A RATIONAL APPROACH TO SPRAY DRYING MULTI-COMPONENT FORMULATIONS CONTAINING LOW-SOLUBILITY ACTIVES

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INTRODUCTION

- Complex formulations with design constraints are costly to develop.
- In this study, an in silico approach was taken to design multi-component D-amino acid formulations, to assess formulation development a priori.
- An equimolar quaternary D-amino acid formulation containing D-Leucine (D-Leu), D-Methionine (D-Met), D-Tryptophan (D-Tyr) and D-Tryptosine (D-Tyr) has been found to have in vitro activity against Pseudomonas aeruginosa. This will be used as a model formulation.

PREDICTED PARTICLE FORMATION

For this formulation, particle formation theory\(^{1}\) predicts (see right):
- D-Tyr and D-Leu achieve saturation early on the surface, and crystallize;
- Trehalose remains amorphous;
- The final particle will likely have a crystalline shell that deforms or collapses.

PROCESS DEVELOPMENT

Step A. Set design targets (right).
Step B. Apply particle formation and spray drying process models to design targets.
Step C. Adjust formulation and process design according to boundary conditions (far right).

RESULTS

Numerical lung deposition model. Simulated deposition of the minority components (D-Tyr, D-Met, D-Leu) was predicted to exceed 4\% throughout lung generations \(^{19}\) by at least three orders of magnitude, regardless of mucus production rate and mucociliary rates.

CONCLUSIONS

- An in silico approach to aerosol formulation and spray dryer process development was successful.
- The powders achieved all design targets, thus no further empirical iterations were required.
- This eliminates significant experimental work for complex formulations.

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REFERENCES