A Comparison of Different Particle Deposition Methods on Dissolution using Transwell® Setup

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Introduction

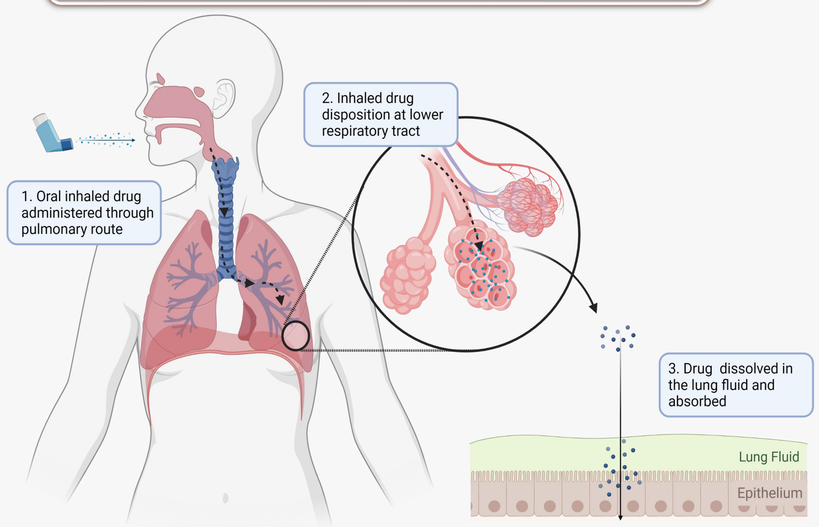

Figure 1. Schematic illustration of drug fate after administration to the lungs

In order to develop drug formulations that will demonstrate efficacy after pulmonary drug delivery, relevant *in vitro* methods that predict drug fate in the lungs are required. The fate of the inhaled drug in the lungs depends on aerosol properties, particle deposition, dissolution, and absorption. It is interesting to consider whether the drug deposition mechanisms that influence particle deposition on the lung surface can affect drug dissolution and absorption.

Particles between 1 – 5 µm diameter size are expected to deposit in the lungs via two mechanisms, impaction and sedimentation. Different particle collection methods can be used to study the impact of different mechanisms of deposition when capturing the aerosol particle sizes that deposit in the lungs.

Aim

To investigate the effect of different particle deposition mechanism on *in vitro* dissolution using a Transwell® system

Method

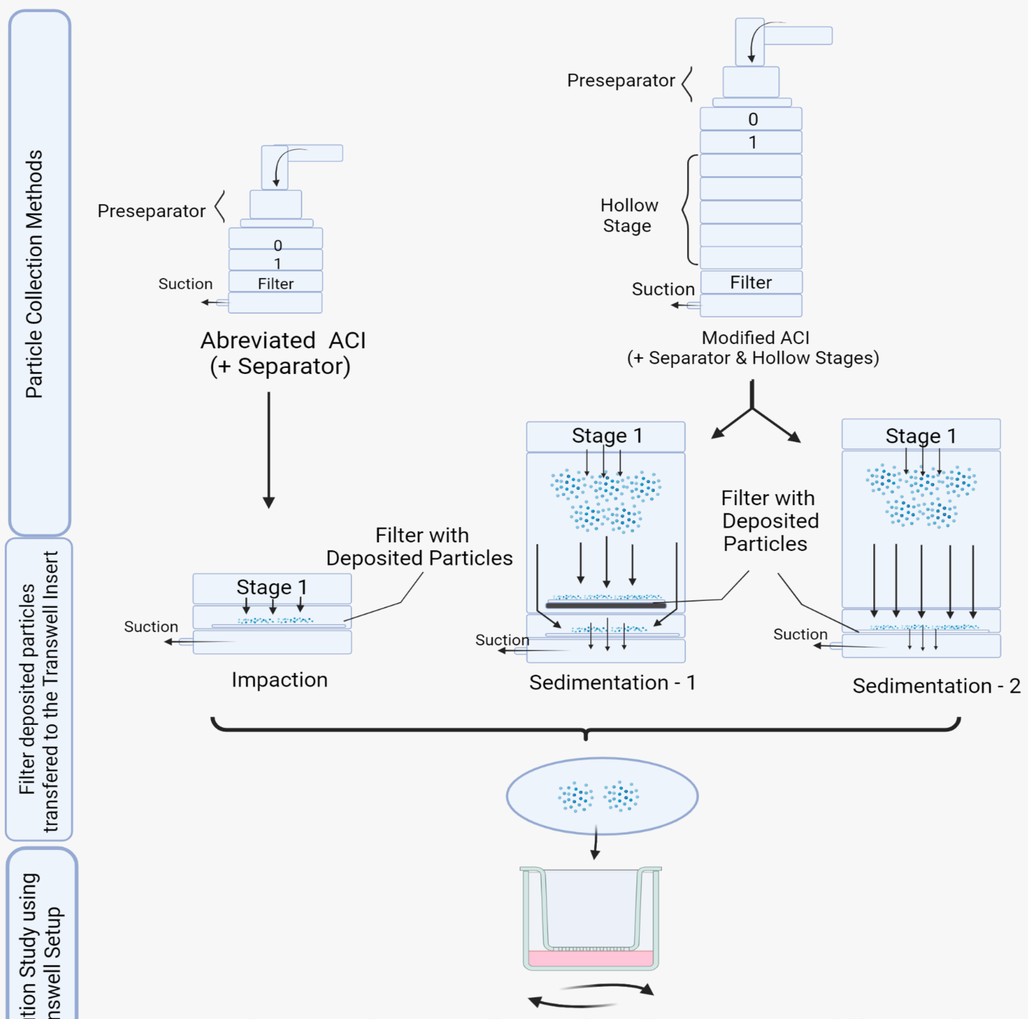

Figure 2. Schematic diagram of particle collection using different disposition mechanisms (Impaction, Sedimentation-1, and Sedimentation-2) for dissolution studies using the Transwell system.

Particle Collection

➢ **Impaction Mechanism**

- Abbreviated ACI consists of mouthpiece, throat, pre-separator, stage 0, stage 1 and filter collection stage.
- Doses were drawn at 60 L/min for 4 seconds onto the filters

➢ **Sedimentation-1 and Sedimentation-2 Mechanism**

- Modified ACI consists of mouthpiece, throat, preseparator, stage 0, stage 1, five hollow stages and filter collection stage.
- Doses were withdrawn at 60 L/min for 0.4 - 0.6 sec and sedimentation time of 20 minutes between actuations
- For Sedimentation-1, the filter was placed at a plate collector above the filter stage. While for Sedimentation-2, the filter was placed at the filter stage.
- Collection filters were cut into 24 mm diameter size and transferred to the Transwell dissolution setup.

Method (continued)

Dissolution and Analysis

- Dissolution profiles were generated using 6-well commercial Transwell system.
- A volume of 2.35 mL media were used as a receptor fluid and 0.1 mL media were placed on top of the filter to initiate dissolution.
- The dissolution condition were using a phosphate buffer saline dissolution medium (pH 6.8) with 0.1% SDS agitated at 60 rpm using a circular motion in an incubator shaker at 37°C.
- Dissolved budesonide were quantified using HPLC – UV and evaluated using deference factor (f1) and similarity factor (f2)

Result and Discussion

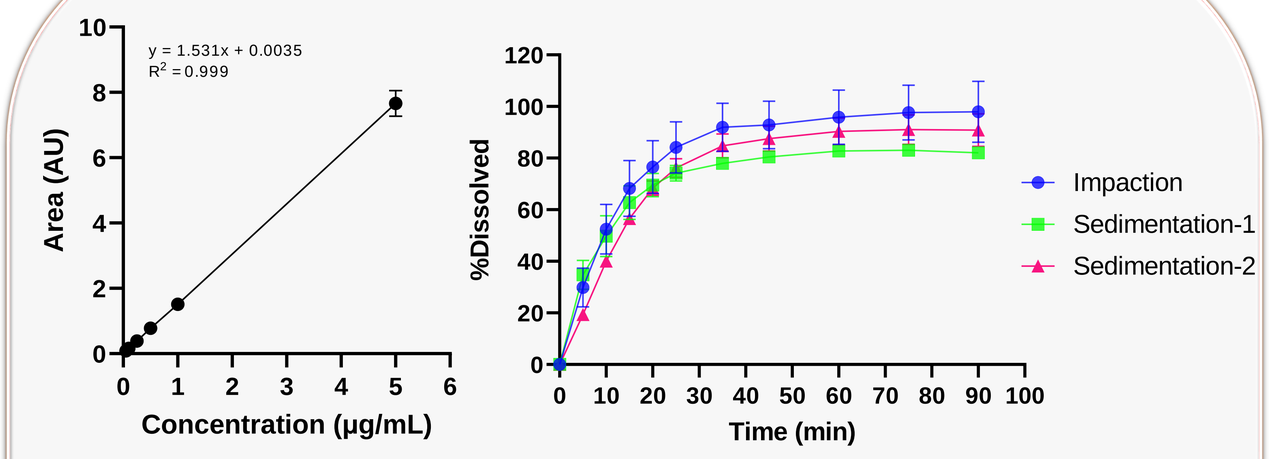

Figure 3. (A) Calibration curve for budesonide analysis; (B) Dissolution profiles for budesonide particles collected by impaction, sedimentation-1 and sedimentation-2 methods. Values represent mean of n=3 measurements, with error bars indicating standard deviation.

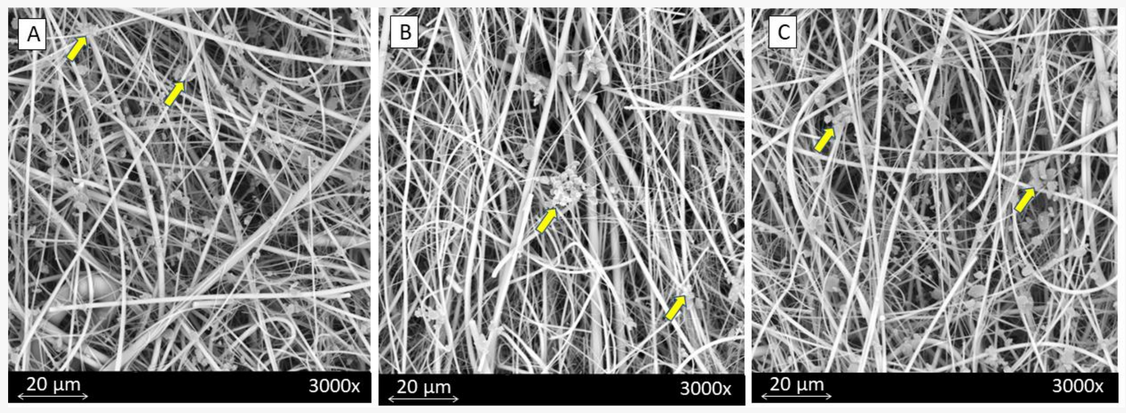

Figure 4. Scanning electron microscope (SEM) micrographs showing budesonide particles collected on a fiberglass filter GF/A using (A), Impaction (B) Sedimentation-1, and (C) Sedimentation-2 collection methods. 3000x magnification. .

- The dissolution profiles illustrated in figure 3B show the difference on drug deposition mechanism on dissolution using Transwell setup. Interestingly, there was no significant difference (f1 and f2) in dissolution profile between aerosol particles collected using the different deposition methods.
- Aerosolized particles collected onto the GF/A fibreglass filter mesh were observed by SEM imaging to be distributed in the mesh of the filter (Figure 4). A greater density of particles resulted from the Impaction and Sedimentation-2 methods compared to Sedimentation-1, even though more actuations were performed by he latter. Aggregates of particles were observed using all particle collection mechanism (yellow arrows; Figure 4).

Conclusion

No significant difference in dissolution profile was seen for particles collected using impaction or sedimentation methods. However, differences in factors including mass deposited and particle dispersion were seen which can in some instances influence aerosol particle dissolution rate. This should be explored further using different drugs and formulations to understand the influence of particle collection on dissolution performance

Reference

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