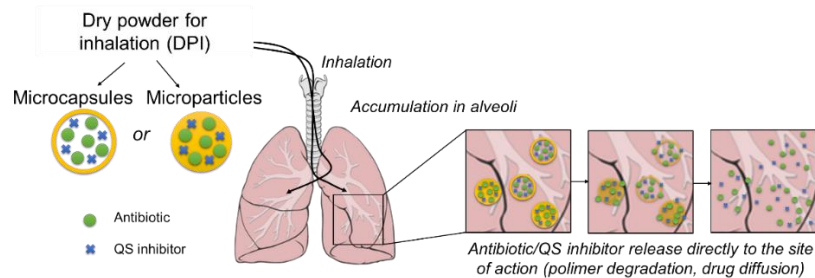


Inhalable polymeric delivery systems of antibiotics and quorum sensing inhibitors for the treatment of respiratory infections

Conventional therapies of pulmonary infections are less effective, due to limited bioavailability of the drug, as only its small portion can reach target site – lower respiratory tract. Pulmonary bacterial infections, occurring e.g. in patients with chronic obstructive pulmonary disease (COPD), are one of the most frequent causes of death worldwide. Conventional treatment based on oral, intramuscular or intravenous administration of antibiotics is often ineffective and causes several negative side effects, e.g. weakness, gastric upset, but can also lead to serious hepato- or nephrotoxicity. **As it is not possible to completely eliminate the use of antibiotics in the treatment of lung infections in COPD patients, novel modes of treatment and drug administration paths should be considered.** Regarding the nature of COPD exacerbations leading to recurrent lung infections, the amount of antibiotics administered to the patients should be well controlled, not only to reduce negative side effects of the drugs, but also to prevent bacteria from gaining resistance against applied antibiotics.

Here we propose a novel approach for eradication of bacterial infections by application of both antibiotics and quorum sensing inhibitors. Quorum sensing (QS) is a type of population density-dependent defence mechanism adopted by bacteria allowing them to avoid both host immunological response and antibiotics. Once the QS system is activated bacterial infections are more difficult to treat. Fortunately QS in bacteria can be disrupted via QS inhibitors, which are promising in context of combination therapies with conventionally used antibiotics.

This project is focused on **development of novel delivery system of antibiotics and QS inhibitors for the treatment of lung infections in acute exacerbations in COPD patients.** Such system will be based on **inhalable polymeric microcapsules and microparticles loaded with antibiotics and QS inhibitors that are effective in suppressing lung infections.** Inhalable administration and synergistic effect of antibiotics/QS inhibitors will allow for reduction of drug dosage delivered to the patient, limit their systemic side effects and increase patient's quality of life. In addition, controlled drug release from degrading carriers will prevent infection recurrence.



Schematic representation of inhalable delivery system of antibiotics and QS inhibitors based on bioresorbable polymer and its principle of action; DPI - dry powder inhaler - will be used to administer drug/QS inhibitors - loaded degradable polymeric microcapsules/microparticles

Broad spectrum of analyses planned in the project will provide knowledge on the synthesis of biodegradable polymers (polyanhydrides), the influence of synthesis parameters on properties of obtained materials and their degradation behaviour. Novel method for manufacturing of highly uniform drug carriers (microspheres and microparticles with a size suitable for inhalation) will be developed using microfluidic devices. *In vitro* studies in contact with human lung epithelial cells, alveolar macrophages and various bacterial strains will provide insight into biological performance of fabricated materials. Evaluation of cytocompatibility and antimicrobial efficacy of the developed drug delivery carries will be done on advanced 2.5D/3D cell co-culture models. Developed drug delivery system will demonstrate superb aerosolization properties coupled with enhanced antibacterial efficacy and in the future may become a successful mode of treatment of lung infections in COPD patients.