DDL Small Research Grant – Successful Submission 2018

Magda Swedrowska – Teaching & Research Fellow – Awarded £1600

‘In vitro deposition of an insulin nasal spray for nose-to-brain delivery in a nasal cast’

1. Aim of the Project

The aim of this study is to evaluate the deposition of insulin (400 IU/mL) in a nasal cast when administered as nasal spray using three nasal pump-actuator configurations. For this, the Next Generation Impactor with a nasal cast model and nasal adapter will be used. We will evaluate the deposition pattern of inhaled insulin aerosols in the nasal cavity to evaluate how much lands in the region associated with nose-to-brain delivery.

This research project is an essential missing part to complete the characterisation of an insulin nasal spray that was shortlisted and presented in the Pat Burnell session at DDL2017 Conference [Wingrove, Swedrowska et al. Characterisation of a nasal spray for nose to brain delivery of insulin 62-65, 2017]. The work included screening of three nasal pump-actuator configurations containing insulin solution (400 IU/mL) and measurement of the droplet size distribution, plume geometry and spray pattern.

Feedback from the committee and external reviewers included a recommendation to address the lack of data about insulin deposition in nasal cavity, this being crucial to complete the characterisation of the nasal spray.

The proposed research visit to Kiel University (Prof Regina Scherließ – an expert in nasal and lung deposition field) will allow access to and training in the use of a nasal cast model connected to an NGI to complete the suggested data package.

2. Programme of Work

Intranasal insulin administration, which takes advantage of the nose to brain pathway, can increase insulin concentration within the brain whilst limiting systemic insulin effects. However, the nasal cavity route requires a device capable of producing posterior-superior nasal drug deposition. Due to variable nasal cavity anatomy between population, achieving maximal delivery for every subject is not always possible using a single device. The general framework of nasal spray pump performance characteristics (spray angle between 30° and 45°, droplet size 20-50 µm) has been established to provide optimal posterior nasal cavity deposition. The parameters dictated by the combination of the device and formulation such as plume area, droplet size, plume angle and particle deposition in nasal cast must be measured using in vitro methods and serves to predict spray distribution and deposition in the human nasal cavity.

In our previous study presented at DDL2017 conference by Wingrove & Swedrowska et al, we have already characterised particle distribution, plume geometry and spray duration using two commercially available nasal spray pumps with three types of actuators containing 400 IU/mL insulin solution. However, the regional insulin deposition within nasal cavity after administration with tested devices is unknown. As regional deposition is an important factor to distinguish between the amount being deposited in different parts of nose and the fraction deposited in the target posterior-superior region, a full characterisation is necessary.

Work summary:

To evaluate nasal insulin deposition, a formulation consisting of 400 IU/mL insulin solution in saline will be delivered using two commercially available nasal spray pumps with three types of actuators. Research objectives are:

1) To optimise an HPLC method for quantification of insulin.
2) To determine the nasal and lung deposition profile of nasal insulin spray (using different pump/actuator device combinations) in the nasal cast either connected to the Next Generation Pharmaceutical Impactor (NGI) and/or used with a filter at the rear end.
3) Identify the fraction of insulin depositing in target region of the nasal cast using the different nasal spray devices

3. Potential Applications

The data collected in this project will characterise the delivered dose in imaging studies in humans to determine the neuropharmacological effects of insulin, such as effects on reward centres. This may lead to treatments for certain cognitive disorders, and more generally will contribute to the growing evidence base for nose-to-brain drug delivery.

This project will be a collaboration between King's College London and Prof Regina Scherließ at Kiel University.
Prof. Regina Scherließ is an expert in respiratory (nasal and pulmonary) drug delivery and has published numorus amount of research articles. Her expertise in aerosol deposition in the nasal cavity and the hospitality and training in her research group will enable the completion of the proposed research project. This outcome of this collaboration will be submitted as a research article to Journal of Drug Delivery and Translational Research.

The research proposal will lead to completion of the characterisation of a human nasal spray for nose to brain delivery of insulin project and will help to interpet findings in an imaging study in healthy volunteers to assess the effects of intranasal insulin on food reward and appetite.
All research findings will be published in Journal of Drug Delivery and Translational Research and at DDL2018.

To support the aims and objectives of the Aerosol Society, the award will enable early career training in biorelevant in vitro aerosol deposition methods. Novel data from this study will be disseminated in apeer-reviewed scientific journal and at the DDL conference (acknowledging Aerosol Society support).

The duration of this project will be 1 month.