Towards personalized drug delivery with semi-solid extrusion

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Introduction

The increasing need for personalized dosage forms requires developing drug delivery systems with tailorable properties. Semi-solid extrusion (SSE) is an attractive film preparation method, offering flexibility in respect to patient-centricity. Poly(vinyl alcohol-co-vinyl acetate) (PVA/PVAc) is a copolymer with varying vinyl alcohol (VA) and vinyl acetate (VAc) monomer ratios. This study aimed to investigate the potential of using five different PVA/PVAc copolymers for SSE and tailoring formulation properties using hydrochlorothiazide (HCT) as a model drug.

Methods

The polymers average VA and VAc sequence lengths and monomer distribution were determined by ATR-FTIR and 1H NMR. To prepare film formulations, each copolymer (40% w/V) was dispersed and HCT (0.5%) was dissolved in 50% ethanol. SSE was employed to prepare the shamrock-shaped films. The wet film formulations were left to dry overnight at ambient conditions. One clover of a shamrock was defined as a single dose. Raman spectroscopy was used to evaluate drug distribution within the films. The drug release experiments were performed using 0.01 M PBS (pH 7.40, V = 10 mL). The permeability and biocompatibility experiments were performed on HT29-MTX cell line.

Results

The ATR-FTIR and 1H NMR showed that the copolymers were partially block-wise distributed. Raman spectroscopy confirmed an even drug distribution within the polymeric matrix on a micrometer level. The HCT release rate from films varied strongly depending on the copolymer. The drug release rate decreased with increasing PVAc proportion in the copolymers, indicating potential hydrophobic interactions with HCT. The flux of HCT through the cell monolayer was significantly higher for PVA/PVAc 98/2 films ($p < 0.05$) than for PVA/PVAc 35/65 and PVA/PVAc 50/50 films, indicating that the monomer ratio, drug release and block distribution may affect HCT permeability. The films did not exhibit toxicity towards the cell line.

Conclusion

The monomer ratio is an important factor in the formulation process and resulting film properties. SSE is a suitable method for film preparation using PVA/PVAc copolymers, and it can be applied for design of appealing shapes for personalized drug delivery, not least attractive for drug delivery to the pediatric population.