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Wang, Yajie

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NANYANG TECHNOLOGICAL UNIVERSITY

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Category: 6 **Student: Wang Yajie** **Project ID: SCBE10030**
School of Chemical and Biomedical Engineering

Aqueous Re-dispersibility of Spray-dried Antibiotic-loaded PLGA Nanoparticle Aggregates for Inhaled Anti-biofilm Therapy

Introduction:

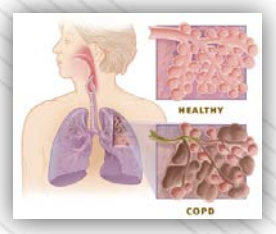


Fig. 1: Infected COPD lungs vs. healthy lungs Source:

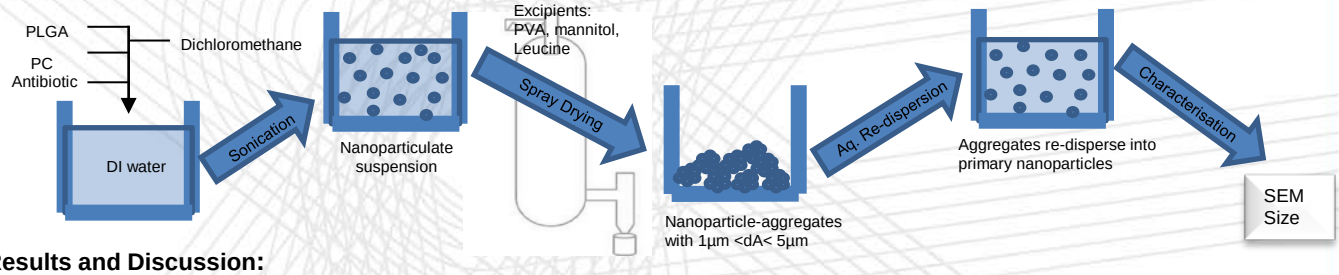
Chronic obstructive pulmonary disease is the fourth leading cause of death globally (Fig. 1). Inhaled antibiotic-loaded nanoparticles (NPs) have emerged as an attractive lung biofilm infection therapy for NPs can penetrate mucus layer surrounding biofilm colonies. NPs made from Poly(lactic-co-glycolic acid) (PLGA), with phosphatidylcholine (PC) as the surfactant (i.e. PLGA-PC) is a biodegradable and biocompatible vehicle for drug delivery. The dry-powder inhaler (DPI) (Fig. 2) is chosen as the delivery platform due to it's high delivery efficiency and stability. To formulate nano-aggregates with aerodynamic characteristics ideal for an effective lung deposition, NP suspension is transformed to DPI by the spray drying technique with different excipients to form aggregates with aerodynamic diameter (d_A) between 1 – 5 µm. The nano-aggregates are specifically designed to re-disperse upon inhalation and transportation to the target.

Fig. 2: DPI for inhalation of NPs Source:

Objective:

To investigate the effect of excipients formulation, poly(vinyl alcohol) (PVA), mannitol and leucine on the re-dispersibility of PLGA-PC nano-aggregates by testing the ratio of diameter of aggregates after re-dispersion (S_f) to diameter of nanoparticles (S_i). $S_f/S_i < 1.5$ is desirable.

Methodology:



Results and Discussion:

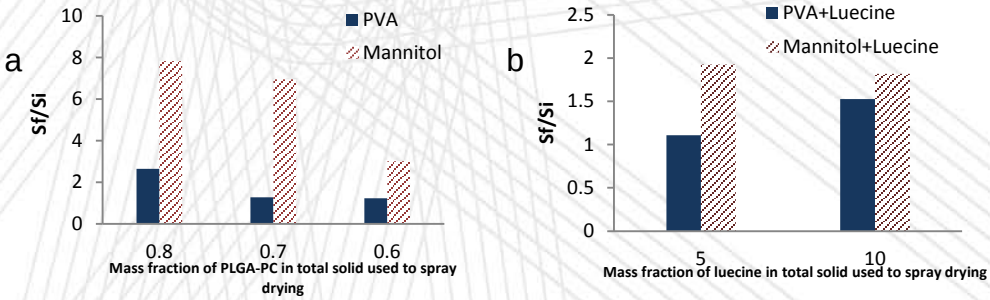


Fig 3. S_f/S_i of aggregates made from (a) NP+PVA or mannitol (b) 60%NP + PVA/Leucine or Mannitol/Leucine

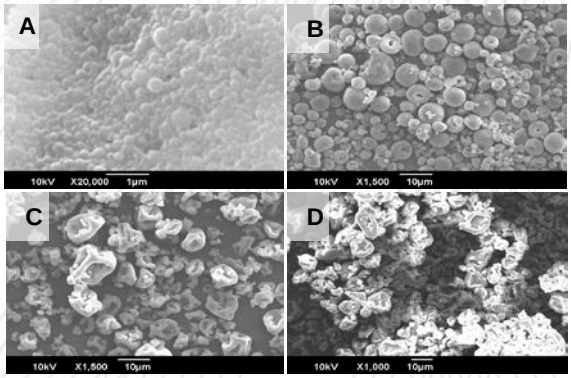


Fig 4. SEM images of (A) PLGA-PC; nanoparticle-aggregates from spray drying 60 w% PLGA-PC nanoparticle suspension with excipients (B) mannitol + Leucine (C) PVA + Leucine (D) PVA only

- Re-dispersibility increases as mass fraction of excipients increasing. PVA makes aggregates be in good redispersibiliy while mannitol could not redisperse aggregates.
- Leucine makes aggregates less cohesive. It improves re-dispersibility at low % while decreases re-dispersibility at high %.
- Aggregates from 60 w% NP, 35%PVA and 5% leucine has best re-dispersion property (S_f/S_i ≈1.11).

Conclusion:

The kinds and the amount of excipients will affect the morphology and re-dispersibility of nanoparticle-aggregates. Ideal nanoparticle-aggregates can be made with PVA and Leucine as excipients. While the re-dispersibility of the nano-aggregates has been achieved, the aggregates will next have to be tested for their aerosol properties, by using (i) flowability and (ii) cascade impactor test.

Project Title: Antibacterial Efficacy of Antibiotic-loaded Nanoparticles against Biofilm Infections by Respiratory Pathogens

Supervisor: Asst Prof Kunn Hadinoto **Collaborators: Katherine Kho, Wean Sin Cheow**