Entinostat-Loaded PLGA Microparticles for Local Mesothelioma Therapy

Obaida Qatawy, Ofra Benny

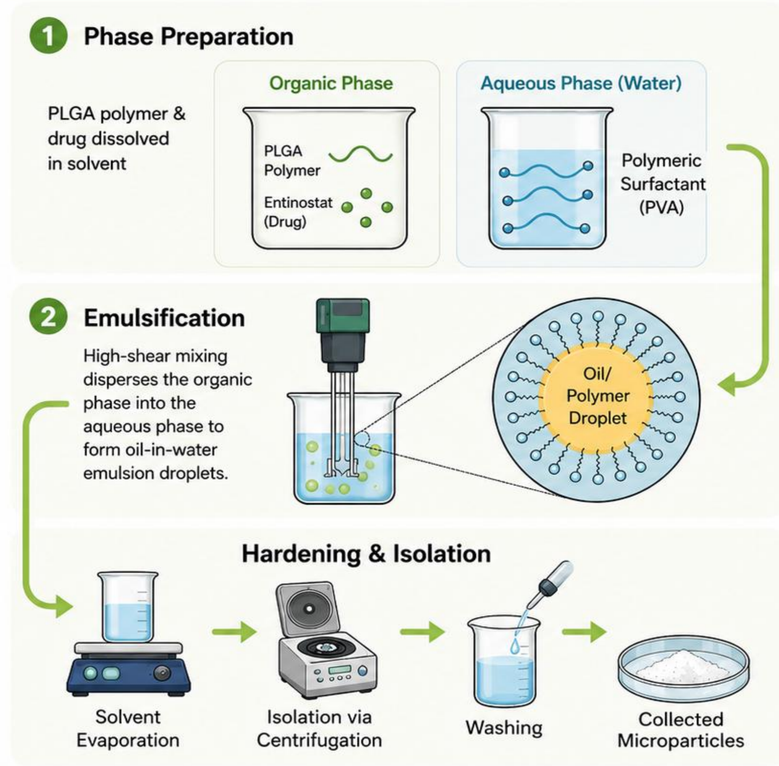
Institute for Drug Research, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem

The Clinical Challenge

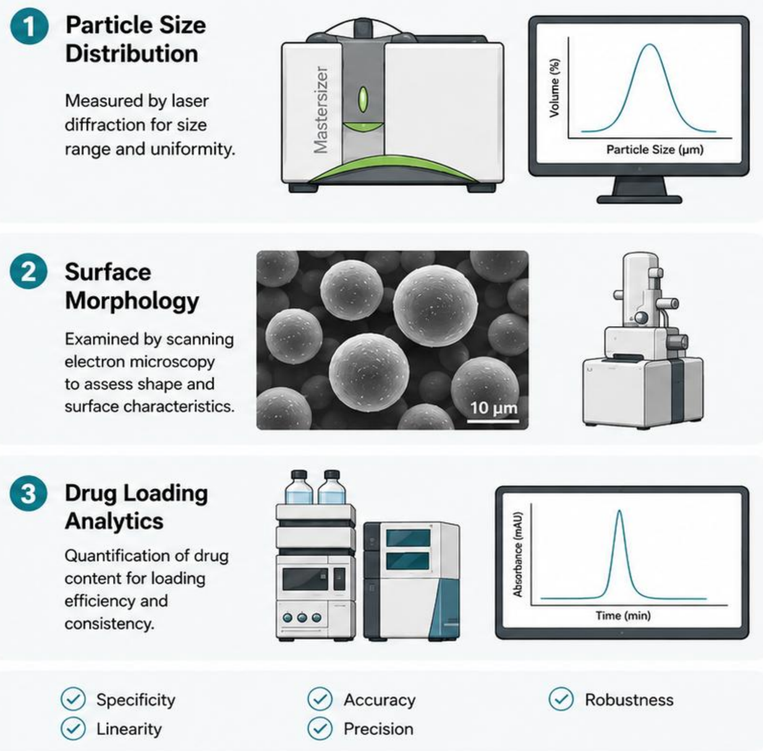
Systemic delivery of the epigenetic drug Entinostat is limited by severe toxicities, while free local injection suffers from rapid lymphatic clearance. To overcome this, biodegradable PLGA microparticles were developed as a sustained-release matrix to stabilize the payload locally. This platform is engineered for cancers that create fluid-filled compartments around themselves, such as Malignant Mesothelioma. Designing the carrier within a precise 2-5 µm size window enables it to evade lymphatic drainage, maximizing long-term regional retention within these specialized anatomical spaces.

Experimental Design

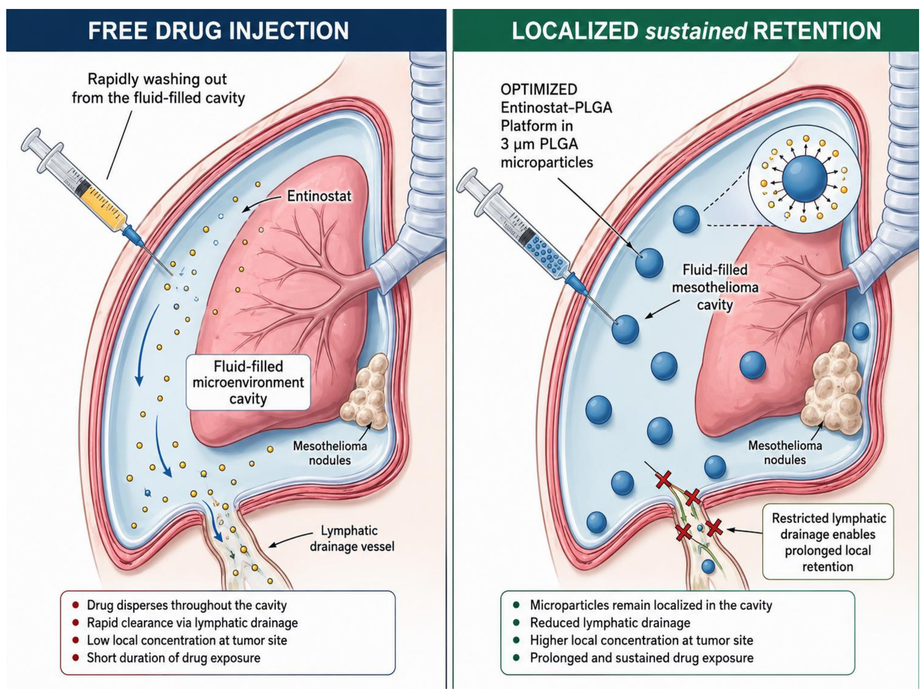
Part A: Microparticle Fabrication



Part B: Physicochemical Evaluation



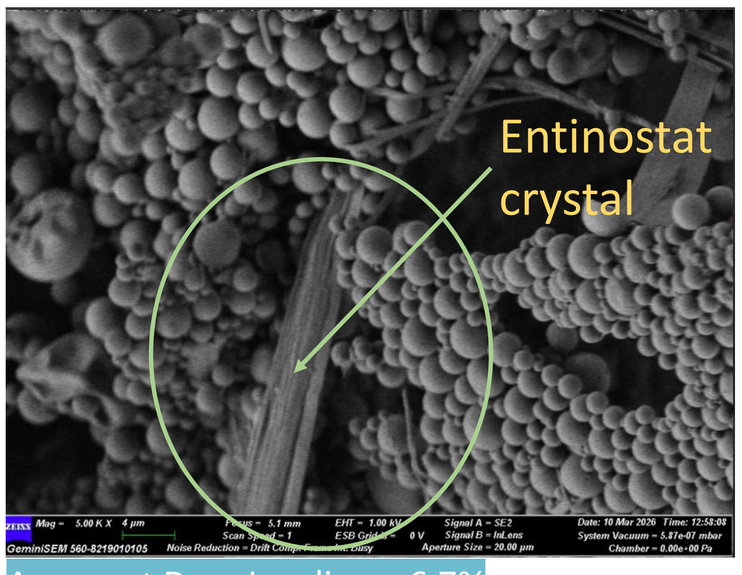
The Scientific Basis: Located Therapy



Localized retention of Entinostat via PLGA microparticles improves drug residence within the pleural cavity compared with free drug injection, enabling sustained release and enhanced tumor exposure.

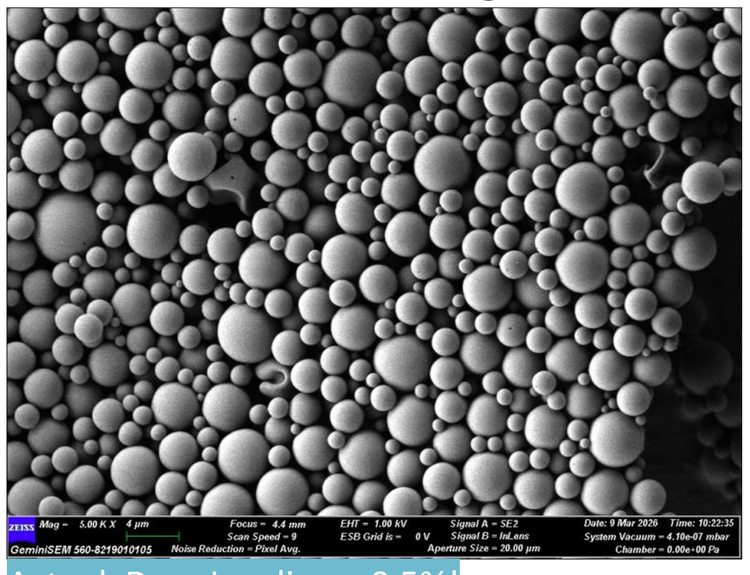
Primary Results and Challenges

Before Washing



Apparent Drug Loading = 6.7%

After Washing



Actual Drug Loading = 0.5%!

Although primary HPLC loading results revealed high drug loading of 6.7%, SEM results revealed drug crystals outside the particles which indicate false positive loading . Thus particles were washed with methanol, which does dissolve the drug but not the PLGA, then particle drug loading reveled results of 0.5% loading

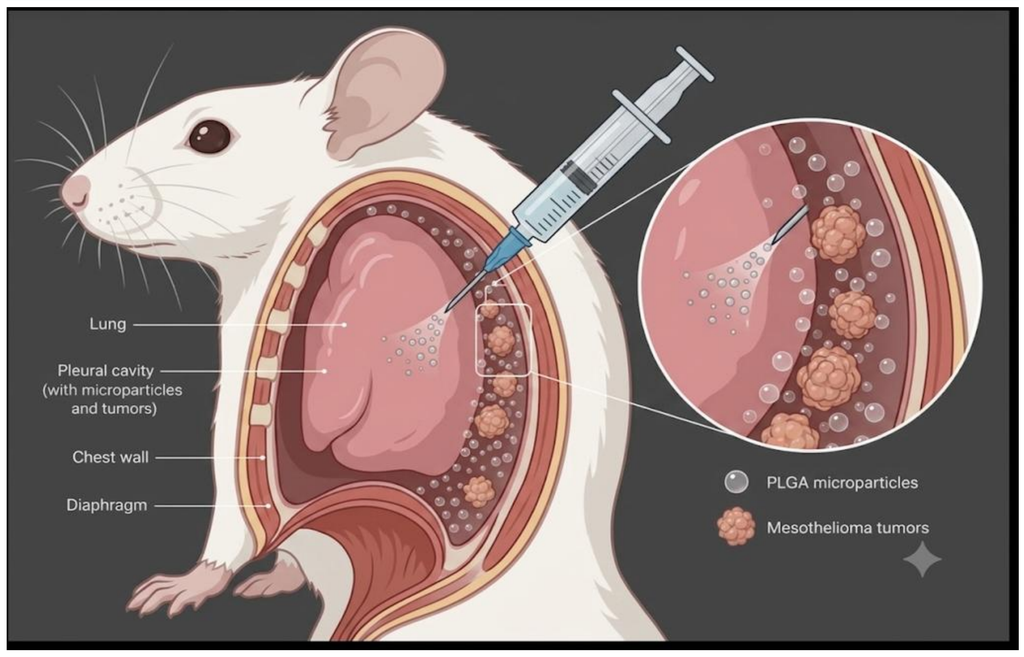
New Approaches to Overcome Encapsulation Challenges

Oil in Oil formulation in development to overcome drug solubility in outer Aqua media (Entinostat logD=1.8).

Summary

Initial O/W processing showed an apparent 6.7% drug loading, but SEM analysis revealed unencapsulated Entinostat crystals precipitating on particle surfaces. Removing these surface crystals via a methanol wash caused true loading to drop to 0.5%, confirming severe drug leakage into the aqueous phase. This limitation justified pivoting to a non-aqueous Oil-in-Oil (O/O) framework to eliminate migration and maximize internal encapsulation.

Future Experiments



Testing the PLGA-Entinostat formulation on Mesothelioma-model mice

Contact:
Ofra.Benny@mail.huji.ac.il
Tel: +972-2-6757268

Obaida.qatawy@mail.huji.ac.il
LinkedIn Obaida Qatawy