RATIONAL POLYMER DESIGN FOR MICROARRAY TRANSDERMAL DELIVERY

Ruslan Mohamed[1], Maria Marlow[1], Mischa Zelzer[1], Pratik Gurnani[2] and Giuseppe Mantovani[1]

[1]School of Pharmacy - University of Nottingham, [2]School of Pharmacy – University College London

Background: Microneedle devices are an attractive route towards painless injection of therapeutics. Microneedle arrays can act as stabilising environments, allowing for the controlled release of biologics, such as peptides. One approach to drug release from microneedles is through the dissolution of the polymeric material comprising the needles once they are inserted into the skin. Achieving reproducible drug delivery profiles relies heavily on the polymeric excipient and the microneedle fabrication. This relationship is not sufficiently understood to enable rational microneedle design. Addressing this knowledge gap is crucial for the wider adoption of microneedle technologies. This project seeks to systematically evaluate different polymers and fabrication parameters to establish a correlation between polymer properties, processing parameters and peptide drug delivery performance via microneedles. To accomplish this, a series of acrylamide-based polymers with defined chain lengths and narrow dispersity have been synthesised and utilised to make microneedle backing layers. These backing layers are integral components of microneedle arrays, providing structural support and potentially enhancing skin penetration. The mechanical properties of these backing layers have been evaluated using a texture analyser, allowing for comparison with commercially available polymers (PVA and CMC) typically employed in microneedle arrays. This process facilitates the identification of suitable materials for backing layers in microneedle formulations.

Methods: Structurally diverse polyacrylamides, both homopolymers and copolymers, are synthesized by ultra-fast RAFT polymerization, offering precise control of molar mass, and creating polymers with narrow dispersity. Their chemical properties are characterized by ^{1}H-NMR, SEC, and DSC techniques. Microneedle backing layers have been fabricated using commercially available polymers alongside the synthesised ones. A TA.XT texture analyser, equipped with a three-point bend rig was used to measure the fracture forces, flexibilities, and toughness of the backing layers. Subsequently, the data has been used to determine the Young's moduli of the corresponding backing layers.

Results: ^{1}H NMR analysis confirms polymer composition and determines monomer conversion and polymer chain length. SEC provides data on polymer dispersity, with values in the range of 1.1-1.3. DSC data identifies the glass transition temperatures of polymers, serving as an indicator for brittleness. Texture analyser data measured the fracture forces for both microneedle arrays and backing layers separately. Additionally, it characterised the flexibility, toughness, and Young's moduli of backing layers. This has enabled comparison between the synthesised polymers and commercially available polymers typically used for microneedle devices.

Conclusions: ^{1}H NMR and DSC analysis indicate that RAFT polymerisation offers a quick approach to producing acrylamide and acrylate-based polymers with well-defined chain lengths and narrow dispersity. DSC data reveals that the synthesised polymers adopt a hard/glassy state, justifying the need for plasticiser in polymer blends. Mechanical testing using a texture analyser demonstrates that both the synthesised polymers and PVA exhibit favourable mechanical properties in comparison to CMC. However, comparisons between the synthesised polymers and PVA are not conclusive yet, necessitating further investigation. Identification of optimal drying conditions for polymer backing layer samples is required to accurately assess mechanical properties and make meaningful comparisons.