POLYELECTROLYTE COMPLEXES AS POTENCIAL TRANSDERMAL DELIVERY SYSTEMS

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Introduction

Transdermal drug delivery is a promising way of drug administration, providing an alternative for standard delivery routes. Transdermal drug delivery systems (TDDS) offer a variety of significant clinical benefits including maintenance of constant drug levels in the blood, decrease of side effects, improvement of bioavailability by circumventing the hepatic first pass metabolism, increased patient compliance. TDDS are able to deliver drugs at a constant rate to the human body. Polyelectrolyte complexes (PECs) are a good alternative to covalently-linked hydrogels because no catalysts or initiators are necessary. The reaction occurs in aqueous solution and mild conditions, avoiding the potential toxicity of free unreacted crosslinkers and purification before administration.

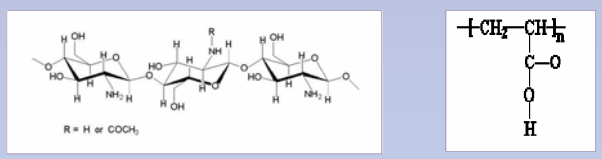

Figure 1: Chitosan structure (left) and polyacrylic acid monomer structure (right)

✓ The aim of this study is to evaluate the drug release profile of polyelectrolyte complexes (PECs) based on chitosan and polyacrylic acid (PAA) for a potential application as TDDS.
✓ For this purpose, four different drugs with log P ranging from 0.92 to 3.48 were used: paracetamol, galanthamine HBr, galanthamine salt and ibuprofen.
✓ The effect of a hydrophilic pressure-sensitive adhesive and several solvents (transcutol, glycofurol, propylene glycol) in the drug release rates was investigated.
✓ The non-occlusive properties were evaluated through the measurement of the water vapour transmission rate (WVTR).

Methods

✓ *In vitro* drug release tests were performed using vertical Franz diffusion cells at 37 ± 1ºC with a receptor medium composed of acetate buffer, pH 5.5. The amount of drug released was determined spectrophotometrically.
✓ The WVTR (g/m^2.h) was measured using a Vapometer (Delfin Technologies Ltd, Finland).

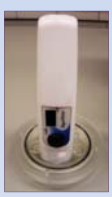

Figure 2: Integrated system used in the in vitro drug release studies. (left)
Illustration of the measurement of WVTR through the films, using the Vapometer®. (right)

Results

✓ Each drug exhibits a release profile characterized by an initial small burst effect followed by a sustained drug release over a long period of time.
✓ The adhesive does not affect the release profile of the drugs with the exception of ibuprofen, the most lipophilic compound, and thus can be used to assure the fixation of these systems to the skin.

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✓ The solvents are compatible with the PECs and may be incorporated in these films as potential penetration enhancers.
✓ The films are non-occlusive and exhibit good bioadhesive properties.

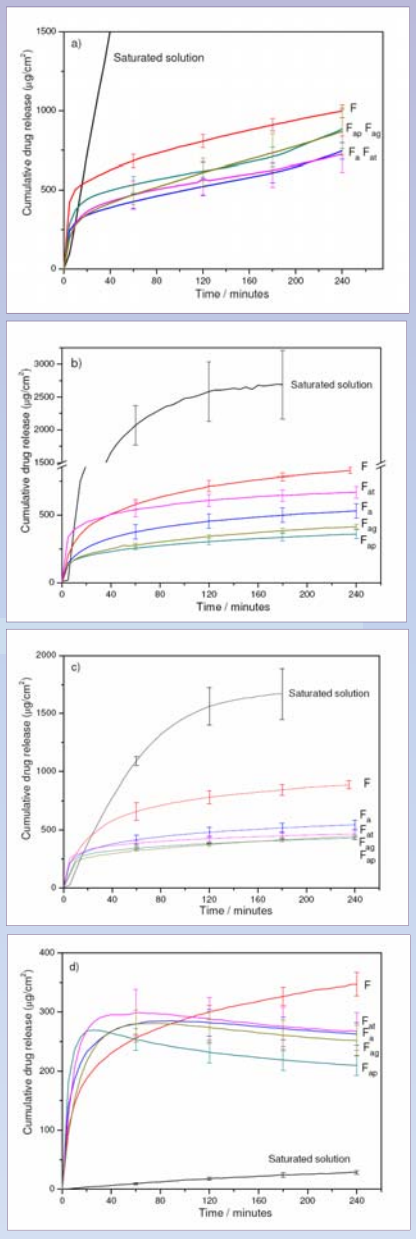

Figure 3: Drug release profiles from the saturated solutions and drug-loaded films of (a) paracetamol, (b) galantamine HBr, (c) galantamine free base and (d) ibuprofen. All films are loaded with 6% of drug. Mean (± SEM); n ≥ 3; F: formulation; F_a: formulation plus adhesive; F_{ap}: formulation plus adhesive and propylene glycol; F_{at}: formulation plus adhesive and transcutol; F_{ag}: formulation plus adhesive and glycofurol.

Conclusions

✓ The sustained drug release and good bioadhesive properties of the PECs indicate that these systems are very promising for the transdermal delivery of drugs with different chemical properties over several days.
✓ The non-occlusive properties reduce the possibility of irritation during the application time.