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| **Incorporation of microneedles into electrospun mucoadhesive patches for improved oral transmucosal drug delivery** |
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| **Background:** Oral transmucosal drug delivery refers to the systemic delivery of drugs through the mucous membranes of the oral cavity. The highly vascularised architecture of the oral mucosa allows for rapid uptake into the systemic circulation, whilst subsequent drug distribution avoids premature hepatic metabolism or enzymatic degradation within the digestive tract. This formulation is limited to drugs that can permeate the oral epithelium at a sufficient rate. Permeation enhancers have been studied to widen this range of drugs, among these, microneedles have been used to physically disrupt the epithelium. These micron-sized projections penetrate the surface tissue to either; directly deposit encapsulated drug or create micropores to aid passive diffusion. Electrospinning is a manufacturing process wherein a polymer is charged with a high voltage to form a mesh-like patch with interfibrous porosity and high surface area. We have developed an electrospun mucoadhesive patch for localised drug delivery where drugs suspended within the fibres can be released at a controlled rate, regulated through altering fibre diameter and composition. The aim of this project is to incorporate microneedles onto an electrospun patch to enhance the permeation of patch-delivered drugs across the oral mucosa and into systemic circulation. |
| **Methods:** Optimal microneedle dimensions were determined through comparison of microneedle heights to human buccal epithelium thickness. Polylactic acid (PLA) microneedles were produced through reverse micromoulding using polydimethylsiloxane (PDMS) to create the negative moulds. Patches were fabricated by electrospinning a polymer solution of 10% w/w poly(vinylpyrrolidone) (PVP) and 12% w/w Eudragit RS100 dissolved in 97% ethanol. Drug-loaded patches incorporated lucifer yellow (LY), used as a fluorescent simulant drug, at 0.3% w/w. Patches were attached to the microneedle baseplates through physical adhesion. Microneedle-assisted LY permeation through 3D cultured buccal epithelium was imaged using confocal microscopy, whilst quantification of LY permeation through collagen hydrogels was measured by fluorescent spectroscopy. |
| **Results:** Human buccal epithelium average thickness was determined to be 712±77 µm, therefore 750 µm microneedle templates were chosen to reflect the dimensions required for epithelial penetration. Dimensional variation was observed between the master microneedles and PLA duplicates, likely due to PDMS contraction. Reproducible PLA microneedles were manufactured with heights of 715±130 µm, and no statistically significant variation. LY was homogenously incorporated within the electrospun patch fibres, which maintained a mesh-like structure. Attachment to the PLA microneedles resulted in a flush baseplate with good residence times of 6 hours. Confocal microscopy revealed that the microneedles formed a clear micropore, which visually confirmed enhancement of LY permeation across the epithelium. When quantified, permeation enhancement using the microneedle-assisted patch was statistically significant, with permeation increasing by two-fold compared to patch only controls. |
| **Conclusions:** The addition of microneedles onto electrospun patches produces enhanced drug permeation across the oral epithelium, with higher peak concentrations and quicker drug absorption times. It is fully anticipated that the resulting micropatterned patches will serve as a superior transmucosal formulation for the administration of poorly permeable drugs. Further work will focus on the incorporation of therapeutics into the design, followed by continued optimisation. |