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Cover Story

Dissolving microneedle vaccine delivery systems

It is well-established that the transdermal route is an attractive alternative for minimally-invasive drug delivery. The potential of the skin as a site for vaccine delivery has been demonstrated over the past decade, with research indicating stronger immune responses and improved duration of immunity compared with conventional intramuscular administration. Benefits of this minimally invasive vaccination approach include avoiding needle and syringe limitations such as the need for qualified medical practitioners, needle-stick injuries, needle-phobia, and disposal costs. To achieve this, the delivery of compounds into and/or through the skin must overcome the barrier of the stratum corneum (the tough outer layer of skin). A range of enhancement methods have been developed to do this, including but not limited to biolistic, iontophoresis, sonophoresis, and most recently, microneedle delivery. One of the simplest embodiments of such a device is to ensure that the delivery vehicle is also the formulation of vaccine — such as with a dissolving microneedle device.

The paper by Professor Mark Kendall and his team in this issue demonstrates the significance of using a unique suite of analytical tools (including FT-FIR using synchrotron radiation, nanoindentation, and skin delivery assays) to identify advantageous microneedle/microprojection device formulations [1]. Their study provided an in-depth mechanistic understanding of the effect that sugar/polyol excipients have on formulation properties of micro-scale formulation delivery systems. The authors analyzed the effects of adding sucrose, trehalose, sorbitol and mannitol at various ratios to carboxymethylcellulose, a well-established excipient within the microneedle field as the core material. These sugars/polyols are often used in the vaccine industry as bulking or stabilizing agents where they can significantly increase the vaccine stability. In a previous cover story in the Journal of Controlled Release, the Kendall team showed this potential in long term stability studies of their silicon Nanopatch, compared to liquid formulations [2]. They highlighted, a promising attribute of these technologies, that the use of solid formulations may make it possible to reduce the need for cold-chain vaccine transport/storage. This could reduce the cost and complexity of getting vaccines to those that need them most, particularly in the developing world.

The Kendall group found that the macro-characteristics of a dissolving microprojection formulation (e.g., brittleness/malleability) did not dictate the micro-characteristics (such as crystalline/amorphous structures). Thus, successful release into skin could be achieved whether an amorphous or crystalline matrix was used. In fact, they were able to deliver their formulation into skin within 5 s, which makes this type of device competitive with the needle and syringe for application time. A particular approach of note within the manuscript was the nanoindentation technique utilized by the authors to investigate the mechanical failure of the microprojections. Individual microprojections were indented within single arrays facilitating insight into the different failure modes and their correlation to formulation, which in principle can also be applied to the larger microneedles. By doing this, the microstructure could be related directly to the functional performance of the microprojections, in strength, ability to penetrate skin and dissolution. This study design more accurately reflects in vivo application of microprojections. The surface roughness of the skin and the small scale of projections mean that skin contact would not be uniform across the array, thereby resulting in different failure modes.

As innovative approaches emerge, it is important to understand the mechanisms, e.g., how micro-devices for vaccination behave on the scale that they operate. Without clear understanding of the mechanisms, any formulation would be nothing more than a shot in the dark. Most of the time, it does not work and there is no good way of finding a solution. If it happens to work, it is still difficult how to improve further. With ever more micro- and nano-technologies introducing into this field, the Journal of Controlled Release provides a forum to discuss the potentials and limitations of the approach, and the path toward developing clinically useful formulations. The paper from the Kendall team serves as good starting point to discuss the assay methods useful or necessary in developing clinical formulations.

References

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