

Cutaneous Drug Delivery System: Characteristics of Drug Loaded Dissolving Microneedle Technology

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Extended Abstract

The microneedle-mediated transdermal delivery system has been developed to provide minimal invasive self-administration method. Especially, dissolving microneedles, which deliver the target drugs as the drug-loaded microneedle dissolves into the skin, have been spotlighted recently [1]. Droplet-born air blowing (DAB) method has great advantages in stability with precise dose control because DAB provide quick manufacturing process with ambient temperature [2].

This study suggests the novel dissolving microneedle fabrication method, droplet-born air blowing (DAB), which provide gentle temperature and fast manufacturing process with precise dose control. The purpose of this study is to show the characteristics of dissolving microneedles and to confirm with the *in vitro* and *ex vivo* models.

Microneedle fabricated by DAB method. Briefly, Biodegradable polymer such as HA (hyaluronic acid) was dissolved in water with active ingredients. The polymer and drug mixture were dropped to a patch, and each droplet is shaped to the microneedle. We tested protein and chemical drug. The loaded amount of drug was analyzed by enzyme-linked immunosorbent assay (ELISA) or HPLC/UV system. Skin permeability of microneedle was confirmed by OCT (optical coherence tomography) and delivered amount of drug into the skin was analyzed using Franz diffusion cell (Logan, FDC-6T). The dissolution performance of protein and chemical drug was evaluated using dissolution equipment (Hanson, Elite 8 Dissolution Tester).

We optimized the DAB process parameters and scaled up without applying any heat. Various ingredients were loaded within microneedles approximately 100% compared to theoretical values independent of microneedle length. *In vitro* and *ex vivo* studies using Franz diffusion cell showed excellent delivery efficiency compared to topical solution. *In vivo* OCT images clearly showed that whole length of microneedles could penetrate into human skin. We developed the appropriate dissolution condition for protein and chemical drugs loaded microneedles. We are studying the pharmacokinetics of small molecule, biomolecule pharmaceutical products in animal models.

DAB technology suggest a way to solve the problems of conventional molding method to fabricate dissolving microneedle. Based on the method, we have successfully developed mass production system to manufacture microneedle-arrayed patch. We loaded lots of active ingredients with precise dose control, and confirmed the delivery efficiency of labile ingredients such as peptide and anti-oxidants within microneedles. We are investigating the formulations for a biopharmaceutics using this platform technology.

References

- [1] S. P. Sullivan, D. G. Koutsonanos, M. P. Martin, J. W. Lee, V. Zarnitsyn, S. O. Choi, N. Murthy, R. W. Compans, I. Skountzou, M. R. Prausnitz, *Nat. Med.*, vol. 16, pp. 915-920, 2010.
- [2] J. D. Kim, M. Kim, H. Yang, K. Lee, H. Jung, *J. Cont. Rel*, vol. 170, pp. 430-486, 2013.