HIGH-THROUGHPUT ELECTRONEBULIZATION FOR THE SCALABLE PRODUCTION OF CONTROLLED-RELEASE PARTICLES

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INTRODUCTION

Polymeric particles:

- Widely used to increase stability and control release of active pharmaceutical ingredients (APIs) in Long-Acting Injectables (LAI) for Subcutaneous (SQ) applications

ELECTRONEBULIZATION[1]:

- Proprietary encapsulation technology[1]:

Innovative, high-throughput (L/h-scale) nebulization of polymer/API solutions within an electric field at temperatures of 30°C or below

- Main characteristics of the technique:
  - ➢ controlled particle morphology and architecture, e.g., core-shell
  - ➢ continuous process
  - ➢ encapsulated material is collected as a free-flowing powder
  - ➢ non-thermal process
  - ➢ ideal for labile APIs, such as biotherapeutics
  - ➢ scalable to any batch size

METHODS

Particle Production:

- Production of polymeric particles encapsulating various APIs at different throughput rates using the proprietary Capsultek® electronebulization technology
- Processing performed at ≤30°C to enable low-temperature particle formation

- Particle Formulation:
  - Single-polymer and polymer-blend systems
  - Various core-shell architectures
  - Different processing conditions to tailor particle properties and release profiles

Model Active Pharmaceutical Ingredients (APIs):

- Caffeine
- A commercially available small-molecule drug

Particle Characterization:

- Particle morphology and size distribution by scanning electron microscopy (SEM)

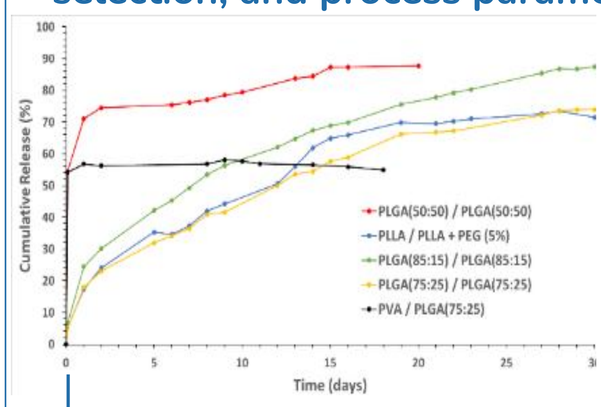
***In Vitro* Drug Release:**

- *In vitro* drug-release kinetics evaluated under simulated subcutaneous (SQ) conditions at 37°C
- API release quantified by UV-Visible spectroscopy

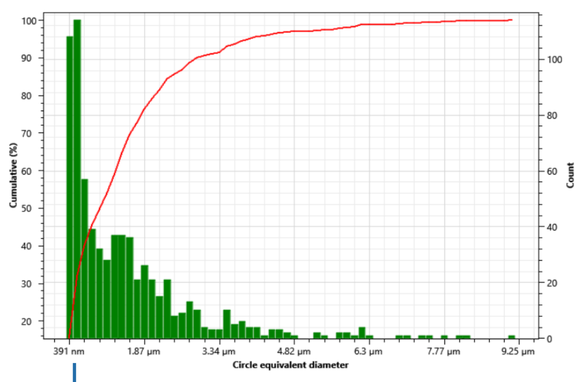
RESULTS

- Electronebulization successfully produced submicron- and micron-sized polymeric particles across a broad range of polymer compositions, polymer blends, core-shell configurations, and processing conditions.

- SEM characterization and *In vitro* release studies revealed that both particle morphology and drug-release kinetics were highly dependent on polymer composition, solvent selection, and process parameters.



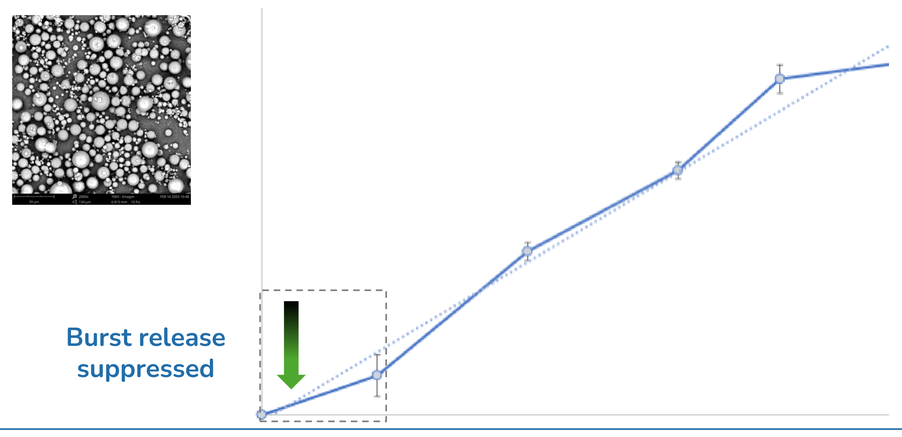
SQ simulation of caffeine release from the various particle compositions:



Typical particle size distribution by SEM

- PLGA(50:50)/PLGA(50:50):
  the fastest profile
  ~70–75% by day 1; plateau at ~86–87% by ~15–20 days
- PLGA(85:15)/PLGA(85:15):
  more gradual release
  ~25-30%: day 1, ~75%: ~20 days, ~85%: ~28-30 days
- PLGA(75:25)/PLGA(75:25) and PLLA/PLLA+PEG (5%):
  intermediate release
  increase to ~70–73% by ~28–30 days
- PVA/PLGA(75:25):
  limited progression after the initial phase
  ~55–57% over ~5–20 days

Accelerated *in vitro* evaluation of LAI API particles predicting 6-month subcutaneous sustained release:



CONCLUSION

- Electronebulization enabled the high-throughput production of diverse polymeric particles with tunable properties governed by polymer composition and processing conditions.

- By optimizing polymer selection and processing parameters, sustained drug release over extended periods was achieved, demonstrating the potential of this technology as a versatile platform for the development of long-acting injectable (LAI) drug formulations.

References
[1]Prieto, C., Evtoski, Z., Pardo-Figuerez, M., Hrakovsky, J., Lagaron, J. M. (2021). Nanostructured valsartan microparticles with enhanced bioavailability produced by high-throughput electrohydrodynamic room-temperature atomization. Molecular Pharmaceutics, 18(8), 2947-2958.

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