**Effect of L-leucine on the Electrostatic Charging of Inhalable Salbutamol Sulfate Powder Aerosols**

**Ayu Lestari1**, Philip Chi Lip Kwok1\*, Hak-Kim Chan1\*.

Advanced Drug Delivery Group, Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney1, Sydney, NSW, Australia

**Background and aims.** Electrostatic charging during aerosolization of pharmaceutical powders can significantly impact drug delivery efficiency in dry powder inhalers (DPIs) [1,2]. L-leucine (LL) is commonly used as a dispersion enhancer in spray-dried formulations, but its role in modifying electrostatic charge behaviour remains unclear. This study aimed to investigate the influence of varying LL content (5–95% w/w) on the electrostatic properties of spray-dried salbutamol sulfate (SS) particles.

**Methods.** Spray-dried composite powders of SS and LL were prepared across a wide range of LL content. Electrostatic charge magnitude and polarity were evaluated using an Electrical Low Pressure Impactor (ELPI) during powder dispersion. Particle crystallinity and surface morphology were analyzed via X-ray diffraction (XRD), while surface chemistry was characterized using X-ray photoelectron spectroscopy (XPS). Thermal transitions and interactions between components were assessed using differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA).

**Results.** The incorporation of LL significantly altered the electrostatic behaviour of the powders. A polarity shift from positive to negative occurred at 5% LL, with peak charge accumulation observed between 5–30% LL. Beyond 40% LL, a decrease in charge magnitude and reversion to positive polarity were observed, coinciding with increased LL crystallinity. XRD confirmed surface crystallization of LL, leading to more stable and consistent charging behavior. Amorphous formulations exhibited higher charge variability, highlighting the role of physical state. XPS analysis identified LL’s isobutyl side chain and hydrogen-bonding interactions with SS as key contributors to charge modulation. Surface corrugation induced by LL reduced particle contact area, further influencing triboelectric charging.

**Conclusion/Discussion.** This study demonstrates that LL content and physical state significantly affect the electrostatic charge profile of SS-based spray-dried powders. The findings highlight the complex interplay between crystallinity, surface composition, and morphology in determining triboelectric behaviour.

**References:**

(1) Hinds, W.C. (1999). Aerosol technology: Properties, behavior, and measurement of airborne particles. John Wiley & Sons, Incorporated.

(2) Pilcer, G., Amighi, K. (2010). Formulation strategy and use of excipients in pulmonary drug delivery. International Journal of Pharmaceutics 392:1–19.