Interest of Cyclodextrins in Spray-Dried Microparticules Formulation for Sustained Pulmonary Delivery of Budesonide

University of Liege

**Purpose**

Cyclodextrins (CDs) are cyclic oligosaccharides made of linked α-1,4-glucopyranose units assembled to form a truncated cone-like structure comprising a hydrophobic cavity. In order to reduce toxicity and to enhance water solubility of natural cyclodextrins, some derivatives were developed. Among them, 2-hydroxypropyl-α-cyclodextrin (2-HP-α-CD) is widely used in pharmaceutical formulations to enhance water solubility, stability and bioavailability of hydrophobic drugs by forming water soluble inclusion complexes. The purpose of this work is to develop a new formulation based on the spray-drying of a solution containing budesonide and 2-HP-α-CD in complex. The impact of cyclodextrin on spray-dried powder aerodynamic properties and lung delivery of budesonide was also investigated.

**Methods**

To this end, an aqueous solution comprising budesonide and 2-HP-α-CD in complex was spray-dried and a design of experiments was undertaken in order to optimize the process. GranuDrum® equipment and Multi stage liquid impinger were used to study aerodynamic properties and lung deposition. In Vitro cell experiments and In Vivo asthma model were used to analyze the impact of cyclodextrin on the budesonide lung permeability.

**Results**

Further to the spray-drying, powders display an interesting “deflated-ball like” shape, associated to a low bulk density (0.11g/cm³). We demonstrate the impact of this particular shape on an increase in air incorporation when the powder is under rotation, leading to a better lung deposition compared to conventional lactose/budesonide formulation (RF: 44% Vs 26%). Moreover, we found that 2-HP-α-CD is able to decrease the budesonide lung permeability, leading to a sustained release and a higher residence time of this corticosteroid. We also showed the positive impact of this sustained release on peribronchial inflammation in a mouse model of asthma.

**Conclusion**

In this study, we demonstrate the double interest of using cyclodextrin in powder for inhalation, both for its ability to increase lung deposition through better aerodynamic properties and for its ability to decrease the lung permeability of complexed API leading to a sustained release and therefore to a better control of airway inflammation in the case of budesonide.