Safety Profiling of a Candidate Decontamination Product: Assessing the Dermal Absorption of Particulate Zirconium Hydroxide through Dry and Sweat-Covered Skin

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Introduction

Following operational deployment, residues of personal decontamination product may persist on exposed human skin surfaces representing a potential hazard due to their inherent toxicity and/or as a potential vehicle for transdermal delivery of contaminants such as chemical warfare agents. As part of a safety profiling exercise, the dermal absorption of a candidate decontamination product (particulate zirconium hydroxide; $Zr(OH)_4$) was compared against FAST-ACT® and A200 (derived from a M295 personal decontamination kit). The study was performed in accordance with OECD guidelines [1], using artificial sweat to mimic conditions reported to enhance metal particle absorption through skin [2, 3].

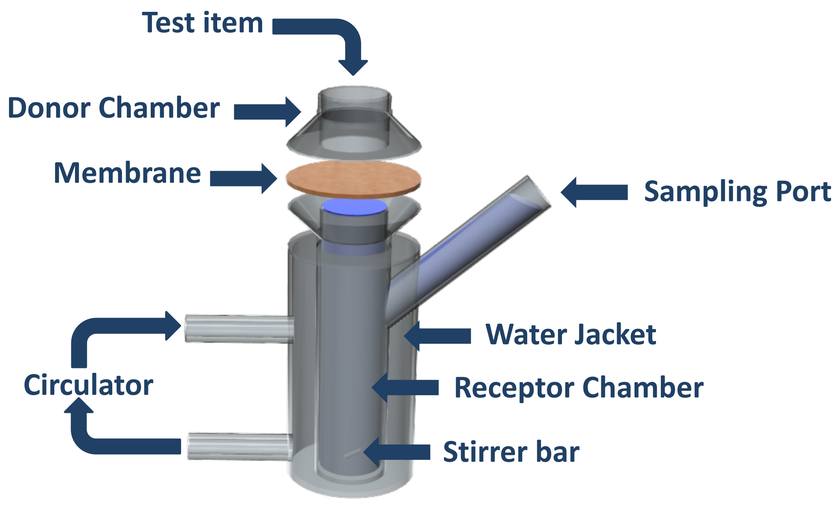

Figure 1: Franz-type diffusion cell.

Materials and Methods

Pig dorsum skin (*sus scrofa*, female, 25 kg) was dermatomed to 500 µm and mounted on Franz-type diffusion cells (1.77 cm^2 diffusion area (**Figure 1**). Citrate-phosphate buffer (pH 4) containing 5% (w/v) EDTA was used as receptor fluid (RF). Experiments were initiated by dosing 1.5 mL of artificial perspiration (EN1811:2011), where applicable, on the surface of the skin, followed by a 90 ± 2 mg of decontaminant product. Receptor fluid was sampled every 3h for a total of 24h.

At 24h post exposure, test powders were removed from the skin surface, which was then washed with 0.5 mL of water and swabbed with cotton wool. Skin was tape-stripped using two D-Squame discs to remove any remaining test product, followed by heat separation into epidermis and dermis. All samples were prepared for induced coupled plasma optical emission spectroscopy (ICP-OES) analysis using zirconium, magnesium or aluminum as surrogates for Zr(OH)4 (LOD/LOD: 0.002/0.016 ppm), FAST-ACT® (LOD/LOQ: 0.001/0.010 ppm) or A200 (LOD/LOQ 0.018/0.177 ppm), respectively.

Results

Penetration profiles for $Zr(OH)_4$, FAST-ACT® and A200 resulted in no penetration into the RF, under both experimental conditions (**Figure 2**). Furthermore, the vast majority (>99%) of all three decontamination products were recovered from the skin surface (**Figure 3A**). When applied to sweat-covered skin, there was an increase in the amount of test products recovered from the epidermis and superficial dermal tissue. However, an excessive amount of sweat was used to represent a worse case-scenario and this increase equated to <0.1 % of the applied dose (**Figure 3B**).

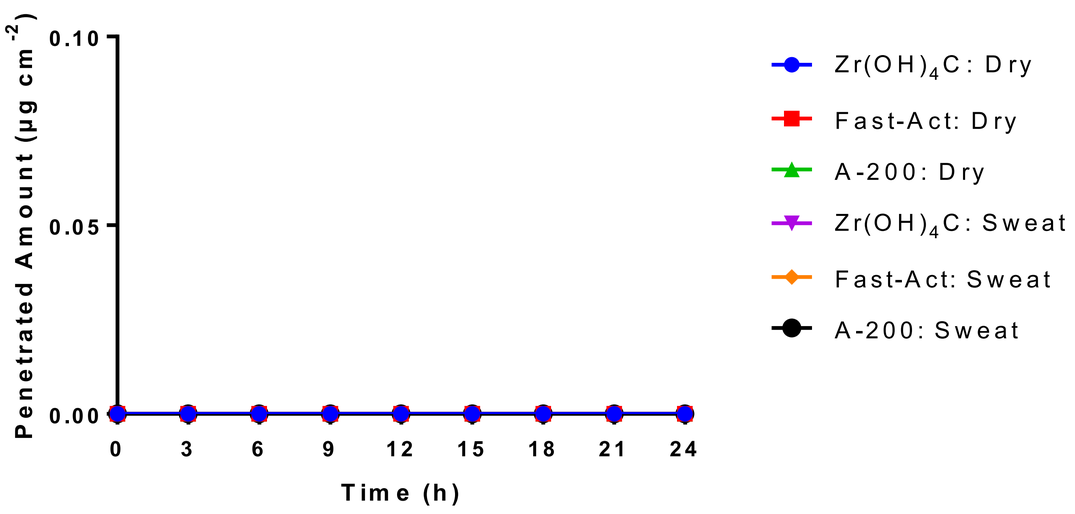

Figure 2: Amount (µg cm^{-2}) of zirconium hydroxide, FAST-ACT® and A200 penetrated into the receptor fluid in presence and absence of artificial sweat.

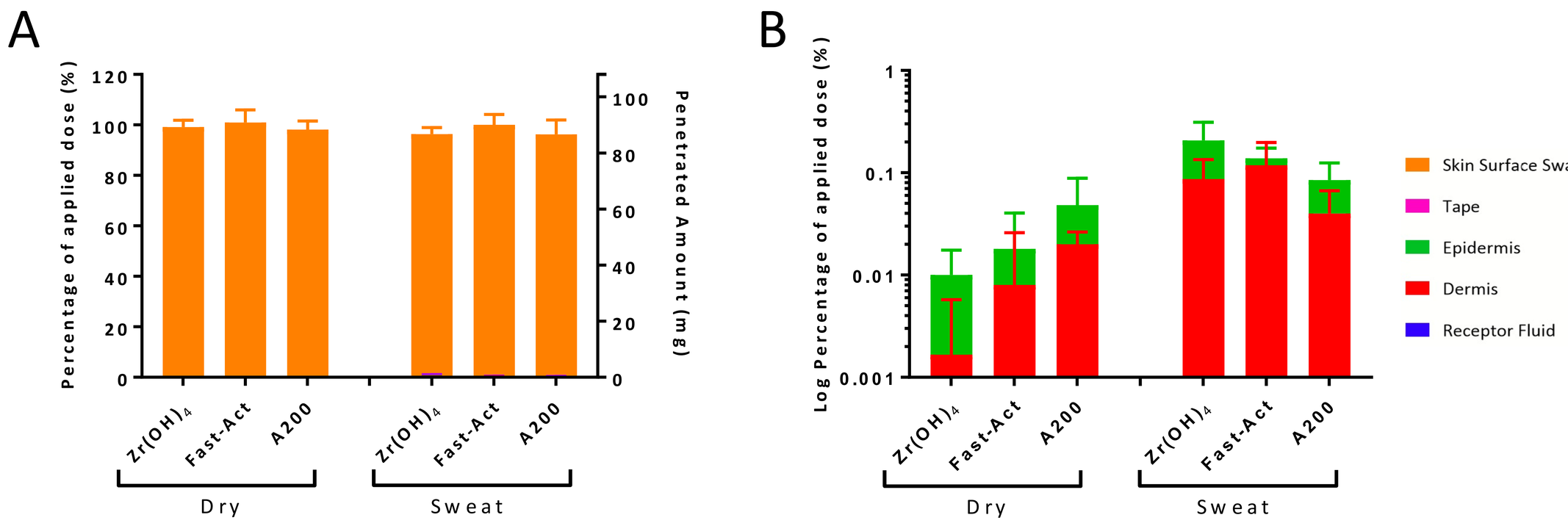

Figure 3: (A) Full mass balance of zirconium hydroxide, Fast-Act and A200 after 24 hours of exposure. **(B)** Epidermis and dermis only for clarity.

Summary

- These data indicate that particles of zirconium hydroxide do not penetrate the skin.
- The marginal enhancement in recovery detected in the skin tissue under sweaty conditions is likely attributed to the dissolution of metal ions from within each formulation, or simply due to their deposition, rather than penetration.
- There is a high probability that this test item will not pose an additional hazard under anticipated conditions of use.

References

[1] OECD, Test No. 428: Skin Absorption: In Vitro Method. 2004.
[2] Midander, K., et al., Testing in artificial sweat–is less more? Comparison of metal release in two different artificial sweat solutions. Regulatory Toxicology and Pharmacology, 2016. 81: p. 381-386.
[3] Sartorelli, P., L. Montomoli, and A.G. Sisinni, Percutaneous penetration of metals and their effects on skin. Prevent Res, 2012. 2(2): p. 158-164.

Acknowledgements

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