Development and characterisation of a library of dissolving polymeric microneedles for targeted drug delivery for basal cell carcinoma.

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Background: Basal cell carcinoma (BCC) is the most common skin cancer in humans. One of the drugs that is frequently employed in the management of BCC is imiquimod (Aldara™). However, imiquimod possesses physicochemical properties that limit its permeation to reach deeper tumour lesions such as those seen in nodular BCC. Thus, such topical treatment with Aldara™ cream is restricted to the management of superficial BCC. In light of these drawbacks, it is hypothesised that the use of microneedles to disrupt the *stratum corneum* may promote the permeation of imiquimod to reach deeper BCC lesions.

Methods: Microneedle moulds of different microneedle architectures were produced using micromachining. The moulds were then used to manufacture dissolving microneedles from the commercial polymer Kollidon® VA 64 as well as from novel polymers that were synthesised via free radical polymerisation reactions. The polymeric microneedles of different designs and chemistries were characterised via microscopy, fracture test and *ex vivo* skin insertion studies. Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) analysis on microneedles was conducted to visualise drug, polymer and excipient distribution along the microneedles in a label free fashion. Drug release studies in *ex vivo* porcine skin was also conducted in comparison to the commercial cream, Aldara™. The capability of the microneedles to puncture and deliver the payload in human skin tumours was evaluated using full thickness *ex vivo* patient BCC tissue (NHS HRA approval ID: 130880) followed by ToF-SIMS analysis to visualise drug and polymer distribution in human skin tumours. In addition, the efficacy of the formulation was also evaluated *in vivo* using a rodent model for skin tumours.

Results: Eight dissolving polymeric microneedle patches of different designs and chemistries were manufactured. These patches displayed sufficient tensile strength and skin insertion properties. ToF-SIMS analysis on the microneedles showed that the microneedles displayed homogenous drug and polymer distribution along the needle length. Drug release studies from *ex vivo* skin tissues demonstrated that some of the patches were capable of achieving higher intradermal delivery of imiquimod relative to the commercial cream, Aldara™ in a dose sparing manner. In addition, ToF-SIMS analysis of patient BCC tumours treated with imiquimod loaded microneedle patches demonstrated significant intradermal delivery of imiquimod within the skin tumour. Furthermore, the parallel detection capabilities of the ToF-SIMS permitted visualisation of the dermal distribution of unlabeled polymer within the native skin tumour milieu.

Conclusions: The current work highlights that dissolving polymeric microneedles is a viable drug delivery platform for the treatment of nodular BCC. Through judicious selection of microneedle design and chemistry, imiquimod loaded microneedle patches were successfully fabricated and characterised. Some of these patches were capable of achieving higher % intradermal delivery of applied imiquimod dose (>25%) relative to the commercial cream, Aldara™ (5.7%). This is further corroborated by the successful delivery of imiquimod into human BCC tumours demonstrating the potential of the microneedle-based approach to treat BCC.