SUBSTITUTION OF L-LEUCINE WITH D-LEUCINE IN SPRAY-DRIED RESPIRABLE POWDERS FOR CONTROL OF PSEUDOMONAS AERUGINOSA INFECTION

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Secondary *Pseudomonas aeruginosa* infection is a significant factor in reducing quality of life for cystic fibrosis patients. L-leucine is a well-known dispersibility agent for respirable dry powders. However, L-amino acids have been implicated as a nutritional source for *P. aeruginosa* biofilm growth. In this study, we instead designed formulations with D-amino acids. Trehalose/D-leucine and trehalose/L-leucine powder formulations (80:20 %w/w) of three batches each, were spray-dried with a Büchi B90 spray drier. The powders were subjected to a number of characterisation techniques. Modulated differential scanning calorimetry and low frequency shift Raman spectroscopy showed that trehalose remained amorphous during spray-drying (Tg ~ 120°C) while L- and D-leucine crystallised. A newly developed, modulated compressed bulk density tester found compressed bulk density of trehalose/L-leucine and trehalose/D-leucine to be similar (700-720 kg/m^3). The spray-dried powders were also dispersed from an Aeroliser DPI, into an Alberta Idealised Throat and filter assembly, at 60 L/min air flow rate (n=9). The filter deposition (representing lung dose fraction) exceeded 40% of loaded dose (20 ± 1mg) for both formulations. The primary particle size, measured by an Aerodynamic Particle Sizer, was 3.82 ± 0.04 um (trehalose/L-leucine) and 3.25 ± 0.03 (trehalose/D-leucine). We have successfully produced dispersible spray-dried L- and D-amino acid powder formulations, using a theoretical approach to study design. The results of our study demonstrate that L-leucine can be substituted with D-leucine without reducing aerosol performance, and remove a biofilm nutrition source from a respirable powder formulation.

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