“Zero Waste” Nanocomposite Patches for Transdermal Delivery of Analgesics

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We have developed a novel biodegradable transdermal nanocomposite patch composed biodegradable polymeric nanofibers containing silica nanoparticles with encapsulated bioactive/s. The nanofiber mats are synthesised by electrospinning a slurry containing the biodegradable polymer and silica-bioactive nanoparticles. The resulting non-woven mat is composed of fibres with a diameter typically around 300nm containing 50-100nm silica particles embedded inside the fibres. Upon contact with moisture, either on the top of the skin or inside a wound, the biodegradable polymer nanofibers dissolve and release the nanoparticles. Subsequently, silica nanoparticles gradually release their payload by diffusion. After a few days, the particles start to dissolve into innocuous water soluble silicates.

The resulting mats were characterised for 1) *in vitro* permeation through human skin using Franz Cell diffusion apparatus and for 2) *in vivo* transdermal permeation in piglets. These studies demonstrated the following features of these Nanocomposite mats:

- **Controlled Release**: The encapsulation in silica matrix did not alter the release profile of lidocaine from the nanocomposite patch *in vitro*. Constant release was achieved up to 72h.
- **Faster Pain Relief**: The Franz cell studies also showed a much shorter induction time of 2H between application and initial release; this was more than 4H for the commercial patch, indicating a strong possibility for faster pain relief. This was confirmed in our animal studies where the release of lidocaine in the blood plasma was evident as early as 1H from the nanocomposite patch verses over 4H for the commercial patch. This added feature of fast pain relief would be ideal for paediatric analgesia, where transdermal patches are becoming the route of choice.
- **Superior efficiency:** In Franz cell studies, despite 60-10-fold lower lidocaine loading in the nanocomposite patch, ~80% of administered lidocaine had permeated through the skin at 24H, which when combined with 17% present in the skin tissue (epidermis and dermis) showed a total of ~97% drug release (i.e. < 5% remaining in the patch after use). In comparison, a total of ~1% of lidocaine from the commercial patch was released. This was confirmed in our large animal studies where, despite a 30-fold smaller dose in the nanocomposite patch, the delivery of lidocaine into blood plasma and the skin was comparable to the commercial patch.
- **Low potential for skin toxicity:** The nanocomposite patch is unlikely to lead to any specific nanoparticle based toxicity, as we found no evidence of skin penetration by fluorescent nanoparticles *in vitro*. This was further confirmed by Draize scoring in our animal trials where the treated skin showed no signs of any irritation/inflammation (redness) or swelling even after 72 H of patch application.

Our nanocomposite patches are now ready for testing in humans and we anticipate that the clinical trials will prove these new patches to be safe and efficacious