Preparation of starch/cellulose acetate structures as drug delivery system using green technology

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Statement of Purpose: Controlled drug delivery systems, using biocompatible or biodegradable polymers, have received considerable attention in the last years. These substances are generally used for the preparation of controlled release formulations, which therefore allow control the rate of assumption of the drug by the body improving its pharmocinetic profile. The objective of this work is to integrate some principles of green technology combining the processing of starch based polymers using ionic liquids as a green solvent together with supercritical fluid technology (SCF) to develop new products for drug delivery applications. Starch based polymers present an enormous potential to be used in biomedical field due to their biocompatibility, renewability and sustainability. However, due to the poor solubility they are extremely difficult to be dissolved in water or organic solvents. This can be overcome using ionic liquids which are recognized as green recyclable solvents to solubilize natural polymers, such as cellulose, lignocellulosic materials, starch, chitin and chitosan. One of the main advantages of using this processing method is the possibility to impregnate active compounds in a subsequent step, after the preparation of the structures. Supercritical fluids, such as (scCO2) has been identified as prime candidates to develop alternative clean processes for the preparation of drug-loaded polymeric matrixes.

Methods: In this work starch/cellulose acetate (SCA) was dissolved in 1-butyl-3-imidazolium acetate at 60-80ºC, followed by regeneration of the polymer in ethanol to obtain membranes. SCA/IL solution was prepared at concentration of 5% and the membranes produced were dried by sc CO2. The starch/ cellulose acetate structures were evaluated by their swelling capability, degradation behavior and morphological features. The influence of thickness on physical chemical properties of the membranes was assessed. Furthermore, a common anti-inflammatory drug such as ibuprofen was incorporated into structures during the drying step, by scf impregnation process and the release profile was evaluated.

Results: The water uptake capability was measured for a period up to 24h by the immersion of the samples in 5mL of PBS at 37ºC and 60rpm. The influence of α-amylase in degradation behavior of SCA materials was investigated up to 21days. In vitro performance demonstrated that SCA membranes with 1,5mm have higher water uptake ability than SCA membranes with 2,5mm, maintaining their shape and integrity upon immersion in PBS solution. From degradation studies in the presence of α-amylase was possible observe a higher degradation rate of SCA membrane with 1,5mm. Furthermore, the results revealed that membranes with lower thickness showed higher water absorption, which by its turn accelerated their degradation rate. Regarding the toxicity potential, the SCA structures have good cell viability, indicating that any possible toxic effects derived from the presence of the IL was not observed. The drug release profiles were similar for all the impregnated samples. Different experimental conditions were tested and the results suggest that SCA membranes may be used as new buccal mucosa drug delivery device.

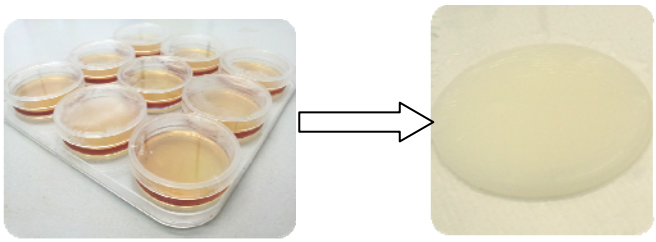

Figure 1. Membranes produced by regeneration of SCA/IL in ethanol.

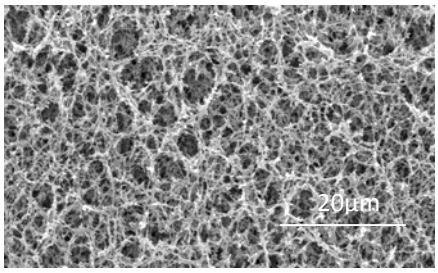

Figure 2. SEM micrographs of cross section of SCA membranes.

Conclusions: The formation of SCA gels in ILs and subsequent removal of IL from SCA gels, with an alcohol is a good way to obtain other architectures such as membranes**.** The morphological analysis performed by scanning electron microscopy, demonstrated that SCA membranes present a porous structure. Additional characterization on the in vitro performance of these membranes revealed their potential to be used in drug delivery systems for instance, in buccal mucosa drug delivery.

References: (Ana Rita C. Duarte et al. J Sup Flu. 2007;42:373-377.)