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Transdermal delivery of insulin using 3D printed microneedles

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Microneedles (MNs) are an attractive approach for transdermal delivery for the delivery of drugs which undergo enzymatic degradation in the gastrointestinal tract or present difficulties to permeate it. MN systems are composed of micrometric needles included in the same array and can be manufactured using different materials and techniques which usually require many steps and are difficult to scale up. Here, we present biocompatible microneedles manufactured by stereolithography (SLA) - a 3D printing technique where MN patches of various designs are built in a layer – by – layer manner. The MN patches are subsequently coated with insulin-carrier formulations via inkjet printing. A stereolithographic printer was employed to print arrays featuring pyramid needle designs. The microneedles were then coated with insulin-sugar formulations at a 5:1 ratio, using inkjet printing. The quality of the produced microneedles and coatings was evaluated by x-ray computer micro tomography (μ CT) and scanning electronic microscopy (SEM). The native structure of insulin was analyzed by circular dichroism and possible changes and interactions of insulin in the formulation were studied by Raman spectroscopy. *In vitro* studies were carried out using Franz diffusion cells and *in vivo* animal studies were done using diabetic mice treated with 0.2 IU of insulin/array and monitored up to 4 hours after administration with a glucometer. The SEM and μ CT evaluations showed that the microneedle arrays were printed with high accuracy and reproducibility. Inkjet printing led to the formation of thin and uniform layers with high precision and reproducibility. All carriers were found to preserve insulin integrity. Franz cell diffusion studies revealed rapid insulin release rates within 30 min. *In vivo* studies showed a remarkable steady state hypoglycemia effect which continued up to 4 hours. In conclusion, 3D printing stereolithographic technique can be employed to fabricate MNs which when combined with a highly accurate coating technique such as inkjet printing can yield microneedle systems that rapidly deliver insulin through the skin.

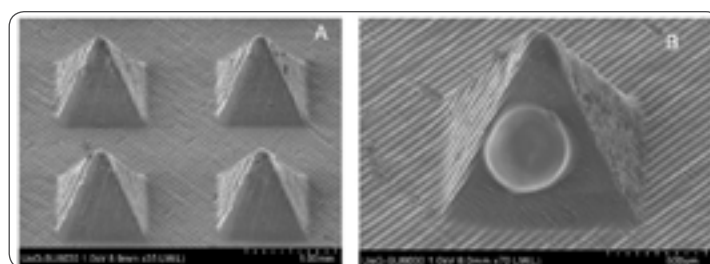


Figure: SEM image of 3D printed microneedles A. Uncoated B. Coated

Recent Publications

1. Pere C P P, et al. (2018) 3D printed microneedles for insulin skin delivery. International Journal of Pharmaceutics 544:425-432.
2. Economidou S N, et al. (2018) 3D printing applications for transdermal drug delivery. International Journal of Pharmaceutics 544(2):415-424.

Biography

Cristiane P Pere has her expertise in drug delivery systems. In her Masters, she worked with nanoparticles obtained by spray drying. In her PhD, she has worked with coated metallic and 3D printed biocompatible MN for insulin delivery. The focus of her work was to develop stable insulin formulations for rapid released using MNs.

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