GLOBAL RESEARCH IMMERSION PROGRAM FOR YOUNG SCIENTISTS

MICRONEEDLE-MEDIATED DELIVERY OF ANTI-IL-31 RECEPTOR FOR TREATMENT OF ATOPIC DERMATITIS

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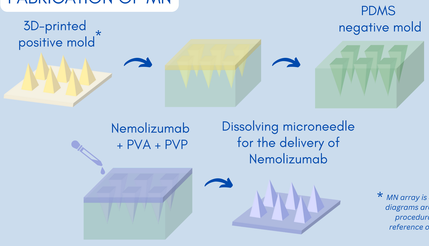
INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by an intense itch, recurrent eczematous lesions and a fluctuating course. Disruption of the epidermal barrier is at the basis of skin inflammation in AD, which is driven by Th2 cell activation and the production of pro-inflammatory cytokines, including IL-4, IL-13 and IL-31. Overall, this results in pruritus and the stimulation of B cells and plasma cells to produce antigen-specific IgE.[1]

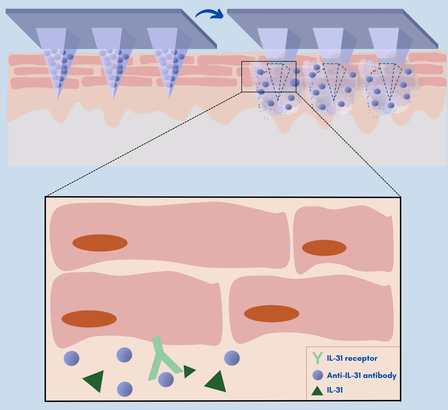
Inhibiting the function of the IL-31 receptor through a monoclonal antibody (Nemolizumab) is an innovative treatment which specifically targets itch and inflammation and has proven effective in reducing symptoms in clinical trials, and has been approved for use in Japan.[2,5] Nonetheless, Nemolizumab has to be administered through a subcutaneous injection every 4 weeks, which may reduce patient compliance due to pain and inconvenience. Our proposal is to enhance the localized delivery of Nemolizumab using a microneedle (MN) patch.

METHODOLOGY

FABRICATION OF MN



DRUG DELIVERY MECHANISM



Nemolizumab competitively inhibits the interaction between the IL-31 receptor and its ligand IL-31, a pro-inflammatory cytokine. By preventing the activation of downstream inflammatory pathways, it effectively targets the pruritus and inflammation that characterizes AD.

CONCLUSION

- This study demonstrated that the designed dissolving MN presents good solubility, adequate mechanical strength, and effective skin penetration capabilities.
- Although PVA 105 and PVA 1795 MNs showed similar solubility, those composed of PVA 105 displayed increased mechanical properties and are therefore preferred in this application.
- This MN patch therefore presents itself as a suitable local delivery mechanism for Nemolizumab which could increase patient compliance, allowing it to become a more widely used and effective treatment for AD.
- Nevertheless, further optimization and evaluation of the MN-based Nemolizumab delivery system are required to validate its suitability and performance in the clinic.

RESULTS

MORPHOLOGY

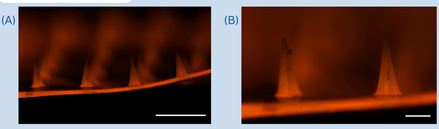


Fig. 1 Fluorescence microscopy of MN patch. (Scale bar: 1mm (A), 250μm (B))

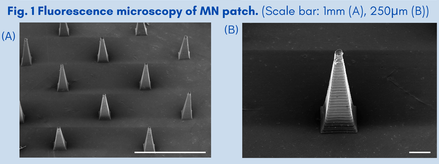


Fig. 2 Scanning electron microscopy (SEM) image. (Scale bar: 1mm(A), 100μm(B))

The above images show the morphology of the microneedles with a base of 0.2 mm x 0.2 mm, height of 0.8 mm, and a 1 mm centre-to-centre displacement.

SOLUBILITY IN PBS

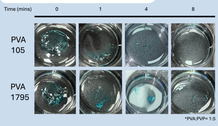


Fig. 3 Dissolution of material stained with dye.

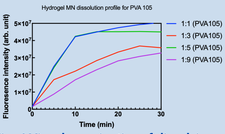


Fig. 4 Visual examination of dissolving 2 types of PVA formulations.

Both PVA formulations (PVA:PVP = 1.5) showed similar dissolving rates and almost completely dissolved at t = 8mins (Fig.3). The 1:1 and 1:5 PVA:PVP ratios dissolved fastest and emitted the highest fluorescence intensity compared to 1:3 and 1:9 (Fig.4).

MECHANICAL STRENGTH TEST

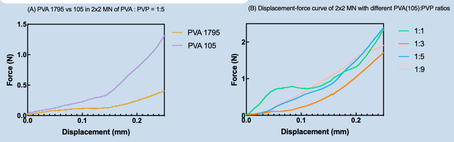


Fig. 5 Comparing the mechanical strength of PVA-PVP MNs across 2 types of PVA formulae (A) and different PVA:PVP ratios (B).

2x2 MN arrays composed of PVP with PVA 105 presented a higher mechanical strength compared to those with PVA 1795 (Fig.5A). Increasing proportions of PVP also increased the mechanical strength; 1:9 and 1:5 ratios demonstrated higher strength than other formulations (Fig.5B).

SKIN PENETRATION TEST

The 8x8 MN array was applied to the back of the mouse skin for 5 minutes. It was then stained with trypan blue for 3 minutes and photographed. Figure 6 shows that the MN successfully penetrated the mice's skin, which would enable efficient drug release.

Fig. 6 Skin penetration efficiency test. (Scale bar: 2mm)

REFERENCES AND ACKNOWLEDGEMENTS

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