Micro-imaging and Microanalysis of PLGA Complex Drug Products by Scanning Electron Microscopy (SEM)

Jing Liang[1,2], Yan Wang[1], Bin Qin[1], Jia Zhou[3], Steven Schwendeman[3], Jiwen Zheng[2]

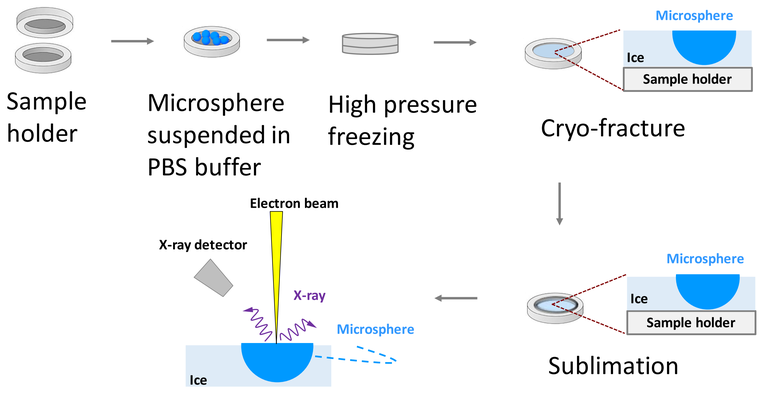
[1.] Office of Research and Standards, Office of Generic Drugs, Center for Drug Evaluation and Research, U.S. FDA, Silver Spring, MD
[2.] Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, U.S. FDA, Silver Spring, MD
[3.] Department of Pharmaceutical Sciences, The Biointerfaces Institute, University of Michigan, Ann Arbor, MI

INTRODUCTION

Due to its outstanding biocompatibility and biodegradability, poly(lactide-co-glycolide) (PLGA) has been extensively used in FDA-approved long-acting drug products (e.g., microspheres and implants). Despite the vast demand, there is no generic PLGA drug products on the U.S. market yet. One of the reasons is the complexity associated with formulation design and physicochemical characterization. It has been well recognized that microstructure/porosity of PLGA matrix plays an important role on drug release and PLGA degradation. However, determining porosity and inner microstructure is often challenging. The goal of the current project was to explore using regular room temperature scanning electron microscope (SEM) and cryo-SEM to characterize both external and internal morphology of in-house prepared PLGA microspheres containing leuprolide acetate and a commercial product (Lupron Depot®, 7.5 mg).

METHODS

- Samples:
  - Lupron Depot® (leuprolide acetate for depot suspension), 7.5 mg
  - In-house leuprolide acetate encapsulated PLGA microspheres (standard condition microspheres in reference [2])
- Components (C: carbon; H: hydrogen; O: oxygen; N: nitrogen.)
  - PLGA (contains C, H, O)
  - Leuprolide acetate (contains C, H, O, N)
  - Gelatin (contains C, H, O, N)
  - Mannitol (contains C, H, O)
- Room temperature SEM/Energy-dispersive X-ray spectroscopy (EDS)
  - External structures
  - Internal structures by razor blade cutting
- Cryogenic –SEM/EDS



Cryo-SEM at -145°C : Imaging; EDS

RESULTS

- SEM/EDS: External morphology and compositional microanalysis

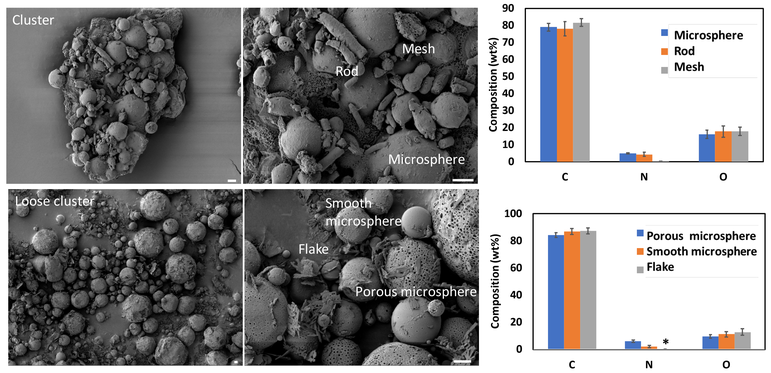
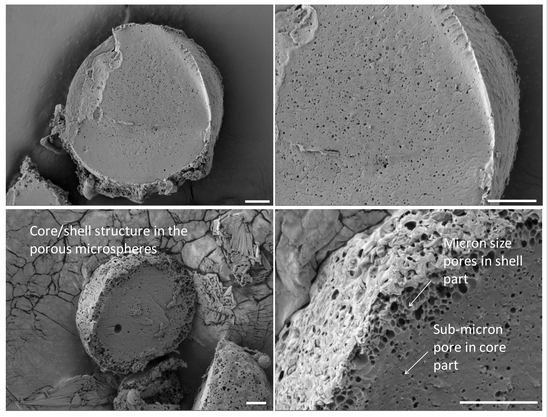


Fig. 1. Room temperature SEM images of Lupron Depot with compositional microanalysis (top) and in-house formulated PLGA microsphere with compositional microanalysis (bottom). All scale bars = 5 µm. EDS: E_0= 5kV. Data are presented as mean ± SD.

- SEM: Internal morphology

Fig. 2. Room temperature SEM images of Lupron Depot cross-section (top) and in-house formulated PLGA microsphere cross-section (bottom). All scale bars = 5 µm. The cross-section is created by razor blade.



- Cryo-SEM: Internal morphology

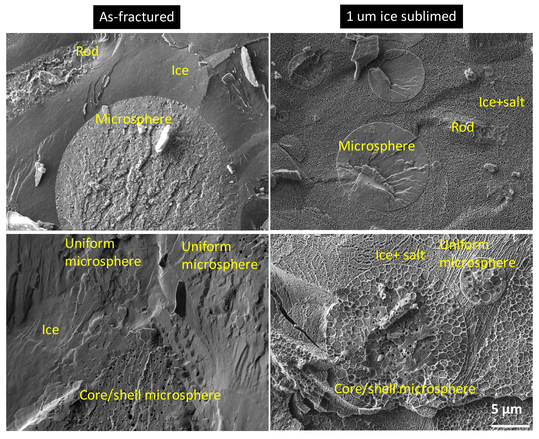


Fig. 3. Cryo-SEM images of Lupron Depot suspension (top) and in-house formulated PLGA microsphere suspension (bottom) with as-fractured cross-section (left) and 1 µm ice sublimed cross-section (right).

RESULTS

- Cryo-SEM/EDS: Compositional microanalysis and water permeability

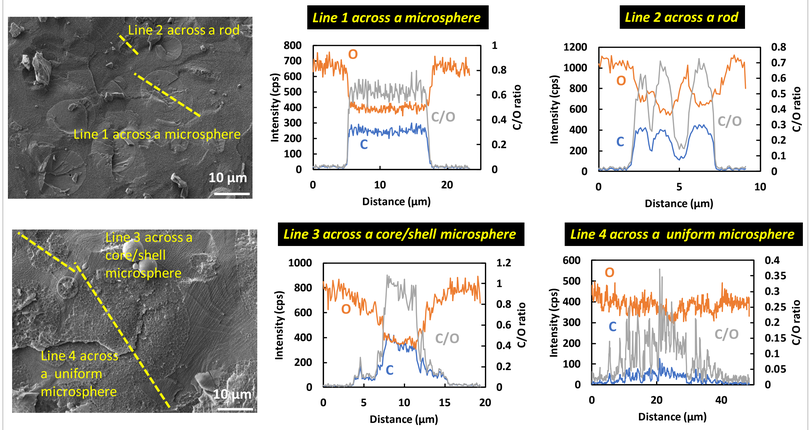


Fig. 4. Cryo-SEM images of Lupron Depot with compositional microanalysis (top) and in-house formulated PLGA microsphere with compositional microanalysis (bottom); ~1 µm ice removed. EDS line scan profile of carbon (blue), oxygen (orange) and C/O ratio (grey) with E_0= 5kV.

CONCLUSIONS

- Lupron Depot is consisted of microspheres with non-permeable pores, water-permeable rods and mannitol in mesh form.
- In-house formulation is consisted of microspheres with water-permeable pores and mannitol in flake form.
- C/O ratio detected by cryo-SEM/EDS could be used to map water distribution and shed light on water permeability.

DISCLAIMER

The views expressed in this poster do not necessarily reflect the official policies of the U.S. Food and Drug Administration; nor does any mention of trade names, commercial practices, or organization imply endorsement by the United States Government.

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