DISSOLVING POLYMERIC MICROARRAY PATCHES LOADED WITH RILPIVIRINE NANOPARTICLES OBTAINED BY BEAD-MILLING

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Background: According to the World Health Organisation, human immunodeficiency virus (HIV) is one of the major global public health issues. Antiretroviral agents are commonly delivered orally or intramuscularly. As a patient-friendly alternative, dissolving bilayered polymeric microarray patches (MAPs) for the intradermal delivery of rilpivirine (RIL) were developed. To achieve high drug loading, a nanosuspension (NS) of RIL was prepared by bead-milling at laboratory scale prior to MAP fabrication.

Methods: The RIL NS was produced in a glass vial (total volume 10 mL) using ceramic milling beads (12 g, 0.1-0.2 mm) and two magnetic stir bars (25 x 8 mm) to facilitate bead movement. RIL (0.25 g) and a surfactant solution (5.5 mL) containing 2% w/w poly (vinyl alcohol) 9-10 kDa and 2% w/w poly (vinyl pyrrolidone) 58 kDa were added to the vial and milled at 1,500 rpm for 24 h at an angle of 75°. The NS was separated from the beads by sieving, made up to a total volume of 6 mL and lyophilised. A NanoBrook Omni Particle size analyser was used for measuring the particle size of obtained nanoparticles.

The lyophilised NS was reconstituted in 710 µL deionised water and immediately used for casting the first layer of MAPs (100 µL/ MAP) using silicone micromoulds (600 pyramidal needles, height 750 µm, base 300 x 300 µm, interspacing 50 µm). After application of a pressure of 5 bar for 15 min, excess formulation was removed and MAPs were dried at room temperature for 2 h. To form a mechanically strong baseplate, 0.7 g of an aqueous poly (vinyl pyrrolidone) 360 kDa blend (30% w/w) was cast on top of the first layer, followed by centrifugation at 3,500 rpm for 15 min.

After further drying for 18 h, MAPs were demoulded, visually inspected using a stereo microscope and tested in terms of their mechanical strength (compression at 32 N against an aluminium surface for 30 s using a Texture Analyser) and insertion efficiency into a previously validated skin model consisting of eight layers of Parafilm M®. Drug content was calculated based on the total needle volume of 13.8 mm^3 and the composition of the prepared NS.

Results: The NS had a mean particle size of 168 ± 2 nm (PDI 0.18 ± 0.02, n = 9) before and 169 ± 3 nm (PDI 0.20 ± 0.05, n = 9) after lyophilisation and reconstitution. Observation of MAPs under the stereo microscope showed two clearly separated layers with RIL visible in the needle shafts only and a clear baseplate. MAPs were compressed 9 ± 6% (n = 48) of their total needle height of 750 µm and approximately 50.8% of the total needle height could be inserted into Parafilm M®. Based on theoretical calculations, MAPs had a total drug load of 2.8 mg/ MAP.

Conclusions: RIL loaded MAPs were mechanically strong and could be easily inserted into a validated skin model. Further studies will now need to be conducted to evaluate in skin dissolution times and RIL deposition.