production in a 3D reconstructed human skin model, when compared to a positive control of 5% w/v sodium dodecyl sulphate. This is in line with other research that has demonstrated the *in vitro* biocompatibility of hydrogels prepared from this type of polymer (Luzardo-Álvarez et al. 2011; Moreno et al. 2014). Hydrogel-forming microneedles prepared from the polymer PMVE/MA have also been shown to exhibit antimicrobial properties, with no microbial growth detected upon storage (Donnelly et al. 2013). This type of hydrogel is, therefore, highly unlikely to cause skin or systemic infection. Indeed, the human studies to date have revealed no skin reactions following use, with swollen arrays removed intact after up to 6 h in place in skin (Donnelly et al. 2014c).

Drug delivery

Hydrogel-forming microneedles been shown to successfully deliver a range of molecules of varying molecular weight *in vivo*, from small, hydrophilic molecules, such as metronidazole, to larger molecular weight peptide and protein molecules, such as insulin and fluorescein isothiocyanate labelled-bovine serum albumin (Donnelly et al. 2012). The combination of the hydrogel-forming microneedles with iontophoresis, with the aim of achieving for pulsatile or bolus delivery, was observed to provoke a marked increase in the rate and extent of in-skin swelling of the arrays. In general, this led to a greater rate and overall extent of transdermal delivery for each of the molecules; however, the difference was only significant for the biomolecules under investigation.

The hydrogel-forming microneedle arrays described as 'super swelling' have also been tested for their drug delivery capabilities (Donnelly et al. 2014a). Paired with a lyophilized drug reservoir, delivery of a clinically relevant dose of a low potency, high dose drug substance (ibuprofen) was achieved, as well as rapid delivery of a model protein (ovalbumin). Hardy et al. (2016) also investigated ibuprofen delivery, using a light-responsive 3,5-dimethoxybenzoin conjugate of the drug incorporated in a pHEMA formulation, in order to test light-triggered transdermal drug delivery. *In vitro*, this hydrogel array was able to deliver up to three doses of 50 mg of ibuprofen upon application of an optical trigger, over a prolonged period of time (up to 160 h). This type of system offers great potential as a stimulus responsive delivery platform, where "on-demand" drug delivery is required, with patient- or physician-controlled analgesia an obvious example.

Application of a 'phase-transition microneedle patch' containing insulin at a dose of 2.0 IU kg^{-1} was able to achieve comparable blood insulin area under curve (AUC) to a 0.4 IU kg^{-1} injection in a diabetic pig model, indicating the relative availability of insulin delivered by the microneedles to be around 20% of the total insulin contained within. In fact, over a 2 month period, the PVA, dextran and CMC microneedle array showed significantly better control of long-term blood glucose over the subcutaneous injection, as measured by HbA1c level, likely due to the post-peak sustained release of insulin from the array. This offers opportunity for non-invasive insulin delivery, with future work hoping to load insulin in selected regions along the microneedle shafts to accommodate the different insulin-dosing regimens. With these alternative polymer