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| **Preliminary development of biodegradable microneedle arrays for delayed burst vaccine release** |
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| **Background:** Repeated dosing is an important hurdle in mass vaccination campaigns, reducing their potentially life-saving impact. Delayed burst release formulations may allow controlled release of vaccines at defined time points to overcome these limitations. Polymeric microcontainers can retain the active ingredient for an appropriate time and release that cargo upon degradation, depending on the polymer characteristics. These can be designed in different shapes, including microneedle (MN) tips for transdermal applications. Antigens can then be incorporated in dry powder form or embedded in an appropriate matrix for delivery at specific time points. Here, we aim to develop biocompatible and biodegradable formulations with polymers such as chitosan (CS), polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA). Optimised polymeric blends will be used to manufacture MN arrays with a hollow cavity for dry powder loading and assessed in terms of their potential use as delayed burst release systems. |
| **Methods:** Polymeric films were prepared from aqueous CS, PVP and PVA solutions (2% w/v each), with and without sodium tripolyphosphate (Na-TPP, 0.1-0.3% w/v) as a crosslinking agent. These were cast in 25 cm2 3D printed moulds and dried at room temperature for 48-72 h. Mechanical properties (tensile strength and elongation at break) were assessed using a Texture Analyser, while thermal properties were evaluated by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). Swelling and erosion were measured upon immersion of the films in aqueous media. Selected formulations were used to prepare MN arrays using PDMS moulds containing 225 pyramidal MNs (15x15) with 600 µm in height and 200 µm base side length. After drying at room temperature for 36 hours, a powder mixture of rhodamine B and mannitol (1:100) was added to the moulds, and a second layer of the formulations was added to seal the MN arrays. Optical and scanning electron microscopy (SEM) imaging were used to visually assess the shape of the MN arrays, and insertion depth was evaluated in a model membrane (Parafilm M®) following application with thumb pressure for 30 s. |
| **Results:** Combinations of CS:PVP and CS:PVA (volume ratio 1:9 to 9:1) were assessed as dried films, with and without crosslinking with Na-TPP. Formulations containing more CS showed increased tensile strength, particularly when crosslinked. The residual water content was similar in all formulations, at 8-12% of initial weight. In terms of swelling and erosion, as expected, films without Na-TPP absorbed more liquid and presented higher weight increases in comparison to those containing the crosslinker. Among all formulations, crosslinked CS:PVP blends with higher CS proportions showed the lowest weight increase by swelling, which can indicate appropriate characteristics for controlled drug release. However, when used to manufacture MN arrays that could be further loaded with a powder mixture, these formulations also showed increased shrinkage, reducing the effective volume available for loading within the MNs. Regardless of their composition, the MN arrays could be inserted into Parafilm M® to sufficient depth. Unfortunately, loading the MN arrays with the powder mixture and further sealing with a second polymeric layer was not successful, requiring optimisation and potentially an alternative loading approach. |
| **Conclusions:** Biodegradable polymeric blends were successfully used to prepare MN arrays with a hollow cavity for drug/antigen loading, with sufficient mechanical strength to achieve effective insertion. Loading of these arrays with dry powder mixtures still requires optimisation before further *in vitro* testing. |