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ENCAPSULATION OF PROTEIN-LOADED MICROPARTICLES WITH A BIODEGRADABLE POLYMER.

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Abstract

Introduction
Microparticles are promising materials for intra-organ delivery of protein pharmaceuticals to treat various life-threatening diseases. This work focuses on the development of a novel microparticulate system for improved renal drug delivery to prevent chronic kidney diseases and make patient-inconvenient therapies (i.e. dialysis and organ replacement) unnecessary.

Supercritical CO_2 ($scCO_2$) technologies offer ample opportunities to produce drug-loaded microparticles and/or microencapsulates that can be used as injectable drug delivery depots for controlled drug release. $ScCO_2$ technologies, such as $scCO_2$ spray drying, offer several advantages over other particle formation technologies, such as minimal exposure of labile drug molecules to organic solvents, mild process conditions, and excellent possibilities to control particle characteristics.

In this study, trehalose microparticles loaded with model proteins lysozyme or bovine serum albumin (BSA) were prepared by $scCO_2$ spray drying, whereafter these protein-loaded trehalose particles were encapsulated into biodegradable hydrophilic SynBiosys multi-block copolymers (MBCPs). The multi-block copolymers were designed in such a way as to provide a water-swollen environment suitable for encapsulated proteins, which allows for long-term protein release.

Materials & Methods
MBCPs were synthesized by InnoCore Technologies. Lysozyme- and BSA-loaded trehalose particles were prepared by $scCO_2$ spray drying of aqueous solutions of their corresponding components. Coating with MBCP was performed by $scCO_2$ spray drying of a lysozyme-loaded trehalose particle suspension in dichloromethane with dissolved MBCP.

Results
Lysozyme- and BSA-loaded trehalose particles in the size range of 1-50 µm were successfully obtained in mass yields of 60-75 % using $scCO_2$ spray drying. In the subsequent coating step, polymer-coated particles with entrapped lysozyme-loaded trehalose particles were obtained.

Conclusions
CO_2 spray drying is a promising technique to create polymer-coated particles containing protein pharmaceuticals that can be applied as injectable controlled release formulations. Optimization in terms of yields, particle structure and protein release kinetics is currently in progress.