Title of the research project: Plant-based nanocarriers for the inhaled delivery of therapeutics

Keywords: nanocarriers, phytoglycogen, pulmonary surfactant, inhalation delivery, drug delivery

Main tasks: Experimental characterization of model biomembranes using surface chemistry techniques and associated data analysis.

Skills required: chemistry lab skills, no prior knowledge of surface characterization required (training will be provided). Interest in nanocarriers for drug delivery and biophysical chemistry.

Objective: This MITACS project aims to investigate the potential of natural materials nanoparticles as nanocarriers for the delivery of inhaled therapeutics.

Problem Statement: Until recently, inhaled drugs were mainly used for the treatment of chronic respiratory diseases, such as COPD, asthma, and cystic fibrosis, with a global market of 23 Billion USD in 2016.[1] Moreover, the World Health Organization has identified respiratory infections, including those associated with respiratory diseases, as the third leading cause of death.[2] Capitalizing on the benefits of pulmonary drug delivery (i.e., rapid action, low metabolism, and high bioavailability) compared to oral or parenteral administration, inhaled formulations and delivery vehicles are increasingly being developed for systemic disease treatment and prevention. Examples include an insulin inhalation powder for diabetes (Afrezza®), nasal flu vaccine (FluMist Quadrivalent®), and nasal spray for smoking cessation (Nicotrol®). The human lungs present many advantages as a delivery route: a large surface area (ca. 70 m^2) for the adsorption of molecules and particles, a thin epithelial barrier, abundant underlying vasculature, low acidity, and low alveolar enzymatic activity.[3] Inhalation delivery is expected to be an ideal approach for the treatment of lung infections, lung cancer and other pulmonary ailments as it allows the site-specific physical delivery of therapeutics.[4] A higher local concentration means that the overall drug concentration in the body is lowered. However, one must ensure that the delivery vehicle itself does not induce severe adverse effects in both healthy and impaired lungs.

Many inhaled drug formulations consist of dry or solution-suspended fine particles. Nanoparticle carriers are broadening the options for the development of targeted drug delivery systems. The key advantages of nanoparticles are a high stability (long shelf life), high carrier capacity, and feasibility of incorporating both hydrophilic and hydrophobic substances.[5] Inhaled nanoparticles preferentially deposit in the alveolar region and peripheral airways.[3] They can translocate to organs by crossing the alveolar epithelium barrier or are retained in the lungs due to slow clearance. In the alveoli, the nanoparticles interact with pulmonary surfactant, a lipid-protein mixture that lines the alveolar air/fluid interface and serves as the primary barrier to uptake. The main function of pulmonary surfactant is to lower the surface tension and facilitate the mechanics of breathing. Nanoparticle-surfactant interactions determine the subsequent clearance, retention, and translocation of the inhaled particles. With increasing evidence that nanoparticles acquire a biomolecular corona during their passage in the lungs and interaction with the pulmonary surfactant monolayer and that it is this corona that determines their fate,[6] the first stage in the development of nanoparticle-based carriers is therefore to identify how the particles themselves interact with and are transported across the surfactant.

Nanoparticles derived from natural materials are good candidates as nanocarriers for pulmonary drug delivery as they are water dispersible, non-cytotoxic, non-immunogenic, hypoallergenic, non-biopersistent, and chemically modifiable. Moreover, their structure enables active ingredients to be physically trapped within the particle or chemically conjugated to the surface and subsequently released upon particle degradation. In this collaborative project, the potential for delivery of therapeutics using the nanoparticles will be assessed via a comprehensive investigation of i) the biophysical interactions of the nanoformulations with the pulmonary surfactant components.

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