MSc Project

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Lab/Institution: Membrane Protein Crystallography Lab (ITQB-UNL) and Associated Lab. for Green Chemistry - Clean Technologies and Processes (LAQV's - REQUIMTE), FCT-UNL
TITLE: Design of Biocompatible Fluorinated Ionic Liquids for Protein Drug Delivery Systems

BACKGROUND

The pharmaceutical market is evolving in a context of increasing economic pressure due to the reduction of healthcare costs by public authorities, the increasing of generic substitution and the rate of failure during drug development, 90% in general. This situation, together with the demand of the society and authorities of more efficient and safety drugs, has contributed to a revival of interest in protein drug candidates. Therapeutic proteins that are natural biological products have emerged since the early 1980s and remain a kind of attainable panacea to all the known diseases.

Nowadays, therapeutic proteins on the market are in clinical trials for therapy of cancers, Alzheimer's disease, immune disorders, infectious diseases, Parkinson's disease, autoimmune disease, AIDS/HIV, among others. However, therapeutic proteins are very sensitive to environmental conditions and have short half-lives in the blood stream due to degradation by enzymes and proteases. All these difficulties in the administration of therapeutic proteins provide us the impetus to develop this project seeking efficient and safety drug delivery systems with reduced immunogenicity that can deliver protein drugs to the body maintaining their therapeutics levels.

OBJECTIVES

The aim of this project is to evaluate the potential application of fluorinated ionic liquids (FILs) as a new and improved strategy for protein drug delivery. The use of novel, biocompatible and greener FILs will hugely improve the bioavailability, stability, structure and efficacy of therapeutic proteins. Playing with the van der Waals, coulombic and hydrogen bonding interactions, the size of fluorinated domain, surfactant behaviour and the solubility in biological fluids will provide the ingredients needed to use FILs in biological applications, where fluorocarbon compounds present a handicap (their solubility in water and biological fluids is, in most cases, too low and the water content in adult human body is ~65%). This project consists of an innovative and multidisciplinary approach involving chemistry, technology and biochemistry areas with a strong biomedical relevancy.

PROJECT DESCRIPTION

FILs can be used to promote the stability of various colloidal systems, including different types of vesicles and tubules that also show promise for controlled release drug delivery due to the strong tendency of these molecules to self-assemble. The stability of fluorinated carrier is superior to those made from standard lipids and as nanocarriers, they appear to be a better drug delivery system contributing to the overall efficacy of the protein drug. This fact is of vital importance to the design of efficient and safety drug delivery systems for therapeutic proteins with high shelf-life stability, controlled/sustained release and absence of clinically significant side effects, providing protection to protein drugs until they have reached their site of action.

The student involved in this project will carry out the experimental work in the Associated Lab. for Green Chemistry (FCT) and Membrane Protein Crystallography Laboratories (ITQB), under the supervision of A. B. Pereiro and M. Archer. The student will work on the following tasks:

Task 1- Synthesis and characterization of biocompatible ionic liquids with fluorinated alkyl chains

Task 2- Evaluation of the solubility of specific protein drugs in various FILs and characterization of their interactions using biochemical and biophysical assays (e.g. microcalorimetry, spectrofluorimeter, FTIR)

Task 3- Functional and structural analysis of the therapeutic proteins “alone” and in complex with FILs. The activity assays will depend on the proteins under study and the structure can be assessed by CD, DLS, X-ray Crystallography and Bio-SAXS.

Task 4- Collection and correlation of all these data to better understand the behaviour of these complex systems. This information is essential for designing novel protein drug delivery systems capable of maintaining or improving the activity, stability and therapeutic efficacy of each protein.

The potential of fluorinated ionic liquids is large and unexplored, and thus can unleash a complete turnaround in the field of biomedical applications. This study involves further collaborations with other groups, which include *in vivo* and *in vitro* assays on cytotoxicity and anti-inflammatory activity, biodistribution, residence time and pharmacokinetics studies in mouse.

TIMELINE (use fill tool for the cells)

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10
Task 1										
Task 2										
Task 3										
Task 4										
Thesis										