ENHANCING THE DEPOSITION OF ASTHMA PHARMACEUTICALS IN THE UPPER AIRWAYS OF THE LUNG

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Background

- Rate of occupational asthma in the United States is 18 per 100,000
- Salts are commonly added to the medication that treats asthma because of their hygroscopic properties
- Hygroscopic growth occurs when a particle enters a high relative humidity environment and absorbs water vapor from the surrounding environment
- The human respiratory system has a relative humidity greater than 90%
- The initial growth phase of hygroscopic particles has not been verified in previous studies, but the initial growth is important because particles reach the bifurcation of the lungs in 0.2-seconds and can deposit within that short time span

Objectives

The overall goal of this research was to analyze initial growth phase of two different hygroscopic salts when the particles were exposed to a high relative humidity environment and compare the results to a mathematical model of hygroscopic growth.

The specific objectives developed for this project were:

1. Develop a system to measure hygroscopic particle growth under different environmental conditions
2. Determine the accuracy of a hygroscopic growth model during the growth phase of salt particles

Methods

- Sodium chloride and potassium chloride were aerosolized using a nebulizer (Figure 1)
  - Microscope slide was dusted with the aerosolized salt
- A second setup was developed to generate a controlled high relative humidity (90%, 95%, and 99.5%) air stream and record the change in the salt's particle diameter when it was exposed to the high relative humidity (Figure 2)
  - The coated microscope slide was placed under the inverted microscope (Figure 2) and a specific particle was videotaped with the high relative humidity air emitted onto it for 30-seconds
  - The video recording was captured using a phone on the inverted microscope and converted into frame-by-frame photographs, which resulted in a photograph every 0.03-seconds
  - The pixel length of the particle in each photograph was measured and the diameter was calculated via a ratio from a stage micrometer and the diameter change over time was graphed
- The Maxwell Equation (Equation 1) was used as the hygroscopic growth model. Two model variations were used.
  - Model A:
    - Assumes that the original dry salt particle first develops a film of saturated salt solution that interacts with the water vapor of the atmosphere according to Maxwell's equation. This process continues until the salt is fully dissolved in the growing droplet, after which the solution becomes progressively dilute.
  - Model B:
    - Assumes that the original dry particle instantaneously becomes a supersaturated salt solution
- The results from the model were graphed and compared to the results that were measured. The models root mean square of error (RMSE) was calculated to see which was closer to the measured, reality.

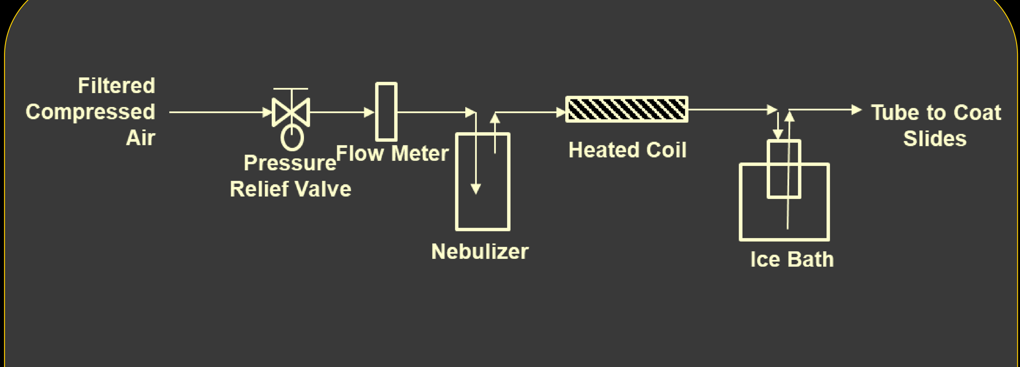

Figure 1: Schematic of salt aerosolization system

$$\Phi \frac{d\Phi}{dt} = \frac{4D_v^* M_w}{R\rho_d}\left[\frac{p_a^v}{T_a} - \frac{p_d^s}{T_d}\right]$$

Φ = droplet diameter
D_v^* = Modified molecular diffusivity
M_w = Molecular weight of water
R = Universal gas constant
ρ_d = droplet density
p_a^v = partial pressure of water vapor at atmospheric condions
p_d^s = saturation pressure of water vapor near the droplet
T_a = ambient temperature
T_d = droplet temperature

Equation 1: Maxwell Equation

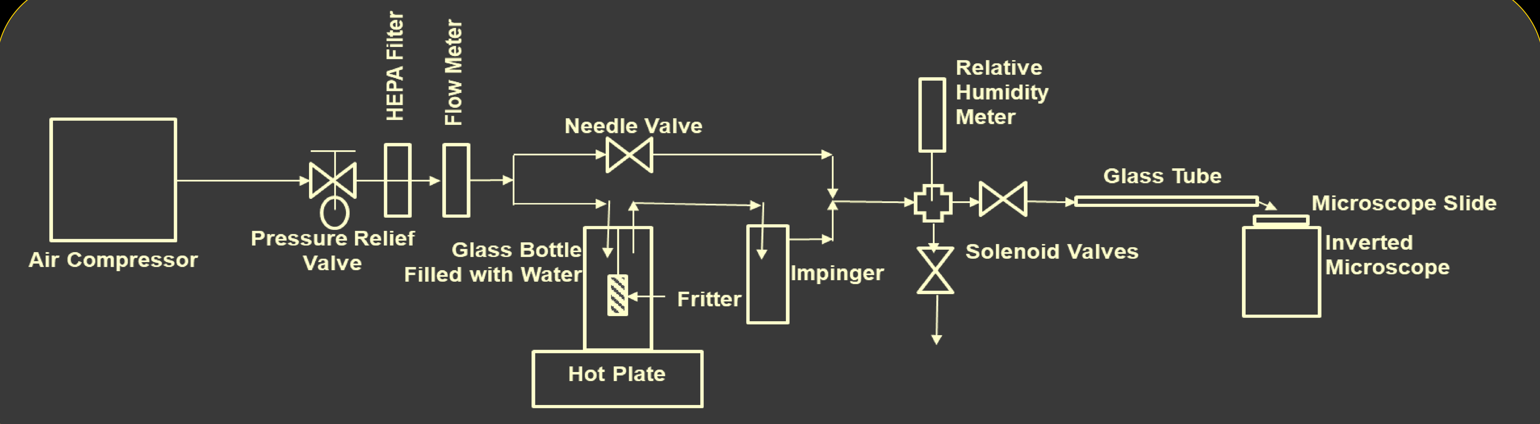

Figure 2: Schematic of the high relative humidity generation and hygroscopic growth analysis system

Results

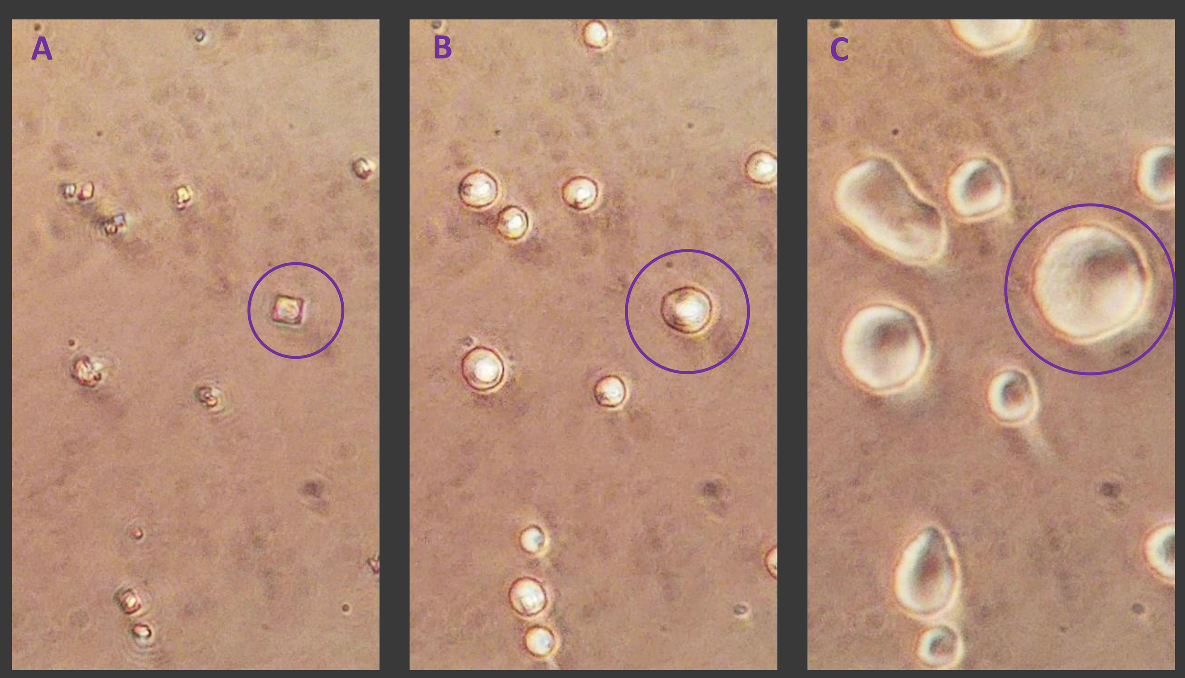

Figure 3: Photographs of the hygroscopic growth of sodium chloride at 95% relative humidity. The particle that was measured for this trial is circled. A is at 0 seconds, B at 0.3 seconds, C at 30 seconds.

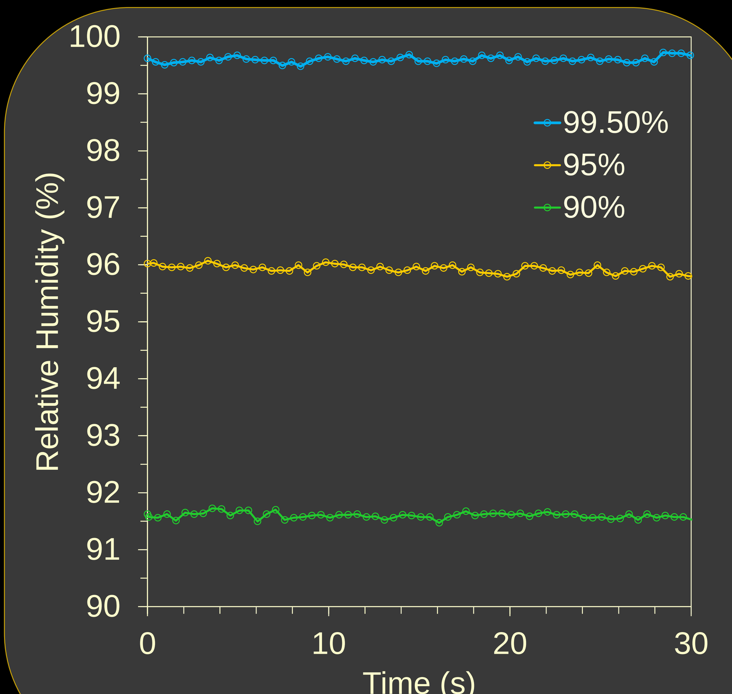

Figure 4: 3 trials of relative humidity level across 30s

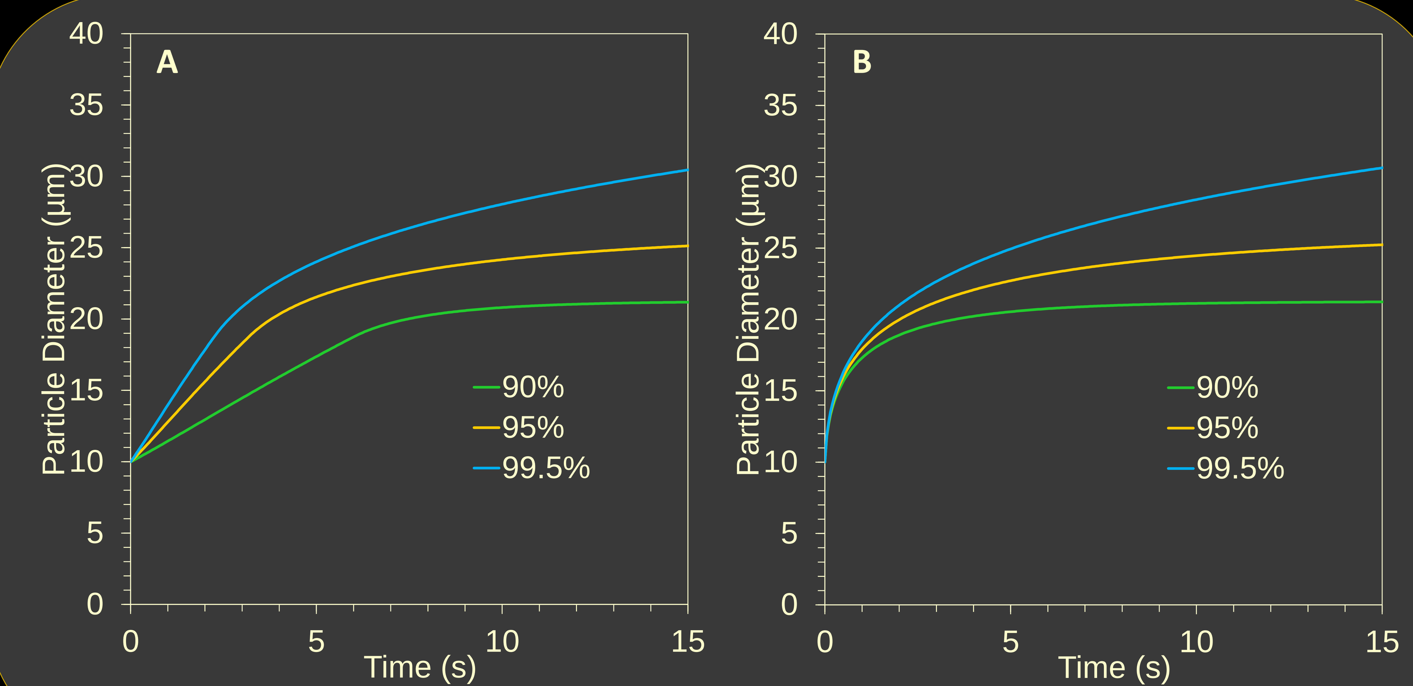

Figure 5: Model prediction of growth of a 10 μm KCl particle when exposed to 3 different relative humidity levels. Model A is in Figure A. Model B is shown in Figure B.

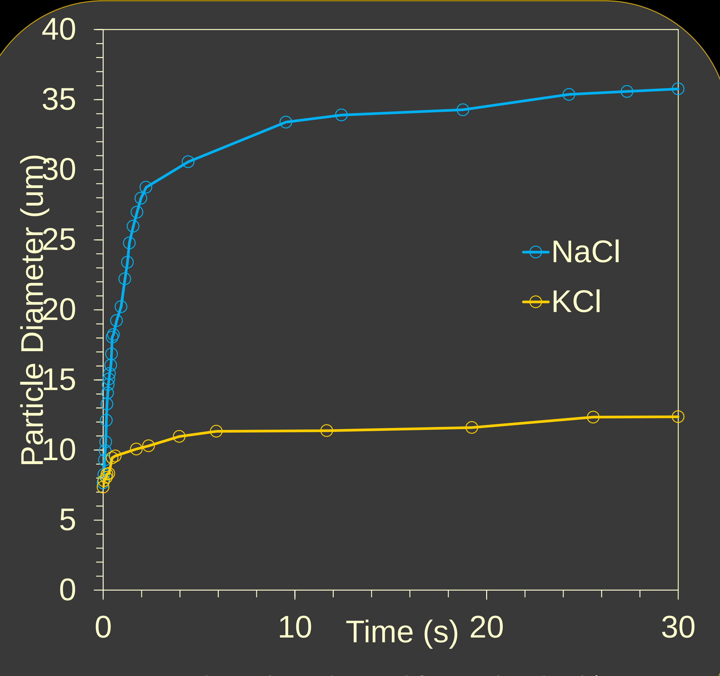

Figure 6: 95% relative humidity trial for NaCl and KCl (starting particle diameters NaCl: 7.66 μm, KCl: 7.35 μm

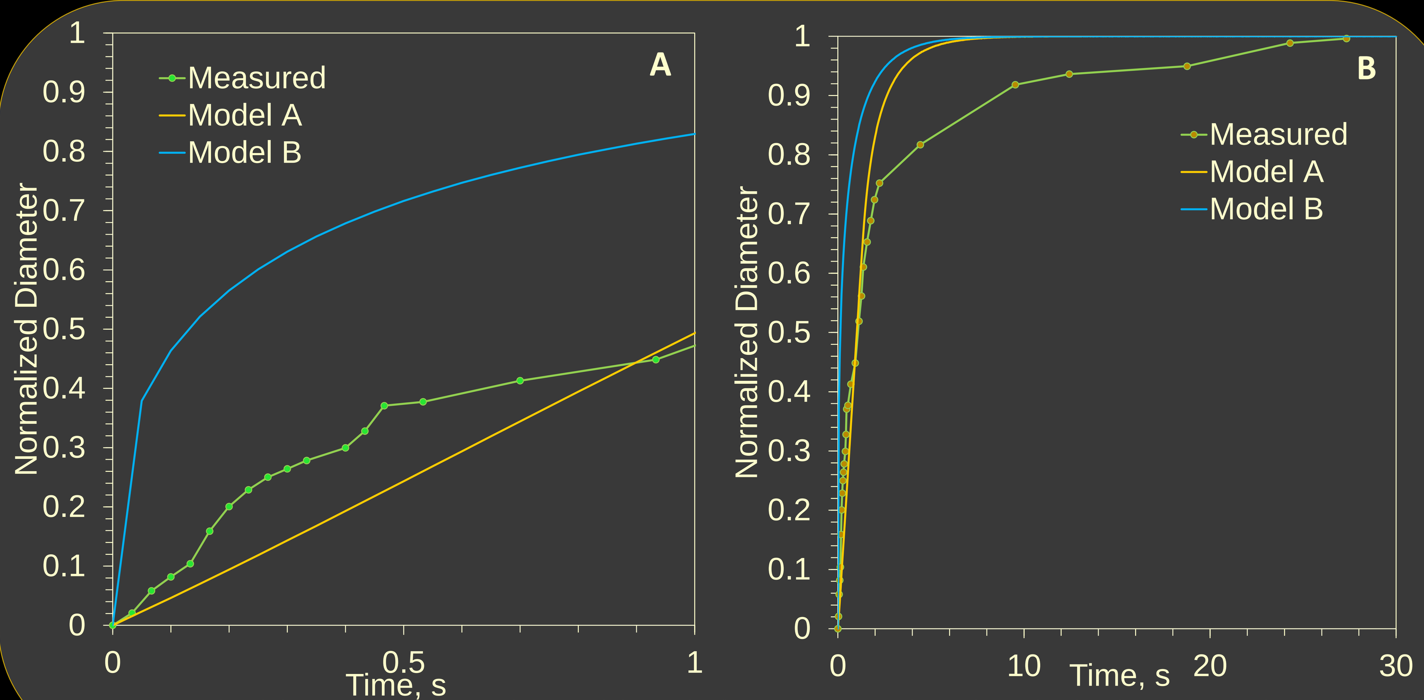

Figure 7: Normalized diameter for measured vs. Model A and B for NaCl at 90% relative humidity level. A is 0-1s and B is 0-30s for the same trial

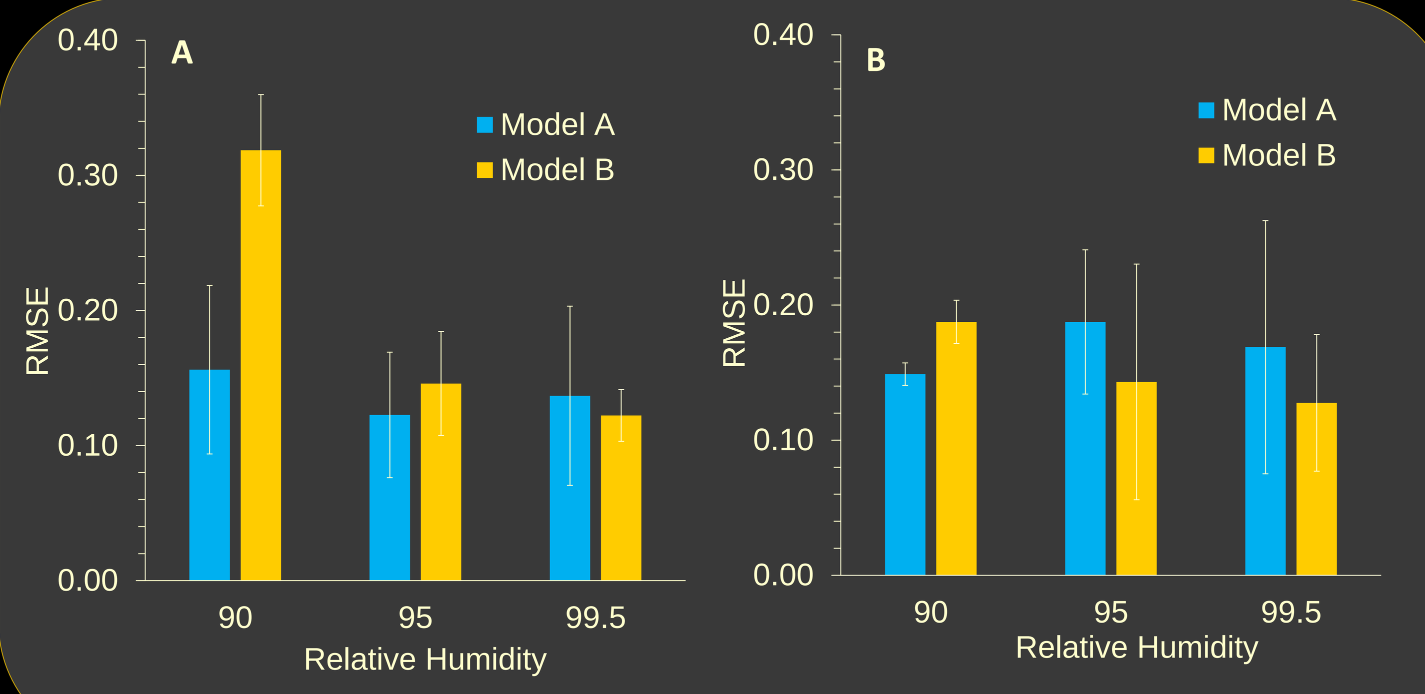

Figure 8: Averaged RMSE for all trials of the same salt type. A is NaCl, B is KCl.

Conclusions

- RMSE was reduced when using Model A over Model B for NaCl at 90% relative humidity
- A longer time was needed for the same salt and size particle to grow to its equilibrium diameter at 90% relative humidity than at 95% or 99.5% relative humidity levels
- Starting particle diameter plays a large role in the equilibrium diameter
- As expected, NaCl is more hygroscopic than KCl; growing to a larger equilibrium diameter with the same size starting particle diameter
- The maximum variability of the relative humidity across a 30-second trial was 1.4%

Future Work

- Test more hygroscopic materials to validate using Model A over Model B
- Add pharmaceuticals to the hygroscopic materials to see their effect on the equilibrium diameter
- Aerosolize the pharmaceutical salt combination using an inhaler to mimic typical delivery methods
- Update lung deposition models to include Model A's starting particle diameter if it continues to be successful

Acknowledgements

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