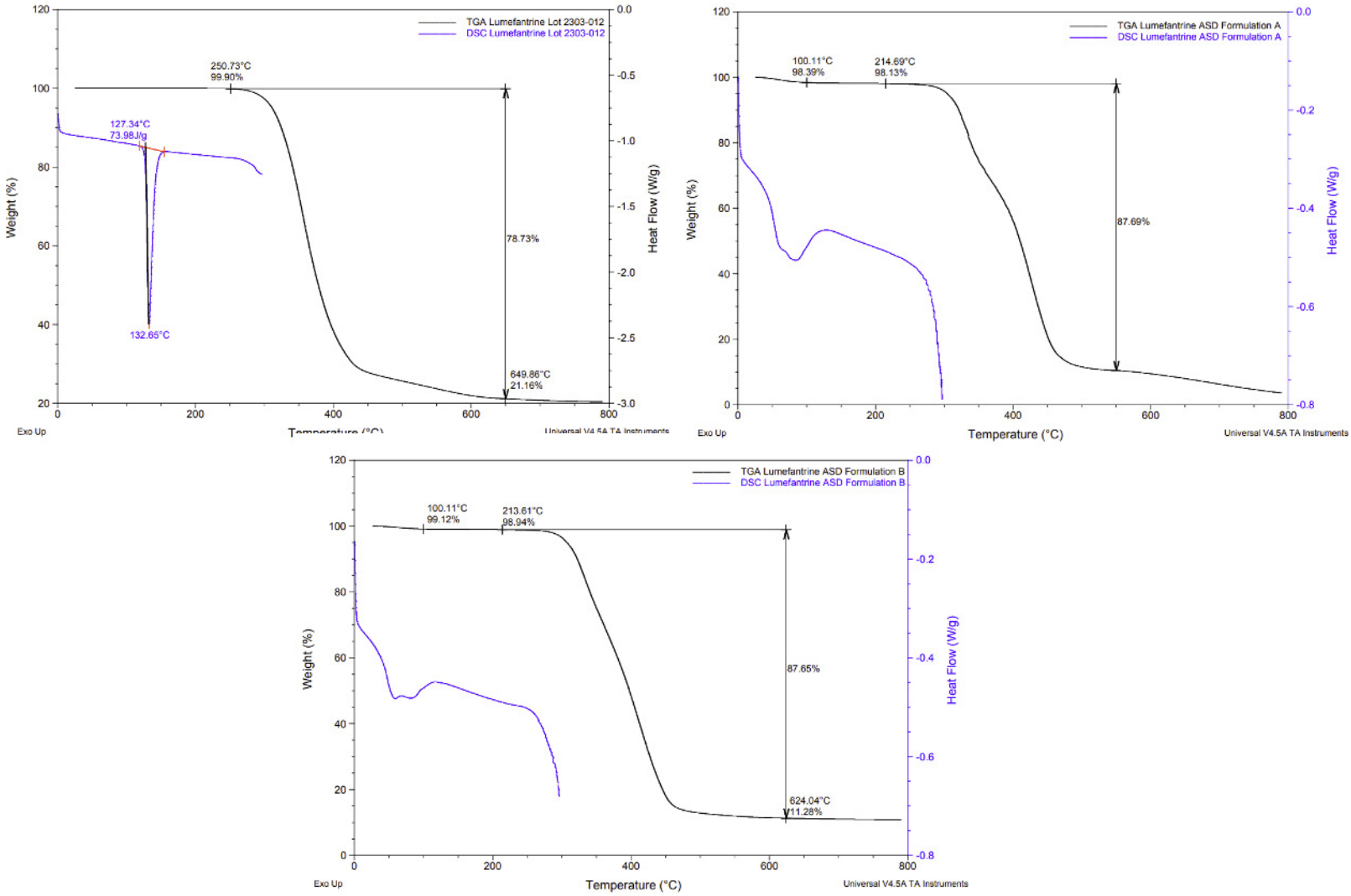

Figure 2. Thermal profiles of Lumefantrine API (D), ASD Formulation A (E), and B (F).

RESULTS & DISCUSSION

Improved Powder and Tablet Properties:

Both ASDs demonstrated superior bulk density and flow behavior (Hausner ratio ≤1.17), translating into consistent die filling and tablet uniformity. Tablet hardness increased markedly when ASDs were blended with MCC, reaching ~22 kp compared to <2 kp for the API.

Enhanced Solubility and Dissolution:

Lumefantrine API showed <1 µg/mL solubility. The 25% ASD achieved ~25 µg/mL solubility in water—a 25-fold increase. In 0.1N HCl, the same formulation exhibited a **six-fold** improvement in dissolution versus crystalline API.

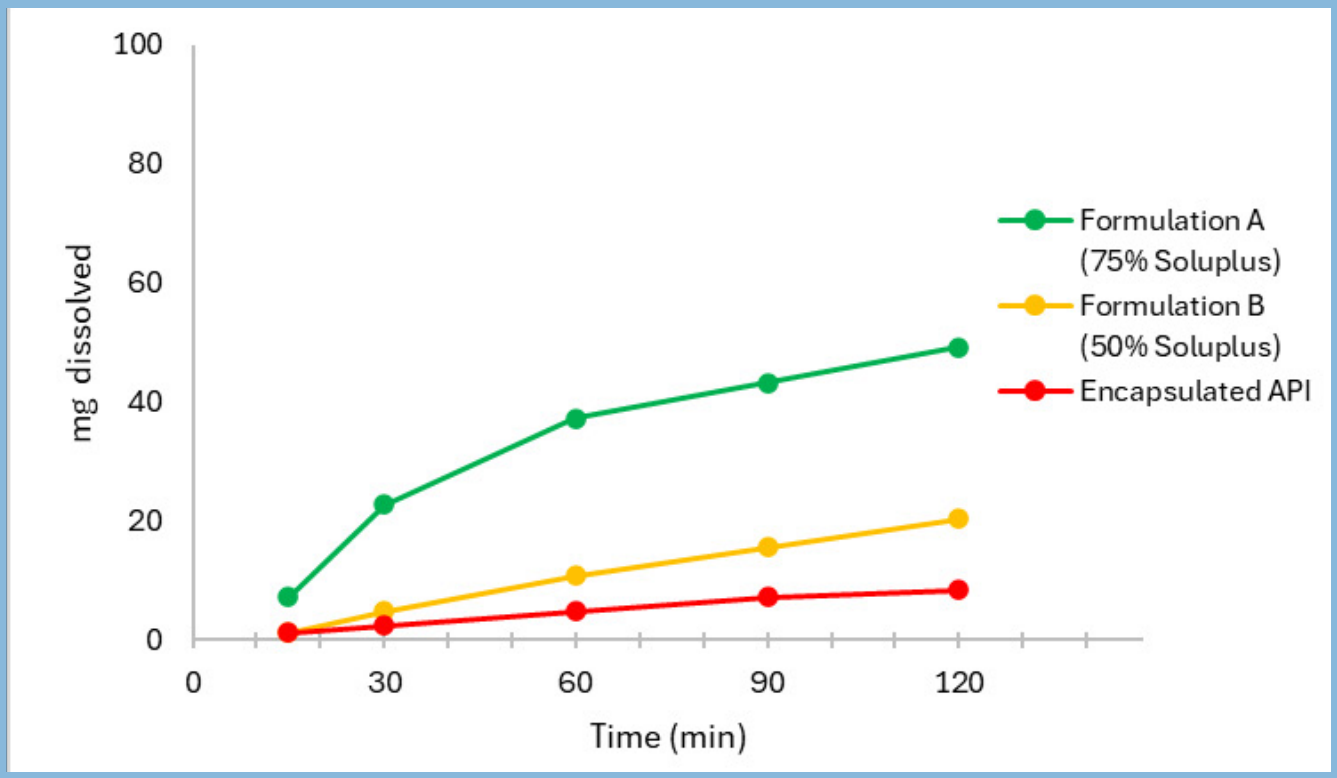

Figure 3. Dissolution profiles of powder loaded capsules: 120 mg in 900mL of 0.3% SDS / 0.1N HCl paddles at 100 rpm

RESULTS & DISCUSSION

Feasibility of High Drug Loading

While the 25% ASD offered optimal solubility–hygroscopicity balance, the 50% formulation validated the technical feasibility of high-load extrudates, key for dose-intensive APIs.

Energy and Process Efficiency

The vertical configuration of the Rondol extruder minimized thermal exposure and footprint, making VHME a sustainable, scalable manufacturing approach aligned with Corealis' continuous process innovation initiatives.

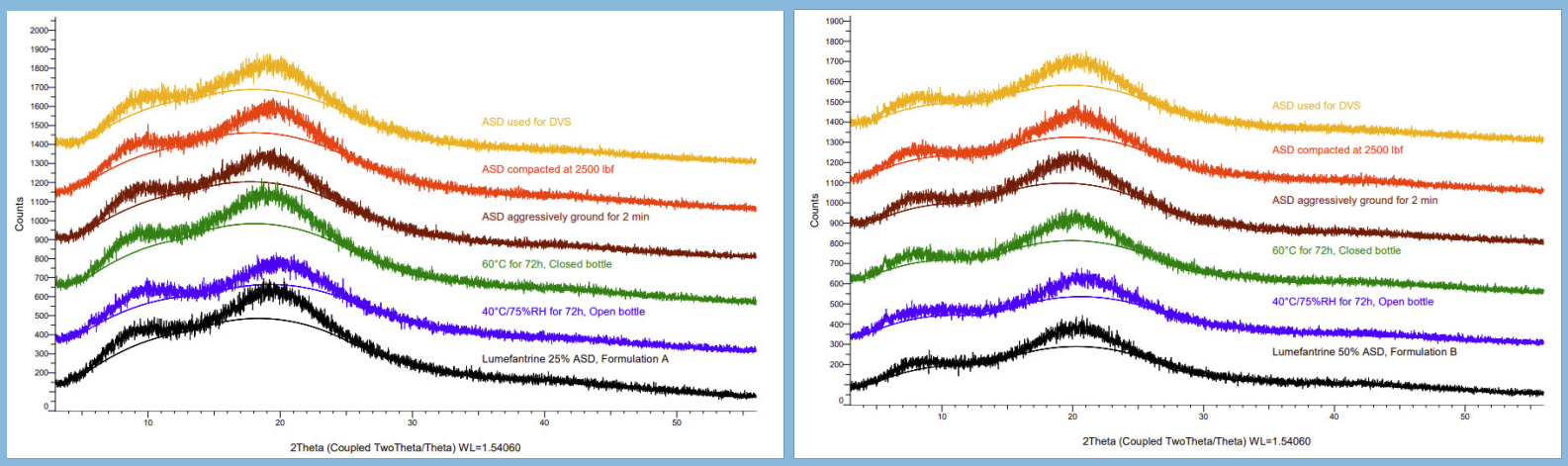

Figure 1. XRPD diffractograms of Lumefantrine API (A), ASD Formulation A (B), and B (C)

RESULTS & DISCUSSION

Particle Morphology

The SEM micrographs revealed that Lumefantrine and ASD formulation A and B were composed of different large irregular particles.

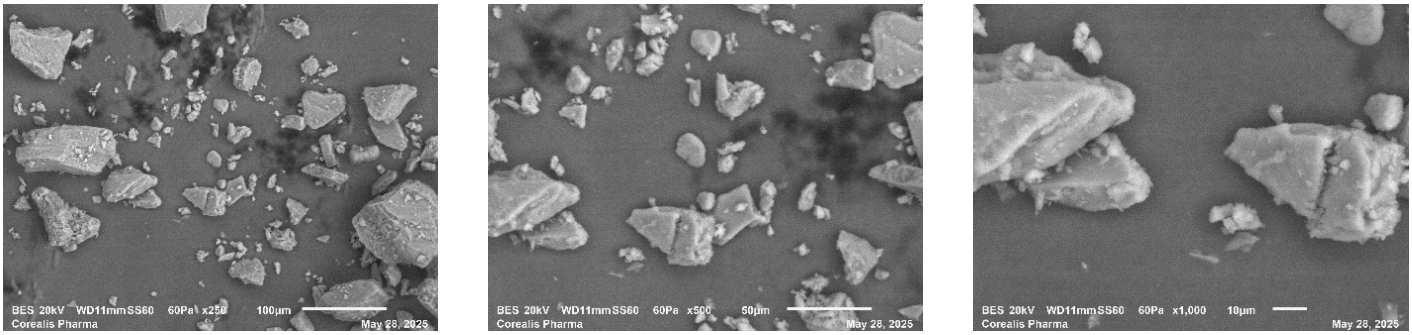

Figure 1: Scanning electron micrographs of Lumefantrine Lot 2303-012 as received at magnification 250X (left), 500X (middle), and 1000X (right).

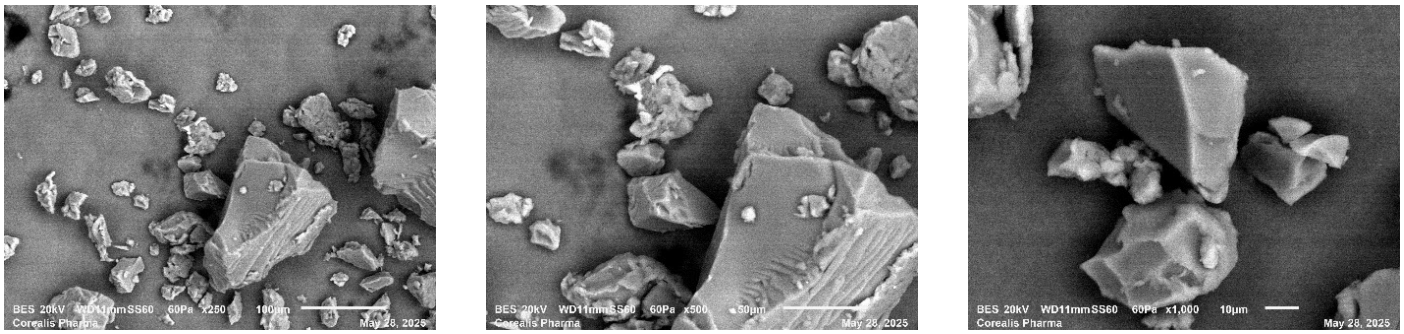

Figure 2: Scanning electron micrographs of Lumefantrine ASD formulation A at magnification 205X (left), 500X (middle), and 1000X (right).

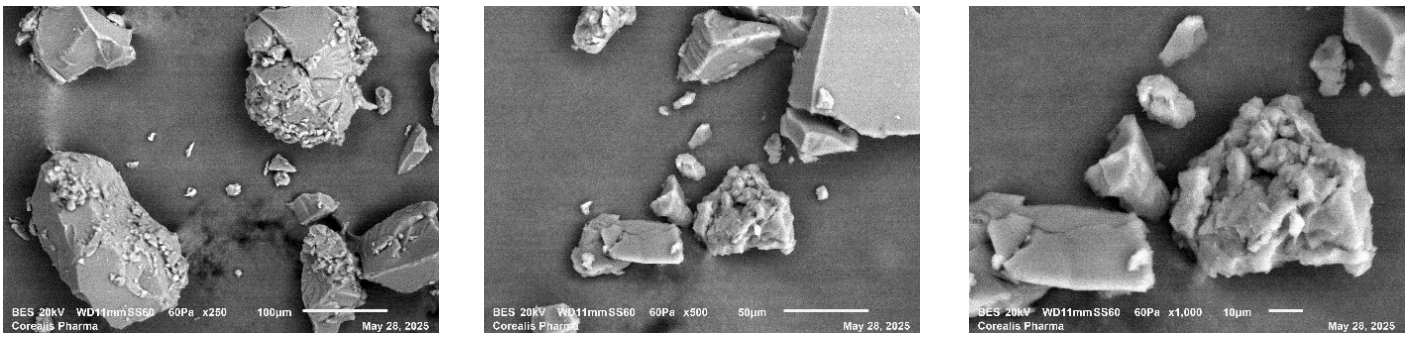

Figure 3: Scanning electron micrographs of Lumefantrine ASD Formulation B at magnification 250X (left), 500X (middle), and 1000X (right).

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CONCLUSION

This collaborative study confirmed that Vertical Hot Melt Extrusion (VHME) is an effective, scalable method to enhance the solubility and manufacturability of poorly soluble Lumefantrine antimalarial drugs.

The 25% Lumefantrine ASD formulation demonstrated superior solubility, stability, and compressibility, offering a strong candidate for pediatric oral solid dosage development. VHME further provides a continuous, energy-efficient pathway for producing high-quality ASDs and expanding access to improved global health treatments.

Corealis Pharma demonstrated a significant enhancement in drug product performance, particularly by improving the solubility of a pediatric formulation.

ABOUT COREALIS PHARMA

Corealis Pharma Inc., based in Laval, Canada, is a specialized CDMO focused on Oral Solid Dose (OSD) development. With expertise in Hot Melt Extrusion, Pre-formulation, and Clinical Trial Supply, Corealis supports clients from early R&D through GMP manufacturing, packaging, and global distribution. The company's mission is to advance innovative, practical solutions for complex formulation challenges—empowering clients to bring better therapies to patients worldwide.

References

1. WHO. WHO guidelines for malaria (consolidated version, 13 August 2025).

2. Li, S., Zhang, Z., Gu, W., Gallas, M., Jones, D., Boulet, P., Johnson, L.M., de Margerie, V., & Andrews, G.P. Hot melt extruded high-dose amorphous solid dispersions containing lumefantrine and Soluplus. Int. J. Pharm. 665, 124676, (2024).

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