Polyelectrolytes as a Plattform for Drug Depots

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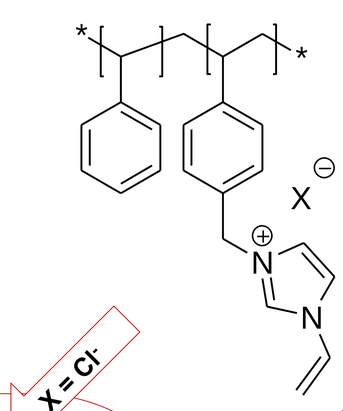
Introduction

Polyelectrolytes are a widely used class of polymers. They can be used as ion exchange membranes, hydrogels or as drug carrier systems among many other applications.[1]
Our aim was to synthesize polyelectrolytes and prepare drug depots out of them, to influence the drug release through the charges. Herein, we present the results of our cooperation project, focusing on synthesis of polyelectrolytes, as well as their use for film casting and electrospinnig.



For the synthesis[2], in a first step, we polymerized styrene and 4-vinylbenzyl chloride in different ratios in a radical polymerization. In a second step we functionalized these polymers with 1-vinylimidazole. With the vinyl group it is possible to crosslink these polymers, which can be used for film casting. To get spinable polymers it was necessary to change the anion to NTf_2^- For that we used lithium trifluromethansulfonate.

Film casting

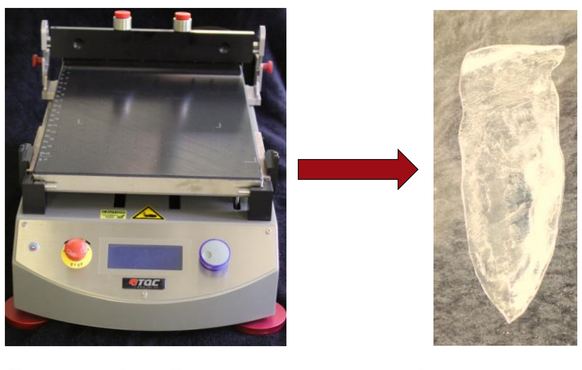


Figure 1: Film preparation: A solution of Polyelectrolyte 28 wt%, N-methyl-2-pyrrolidon 72 wt% and 2-Hydroxy-2-methylpropiophenone as a photoiniator was cast with a 200 µm casting knife and irradated with UV-light for 6 min.

The film was cast with an automatic film applicator. It was possible to prepare four different films with a proportion of PCMS from 10 to 40 %. We could also incorporate ibuprofen up to 10 wt% in relation to the polymer in these films.

The release of ibuprofen increased with a lower proportion of PCMS in the polymers 10>20>30. A complete release was reached after 16.5 h for PCMS-Sty-10-VIm and it increased for the 30 to 31.5 h.

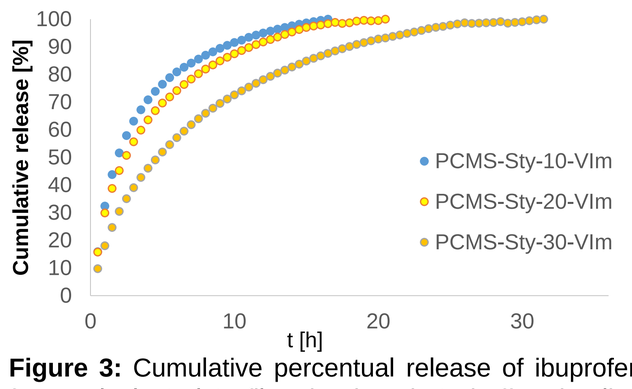


Figure 3: Cumulative percentual release of ibuprofen from polyelectrolyte films in phosphate buffered saline pH=7.4.

Figure 2: Direct Cell Contact Test on L929 mouse fibroblast: a) PCMS-Sty-40-VIm, b) PCMS-Sty-30-VIm c) PCMS-Sty-20-VIm

The direct cell contact tests showed no cell toxic behavior and a good cell morphology. For the PCMS-Sty-40-VIm only a low cell adhesion was observed, whereas a good cell adhesion could be achieved for 20 and 30.

Electrospinning

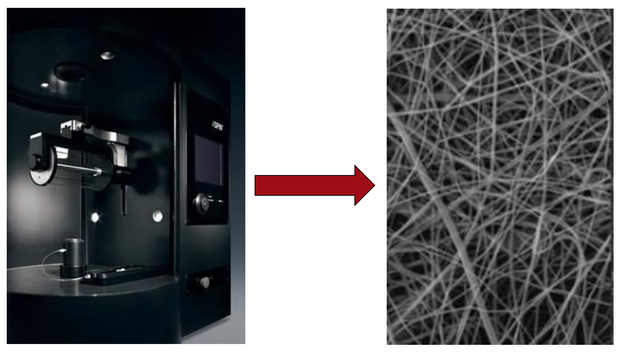


Figure 4: Preparation of fiber mats[3]: Polyelectrolyte 25 wt%, polyvinylpyrrolidone 9 wt% as a support polymer, DMF 66 wt% and 2-Hydroxy-2-methyl-propiophenone.

A 4SPin elctrospinning device from Contipro a.s. was used to produce fibers from polymers up to 100 % PCMS. In contrast to film casting, it was possible to achieve a higher variation of polyelectrolyte contents.

The release from the fibers was much faster than from the films. Both films released nearly 100 % after 24 h. No major difference could be detected between the release from the two polymers.

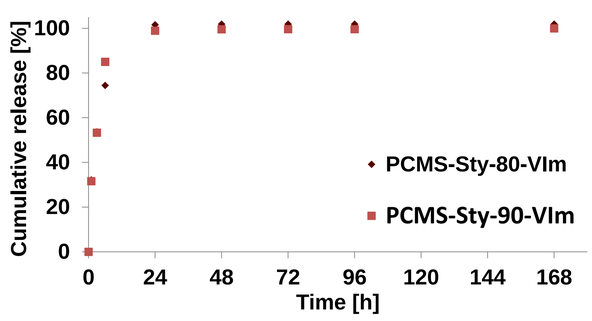


Figure 5: Cumulative percentual release of ibuprofen from polyelectrolyte fibers in NaCl-solution pH=7.4 with N=1.

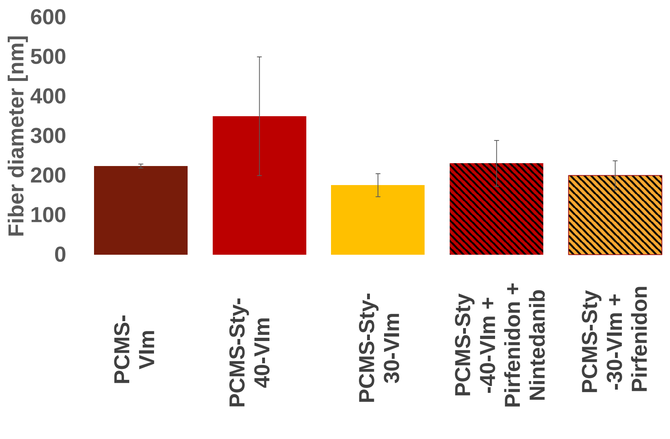


Figure 6: Fiber diameters of the electrospun mats from the polyelectrolytes

The diameter of the electrospun fibers is in the range of 170 to 500 nm, which resembles similar polymers[3]. A clear influence of drug incorporation on fiber diameter could not be detected.

Summary and Outlook

- successful preparation and crosslinking of polyelectrolytes
- electrospinning using X = NTf_2^-
- incorporation of ibuprofen in film and nonwoven
- characterization of the influence of charges
- investigation of drug release from fibers
- biocompatibility tests of electrospun fibers

Acknowledgement

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