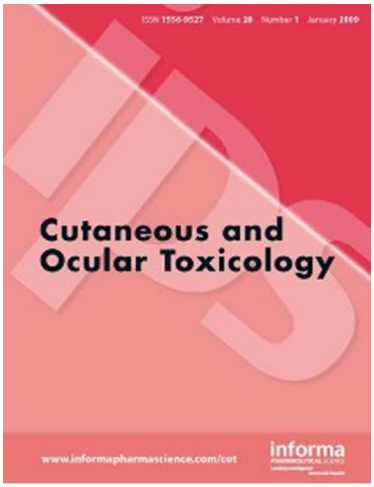

Preliminary evaluation of military, commercial and novel skin decontamination products against a chemical warfare agent simulant (methyl salicylate).

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Abstract

Rapid decontamination is vital to alleviate adverse health effects following dermal exposure to hazardous materials. There is an abundance of materials and products which can be utilised to remove hazardous materials from the skin. In this study, a total of 15 products were evaluated, 10 of which were commercial or military products and 5 were novel (molecular imprinted) polymers. The efficacies of these products were evaluated against a 10µL droplet of ^{14}C-methyl salicylate applied to the surface of porcine skin mounted in static diffusion cells. The current UK military decontaminant (Fuller's earth) performed well, retaining 83% of the dose over 24 hours and served as a benchmark to compare with the other test products. The five most effective test products were Fuller's earth (the current UK military decontaminant), Fast-Act® and three novel polymers (based on itaconic acid, 2-trifluoromethylacrylic acid and N,N-methylene bis acrylamide). Five products (medical moist-free wipes, 5% FloraFree™ solution, normal baby-wipes, baby-wipes for sensitive skin and Diphotérine) enhanced the dermal absorption of ^{14}C-methyl salicylate. Further work is required to establish the performance of the most effective products identified in this study against chemical warfare agents.

Introduction

The deliberate release of chemical, biological, radiological and nuclear (CBRN) materials poses a significant threat to civilian populations as exemplified by the 1995 Tokyo sarin incident (1). Skin decontamination of civilians following exposure to hazardous materials is vital to mitigate local or systemic absorption and subsequent toxicity. Current UK mass casualty decontamination procedures require the casualty to disrobe and decontaminate within bespoke showering units. This procedure has many logistical issues such as time taken to erect the shower units, potential crowd management issues and triage of casualties which may delay decontamination (2, 3). Moreover, previous studies have shown that water may enhance the penetration of certain chemicals through the skin via the 'wash-in effect' (4-7). Within the current procedure there is a window in which to perform rapid decontamination prior to or in lieu of showering within the bespoke showering units. Therefore, the identification or development of an effective decontamination product which can be used at the scene of an incident by members of the public may represent a significant improvement for managing mass casualty incidents requiring decontamination. Clearly, such products need to be evaluated to ensure their effectiveness against a range of toxic chemicals.

Methyl salicylate is generally regarded as an appropriate chemical warfare agent simulant for sulphur mustard (bis(2-chloroethyl) sulphide) based upon its physiochemical properties and dermal absorption kinetics (8). It has been applied in various scenarios from evaluating medical countermeasures to assessment of protective clothing (9-13).

The purpose of this study was to identify an effective product which can be rapidly deployed at the scene of a CBRN incident prior to the availability of bespoke decontamination facilities. A range of products were selected for evaluation: Commercial-off-the-shelf (COTS) products were selected on the basis of suppliers' claims of efficacy; some were chosen as they may be readily available (such as baby-wipes). Novel polymers were selected based upon their binding affinities to methyl salicylate, sulphur mustard, soman and VX which was determined by *in silico* modelling using the LEAPFROG algorithm. Military products were chosen on the basis that they may serve as a benchmark of 'standard efficacy' and also to evaluate their efficacy against the chemical warfare agent simulant methyl salicylate.

Materials and Methods

Ring-labelled (^{14}C) methyl salicylate (55 mCi mMol^{-1}) was purchased from ARC (UK) Ltd (Cardiff, UK). Non-radioactive methyl salicylate (MS) was purchased from Sigma Aldrich (Poole, UK) and was reported to be >99% pure. These were mixed in an appropriate proportion to give a working solution with a nominal activity of 0.2 µCi µl^{-1}.

Soluene®-350 and Ultima Gold™ liquid scintillation counting (LSC) fluid were purchased from PerkinElmer, Cambridgeshire, UK. Propan-2-ol and ethanol were obtained from Fisher Scientific, Leicestershire, UK.

Proprietary products obtained for evaluation were Fuller's earth (Sigma Aldrich, Poole, UK), KBDO (potassium butadiene monoximate) liquid (E-Z-EM Inc., Canada; free-flow bottle and sponge formulations), normal baby wipes ('Pampers baby fresh', Proctor & Gamble), Diphotérine eye wash (Prevor, Valmondois, France), Fast Act chemical containment and neutralisation system (NanoScale, Manhattan, USA), FloraFree detergent (DEB Ltd, Belper, UK), alcohol free medical wipes (Safety First Aid Group, London, UK) and an industrial skin decontamination cream (DTAM SKIN™, Colormetric Laboratories Inc., Illinois, USA).

Novel polymers were prepared by the University of Cranfield (Cranfield, UK) as previously described in a patent (14). The materials were synthesised using ethylene glycol dimethacrylate (EGDMA) cross-linker and various monomers which confer different functional groups (e.g. amide, amine, carboxylate) to the resulting polymer. The cross-linker and functional monomer were mixed in a 4:1 molar ratio with a free-radical initiator (1, 1'-azobis(cyclohexanecarbonitrile), 1% w/w of total mixture) which decomposes under UV light or heat. Dimethylformamide (DMF, volume equivalent to the combined mass of reactants) was used as solvent and porogen. The monomers, initiator and solvent were mixed in a glass bottle and degassed with nitrogen for 5 minutes. The bottle was then sealed with a screw cap and the reaction initiated by heating to 80 °C for 18 hours. Control polymers were prepared with EGDMA in the absence of any functional monomers. Following polymerisation, the resulting material was ground then wet-sieved with methanol to collect particles ranging from 40 to 90 µm diameter which were subsequently washed with hot methanol for 24 hours and dried at 80 °C overnight.

Full thickness skin was obtained post mortem from female pigs (Sus scrofa, large white strain, weight range 15-25 kg) purchased from a reputable supplier. The skin was close

clipped and excised from the dorsal aspect (full thickness) from each animal. The skin was then wrapped in aluminium foil and stored flat at -20ºC for up to 3 months before use. Prior to the commencement of each experiment, a skin sample from one animal was removed from cold storage and thawed in a refrigerator (5ºC) for approximately 24 hours. The skin was then dermatomed to a nominal depth of 500 µm using a Humeca Model D42, (Eurosurgical Ltd, Guildford, UK) and the thickness of the resulting skin section confirmed using a digital micrometer gauge (Tooled-Up, Middlesex, UK). Once dermatomed, the skin was cut into squares (3 x 3 cm) in preparation for mounting onto diffusion cells.

Static skin diffusion cells were purchased from PermeGear (Chicago, Illinois, USA) and based upon the design of the Franz diffusion cell (15). Each diffusion cell comprised an upper (donor) and lower (receptor) chamber with an area available for diffusion of 1.76 cm^2. Dermatomed skin sections were placed between the two chambers (epidermal surface facing the donor chamber) and the ensemble was securely clamped. The receptor chambers were filled with 50% (v/v) aqueous ethanol (approximately 14 ml ± 0.8 ml), so that the meniscus in the sampling arm was level with the surface of the skin sample. Each diffusion cell was placed in a Perspex™ holder above a magnetic stirrer which constantly mixed the receptor fluid via a (12 x 6 mm) Teflon™-coated iron bar placed within the receptor chamber. The receptor chambers were of the jacketed variety through which warm (36ºC) water was pumped from a circulating water heater (Model GD120, Grant Instruments, Cambridge, UK) via a manifold to ensure a constant skin surface temperature of 32ºC (as confirmed by infrared thermography; FLIR Model P620 camera, Cambridge, UK). Once assembled, the diffusion cells were left *in situ* for an equilibration period of up to 24 hours.

Thirty six diffusion cells were used in each experiment, divided into to six treatment groups (each comprising n=6 diffusion cells). Each experiment was initiated by the addition of 10 µl ^{14}C-radiolabelled methyl salicylate (MS; 0.2 µCi μl^{-1}) to the skin surface of each diffusion cell. Samples of receptor fluid (250 µl) were withdrawn from each diffusion cell at regular intervals (i.e. every 3 hours) up to 24 hours post exposure and were placed into vials containing 5 ml of liquid scintillation counting fluid. Each receptor chamber was replaced with an equivalent volume (250 µl) of fresh fluid to maintain a constant volume in the receptor chamber.

Decontamination was conducted 5 minutes post exposure by the addition of a test product comprising powder (200 mg), liquid (200 µl) or swab/wipe (5 x 5 cm) to each contaminated

skin surface. Each product remained *in situ* for 24 hours at which point they were removed and placed into 20 ml glass vials. Twenty four hours post exposure, test products were recovered from each skin surface. The powder or liquid formulations (KBDO-sponge, KBDO-liquid, Fuller's earth, FloraFree, DTAM, Diphotérine, Fast Act and all polymers) were placed into glass vials containing 20 ml LSC fluid whereas the wipe, swab or sponge formulations (~~M~~medical sterile swabs, Baby wipes normal and sensitive formulations, polymeric sponge formulations; Itaconic acid sponge (IA-SP) and 2-Trifluoromethyl acrylic acid sponge (TFMAA-SP)) were placed in 20 ml of isopropanol. The contents of each receptor chamber were removed and placed into 20 ml glass vials. Each skin surface was then swabbed with a dry gauze pad which was subsequently placed in 20 ml isopropanol. Finally, the skin from each diffusion cell was removed and placed into pre-weighed vials. The difference in the weight of each vial before and after addition of each skin sample allowed a calculation of the skin weight. Each skin sample was then dissolved in 10 ml of Soluene-350.

All vials were stored at room temperature (with occasional shaking) for up to 5 days after which aliquots (250 µl) were removed and placed into vials containing 5 ml LSC fluid. Standard solutions were prepared on the day of each experiment by the addition of 2 µl ^{14}C-radiolabelled methyl salicylate to (a) known weights of fresh test products in 20 ml LSC fluid or 20 ml isopropanol, (b) unused gauze pads in 20 ml isopropanol and (c) unexposed skin tissue dissolved in 10 ml Soluene-350. Each of the standard solutions was prepared in triplicate and was then subject to an identical sampling regime (250 µl aliquots into vials containing 5 ml LSC fluid). A standard receptor chamber solution was also prepared in triplicate by the addition of 10 µl of ^{14}C-MS, to 990 µl of fresh receptor fluid (50% aqueous ethanol) from which a range of triplicate samples (25, 50, 75 and 100µl) were placed into vials containing 5 ml of LSC fluid to produce a standard (calibration) curve. Aliquots (250 µl) of each the samples (i.e., skin, receptor fluid, swabs, and decontaminants) were placed into vials containing 5 ml of liquid scintillation fluid and were subject to liquid scintillation counting.

The radioactivity in each sample was quantified using a Perkin Elmer Tri-Carb liquid scintillation counter (Model 2810 TR), employing an analysis runtime of 2 minutes per sample and a pre-set quench curve specific to the brand of liquid scintillation fluid (Ultima Gold™). The amounts of radioactivity in each sample were converted to amount of ^{14}C-radiolabelled chemical warfare simulant by comparison to the corresponding standards (measured simultaneously). Quantification of the amounts of methyl salicylate recovered in

each receptor chamber enabled a calculation of the cumulative dermal absorption over 24 hours. These were averaged at each time point for each treatment group and plotted as total amount penetrated (μg cm^{-2}) against time for each experiment.

In order to permit an inter-experimental comparison of the performance of each treatment, the data were normalised relative to controls within each experiment (Equation 1).

$$\%CD_{24} = \left(\frac{QT_{24}}{QC_{24}} \right) \times 100 \quad \text{…Equation 1}$$

Where $\%CD_{24}$ is the percentage of the control dose penetrating the skin, QT_{24} is the quantity of contaminant penetrating the skin at 24 hours following treatment (decontamination) and QC_{24} is the quantity of penetrant penetrating control (untreated) skin at 24 hours. A surrogate measure of flux (percentage of control dose penetrating the skin at 3 hours; $\%CD_3$) was calculated in a similar fashion (by substituting the amount penetrated at 3 hours for that penetrated at 24 hours).

A test for normality (Kolmogorov-Smirnov) was conducted on all data acquired from the *in vitro* studies: the data were found to be not normally distributed (non-Gaussian) and so analysed using non-parametric statistical tests. Treatments effects were analysed using the non-parametric equivalent of a one way ANOVA (Analysis of variance; KruskalWallis) followed by Dunn's post-test which allow comparisons of each group against a control group.

Results

There was substantial variation in the ~~qualitative~~ performance of the 15 test decontamination products: ~~ten~~ 10 reduced the dermal absorption of ^{14}C-MS, one had no demonstrable effect and four enhanced absorption (Figure 1). When assessed using the Kruskal-Wallis ANOVA with Dunn's post-test, treatment with Fuller's earth (FE), D-TAM™, Fast-Act® (FA), itaconic acid (IA), 2-trifluoromethylacrylic acid (TFMAA) and N,N-methylene bis acrylamide (MBA) caused a statistically significant ($p<0.05$) reduction in the total amount of ^{14}C-MS penetrating the skin at 24 hours (expressed as percentage of control dose; $\%CD_{24}$) in comparison with their respective controls.

Correspondingly, decontamination with FE, IA, TFMAA and MBA resulted in a significant decrease in maximum penetration rate (J_{max}); Figure 2. In addition, urocanic acid (UA) and methacrylic acid (MA) also significantly reduced J_{max} ($p<0.05$), but in the absence of a statistically significant effect on $\%CD_{24}$.

In contrast, sensitive and normal baby-wipes (BW-S and BW-N, respectively) and Diphotérine significantly ($p<0.05$) enhanced both dermal absorption ($\%CD_{24}$; Figure 1) and J_{max} (Figure 2), whereas medical moist-free wipes (MMFW) and FloraFree™ solution significantly ($p<0.05$) enhanced J_{max} only (no significant effect on $\%CD_{24}$).

No significant effects on T_{max} (time at which maximum rate of penetration (J_{max}) was achieved) were observed for any of the products (Figure 2).

In terms of recovery of ^{14}C-MS, a wide range (10-80%) of applied dose was sequestered by the decontamination products. The majority of products were not significantly different to FE in terms of dose recovery. However, FloraFree™, D-TAM™ and Diphotérine were significantly ($p<0.05$) less effective (Table 1).

All of the polymers (UA, MA, IA) and both baby wipe formulations (BW-S, BW-N) significantly reduced the amount of ^{14}C-MS on the skin surface in comparison with respective controls (Table 1; $p<0.05$). All the other test products had no significant effect on skin surface recovery.

Five products (FE, FA, IA, TFMAA and MBA) significantly reduced the amount of ^{14}C-MS retained within the skin at 24 hours (Table 1; $p<0.05$).

All experiments resulted in a significant correlation between maximum rate of penetration (J_{max}) and percentage of control dose at 3 hours ($\%CD_3$), r=0.9750, 0.9658 and 0.9887 for experiments 1, 2 and 3 respectively (Figure 3; $p<0.05$).

When expressed as %CD at 3 versus 24 hours, the baby-wipe formulations (normal & sensitive), Diphotérine and 5%FloraFree™ enhanced both the rate and amount penetrated (Figure 4; quadrant D). Interestingly, ~~M~~medical moist free wipes led to an increased rate, but did not result in higher amounts of ^{14}C-MS penetrating over 24 hours (Figure 4; quadrant C). No products enhanced the extent of penetration and decreased the rate of ^{14}C-MS absorption (Figure 4; quadrant B). Of the products which decreased both the rate and extent of ^{14}C-MS absorption, IA, MBA, FE, TFMAA and Fast-Act® reduced both $\%CD_3$ and $\%CD_{24}$ by 95% and 88% respectively. In contrast, D-TAM™, KBDO-L, KBDO-S, MA and UA did not perform as well, with the reduction in $\%CD_3$ and $\%CD_{24}$ being approximately 70% for either parameter. Products delineated by the ring (IA, TFMAA, MA, FE and FA; Figure 4) were the top five efficacious products.

Discussion

This study has successfully identified a number of effective decontamination products that may have potential for use at the scene of a chemical incident.

The effectiveness of decontaminants was measured *in vitro* using a static diffusion cell system with (previously frozen) skin exposed to radiolabelled contaminants. Whilst this model is considered to be appropriate and validated for the assessment of skin absorption (16) the corresponding data needs to be interpreted with some caution due to several experimental drawbacks of the model. The skin used in these studies was obtained from the dorsal aspect of pigs whereas human skin is the skin of choice for assessing dermal absorption. Due to cost and availability it was necessary to use a viable alternative. Several animal models have been evaluated as to their suitability as a surrogate for human skin (17, 18). Pig skin has been shown to have similar histological and morphological properties to human skin (19, 20) and is generally more akin to human in terms of permeability to xenobiotics. Skin was excised from the dorsal aspect in comparison to porcine ear, the latter being generally more comparable with human (21, 22). To reduce animal numbers in accordance with the 3Rs (23), the back provided the greatest surface area for dermatoming skin for up to 36 diffusion cells. Additionally, skin from one region of the animal may reduce inter-individual variability in percutaneous permeability (24, 25), thus allowing statistical differences to be confidently attributed to treatment effects. The practice of using previously frozen skin for *in vitro* dermal absorption studies has not been shown to significantly affect penetration (26). The use of radiolabelled chemicals in this study also has inherent limitations, as liquid scintillation counting cannot distinguish between the parent molecule and its metabolites or hydrolysis products. The choice of receptor media will also influence the extent of percutaneous absorption of chemical warfare agents and simulants (27). In this study, aqueous ethanol (50:50) was chosen to aid partitioning of methyl salicylate, a lipophilic compound (28, 29). Whilst there are some concerns over the use of 50% ethanol (aq) in terms of potential ability to increase skin permeability (16), it could be argued that an overestimate of dermal absorption (if present) would result in a conservative assessment of decontamination and thus provide a more rigorous assessment of test products. This model also lacks physiological relevance with regards to metabolic processes, systemic clearance and toxicological end-points (non-viable skin) (30). Diffusion cell studies are also susceptible to inter and intra-laboratory variations (31, 32). Despite these drawbacks, *in vitro* diffusion cells are a useful tool and have historically been used for the assessment of percutaneous absorption (33). This

model has also been used for similar work assessing product efficacy for decontamination (21, 34, 35). Thus overall, the system is well characterised and so the following interpretations appear to be justified.

Initial screening of decontamination products demonstrated that a number of products were effective when applied to the skin 5 minutes post exposure. Notably, all of the polymeric formulations (IA, TFMAA, MBA) tested were highly effective. The benchmark decontaminant (Fuller's earth; a ~~processed~~ fine powder of natural aluminium silicate clay containing an abundance of minerals) removed 83% of ^{14}C-MS which compares favourably to the 91% achieved against sulphur mustard on pig ear skin (21). From the total of 15 test products, 5 products (~~M~~medical moist free wipes, 5% FloraFree™ solution, Baby-wipe Normal, Baby-wipe Sensitive and Diphotérine) enhanced the rate and amount of penetration, thus justifying their elimination from further testing. It is conceivable that water based products (i.e. FloraFree™ and Diphotérine) may have enhanced dermal absorption due to the 'wash in effect' (5, 6, 36). Additionally, the baby-wipes may have enhanced penetration due to the presence of solvents and or detergents in these wipes as they may have disrupted the lipid structure of the stratum corneum and therefore resulted in enhanced penetration (37, 38).

Of the remaining 10 effective products, 5 (urocanic acid (UA), methacrylic acid (MA), D-TAM™ and the sponge and liquid KBDO formulations) were discounted as they were generally not as effective as FE, Fast-Act®, IA, TFMAA and MBA (Figure 4). Furthermore, D-TAM™ was excluded on the basis of the manufacturer's instructions which contraindicate application onto wet skin: a practical point which would clearly limit its use ~~in the UK~~.

It is perhaps worth emphasising that the sponge and liquid KBDO formulations were specifically designed to decontaminate chemical warfare agents (not methyl salicylate) and were not used in accordance with the manufacturer's instructions (being left on the skin rather than immediately removed after application). A lack of broad spectrum effectiveness is considered a disadvantage. However, the main constituent of KBDO liquid is polyethylene glycol, the primary function of which is to solubilise contaminants within the lotion (39). Indeed, PEG may contribute to the generic effectiveness of such decontamination products through preferential partitioning of contaminants (40).

A strong correlation between $\%CD_3$ and J_{max} was obtained (Figure 3) indicating that $\%CD_3$ is a good surrogate for measuring skin absorption kinetics. The use of $\%CD_3$ in future studies could provide practical benefit in reducing the frequency of receptor chamber samples

required to characterise the performance of a decontamination product. More importantly, $\%CD_3$ eliminates the inherent variation in skin permeability between different skin samples. Normalising the J_{max} values (using $\%CD_3$) allows the performance of all products to be directly compared regardless of the experiment-specific differences in skin permeability.

Further work is required to fully evaluate the 5 most effective products, consisting of one military product (Fuller's earth), one commercial off the shelf product (Fast Act®) and three novel polymers (Itaconic acid, *N*,*N*-Methylene Bis Acrylamide and 2-Trifluoromethylacrylic acid) against chemical warfare agents: sulphur mustard (HD), soman (GD) and VX.

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Declaration of interest

The authors report no declarations of interest

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Experiment	Treatment	Skin	Skin Surface	Decontaminant	Receptor Fluid
1	Control	9.2 ± 1.8	0.9 ± 0.5	NA	3.1 ± 1.2
	Fuller's Earth	0.4 ± 0.7§	0.1 ± 0.1	83.0 ± 10.9	0.1 ± 0.2
	Medical moist free wipes	2.1 ± 3.9	0.1 ± 0.1	28.0 ± 11.6	2.5 ± 1.4
	KBDO Sponges	4.4 ± 5.3	1.7 ± 2.0	36.8 ± 43.3	0.3 ± 0.3
	KBDO Liquid	4.1 ± 2.8	4.6 ± 1.1	18.9 ± 23.0	0.4 ± 0.2
	5% Florafree	6.7 ± 2.5	1.6 ± 0.5	2.4 ± 2.1*	4.6 ± 1.9
2	Control	8.0 ± 3.9	3.7 ± 1.4	NA	2.5 ± 1.2
	DTAM	2.9 ± 2.4	4.2 ± 3.5	12.1 ± 18.7*	0.5 ± 0.1
	Baby-wipe Sensitive	1.7 ± 0.3	0.7 ± 0.2#	19.5 ± 6.6	10.1 ± 5.5
	Diphotérine	12.0 ± 7.3	1.0 ± 0.4	2.2 ± 2.5*	6.2 ± 3.4
	Baby-wipe Normal	4.8 ± 6.2	0.6 ± 0.1#	20.0 ± 11.5	8.4 ± 1.4
	Fast Act	0.9 ± 0.6§	0.7 ± 0.6	49.5 ± 15.1	0.0 ± 0.0
3	Control	16.3 ± 7.7	3.9 ± 2.0	NA	4.3 ± 1.4
	IA	0.9 ± 1.3§	0.3 ± 0.2#	81.8 ± 21.3	0.2 ± 0.3
	TFMAA	0.1 ± 0.0§	0.2 ± 0.1#	71.0 ± 28.3	0.1 ± 0.1
	MBA	0.5 ± 0.9§	0.2 ± 0.1#	98.5 ± 40.6	0.2 ± 0.3
	UA	1.0 ± 1.4	0.3 ± 0.2#	77.0 ± 43.5	0.4 ± 0.4
	MA	1.9 ± 1.6	0.5 ± 0.3#	79.4 ± 6.9	0.5 ± 0.4

Table 1: ***Dose distribution on the percentage of dose applied of ^{14}C-Radiolabelled methyl salicylate penetrating untreated (control) or decontaminated pig skin over a 24 hour period.*** *Skin surface decontamination was conducted five minutes post-exposure using Baby-wipe Normal, Baby-wipe Sensitive, Diphotérine , FloraFree™ detergent, Medical moist free wipes, D-TAM™, KBDO liquid, KBDO sponge, Methacrylic acid (MA), Urocanic acid (UA), N,N-Methylene Bis Acrylamide (MBA), Fast-Act®,2-Trifluoromethylacrylic acid (TFMAA), Fuller's earth and Itaconic acid (IA). All points are mean ± standard deviation of up to n=6 diffusion cells. Porcine skin was obtained from the dorsum of one animal. Section symbol (§) indicates significant reductions ($p<0.05$) in the amount of ^{14}C-MS remaining within the skin at 24 hours compared to controls (untreated) skin. Hash symbol (#) indicates significant ($p<0.05$) reductions on amount remaining on skin surface against respective controls. Asterisk (*) indicates recovery of ^{14}C-MS from decontaminant was significantly different ($p<0.05$) to FE.*

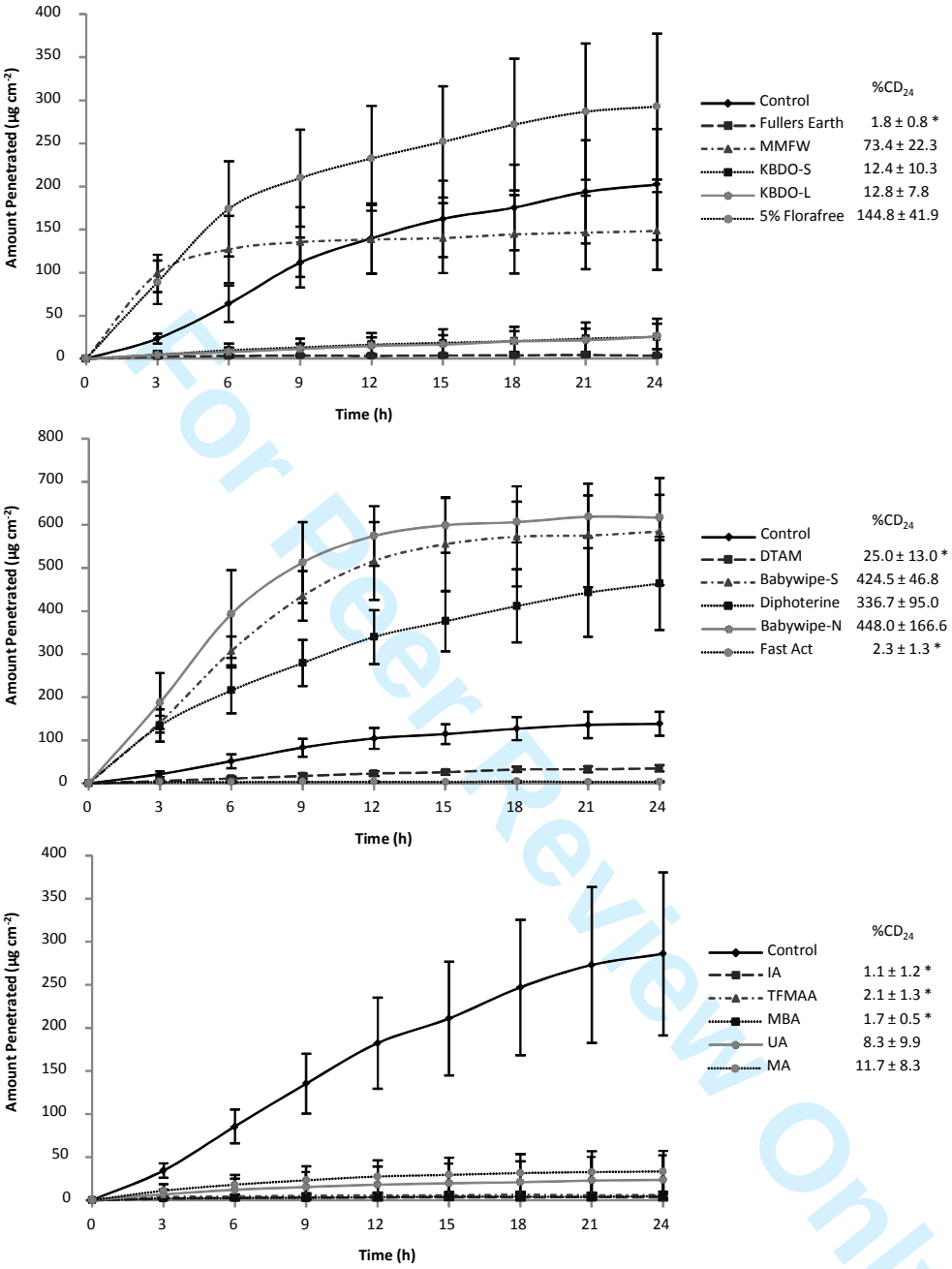

Figure 1: ***Cumulative amount of ^{14}C-Radiolabelled methyl salicylate penetrating untreated (control) or decontaminated pig skin over a 24 hour period***. *10µl of ^{14}C-methyl salicylate (2µCi total per cell) was applied to the skin surface. Skin surface decontamination was conducted five minutes post-exposure using Fuller's earth, Medical moist frees wipe (MMFW), Potassium butadione monoximate (KBDO) Sponge, KBDO liquid and 5% FloraFree™ detergent solution (A), D-TAM™ skin cleanser, Baby-wipe Sensitive, Diphotérine , Baby-wipe Normal, Fast-Act®, (B), Itaconic acid (IA), 2-Trifluoromethylacrylic acid (TFMAA), N,N-Methylene Bis Acrylamide (MBA), Urocanic acid (UA) and Methacrylic acid (MA (C). Asterisk (*) indicates significant ($p<0.05$) reductions in amount penetrated at 24 hours compared to control. All points are mean ± standard deviation of up to n=6 diffusion cells. Porcine skin was obtained from the dorsum of one animal.*

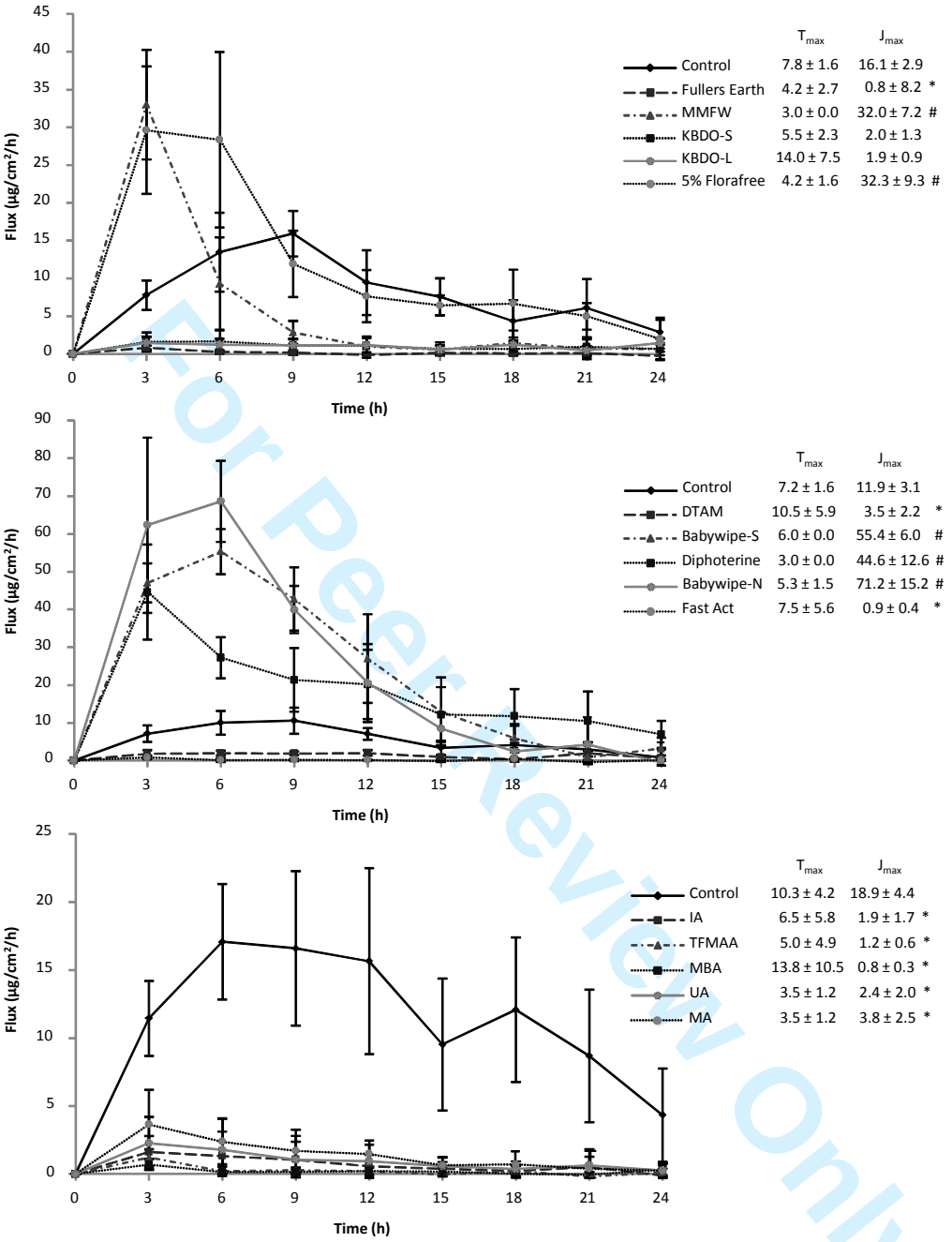

Figure 2: ***Flux profile of ^{14}C-Radiolabelled methyl salicylate penetrating untreated (control) or decontaminated pig skin over a 24 hour period***. *10µl of ^{14}C-methyl salicylate (2µCi total per cell) was applied to the skin surface. Skin surface decontamination was conducted five minutes post-exposure using Fuller's earth, Medical moist frees wipe (MMFW), Potassium butadione monoximate (KBDO) Sponge, KBDO liquid and 5% FloraFree™ detergent solution (A), D-TAM™ skin cleanser, Baby-wipe Sensitive, Diphotérine , Baby-wipe Normal, Fast-Act®, (B), Itaconic acid (IA), 2-Trifluoromethylacrylic acid (TFMAA), N,N-Methylene Bis Acrylamide (MBA), Urocanic acid (UA) and Methacrylic acid (MA (C). Asterisk and hash (* & #) indicates significant ($p<0.05$) reductions and enhancements in J_{max} compared to control respectively. All points are mean ± standard deviation of up to n=6 diffusion cells. Porcine skin was obtained from the dorsum of one animal.*

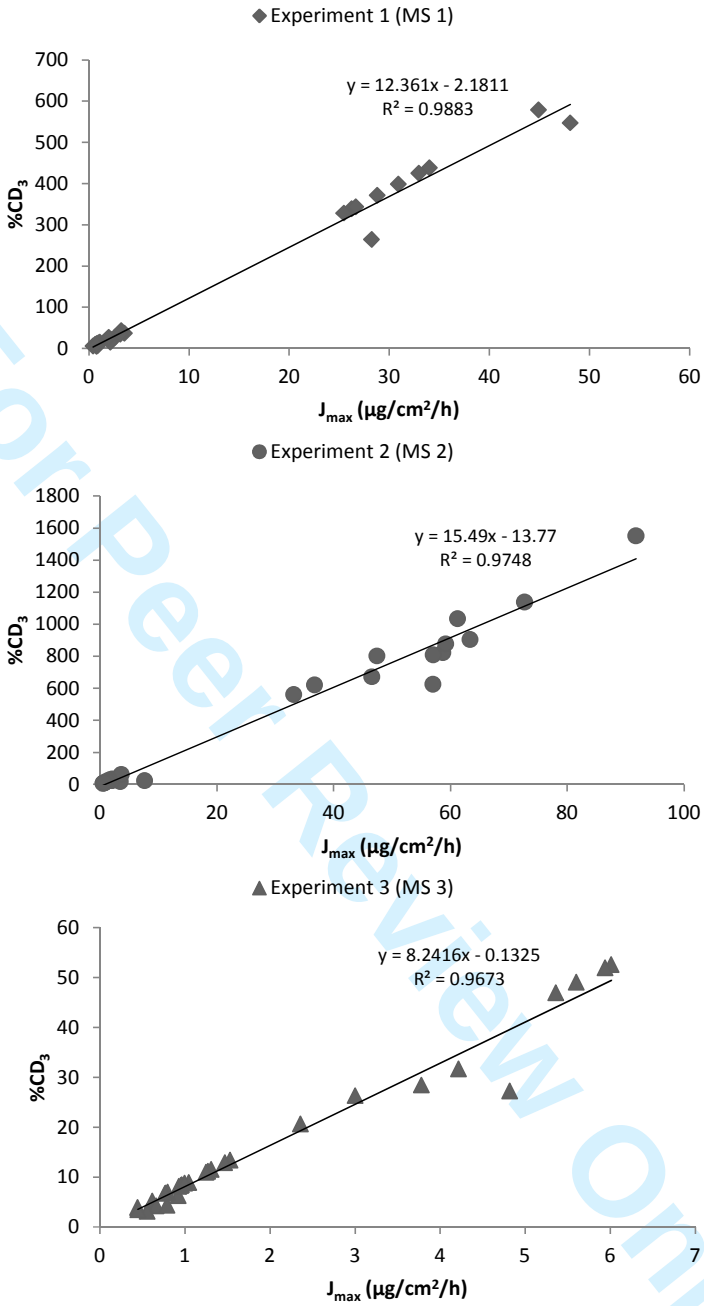

Figure 3: Comparison of maximum rate of penetration (J_{max} µg/cm^2/h) against surrogate marker for rate of penetration (%CD_3; see equation 1). Each data point is n=1 diffusion cells for each of the treatments for the respective experiments totalling n=36.

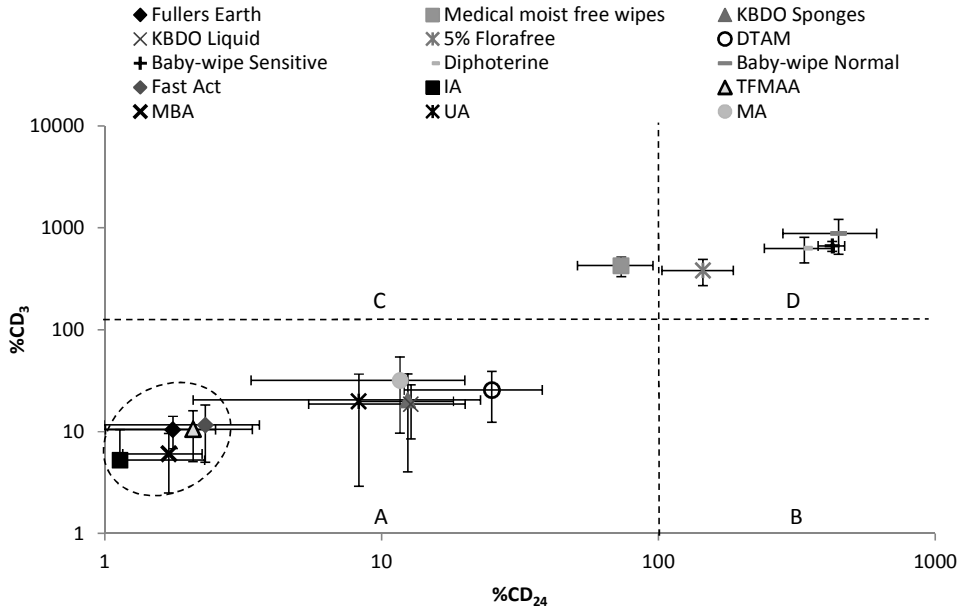

Figure 4: Summary of decontaminants evaluated against ^{14}C-methyl salicylate normalised as percentage control dose at 3 and 24 hours (%CD$_3$ and %CD$_{24}$) plotted on a log scale for clarity. *Skin surface decontamination was conducted five minutes post-exposure using Baby-wipe Normal, Baby-wipe Sensitive, Diphotérine , FloraFree™ detergent, Medical moist free wipes, D-TAM™, KBDO liquid, KBDO sponge, Methacrylic acid (MA), Urocanic acid (UA), N,N-Methylene Bis Acrylamide (MBA), Fast-Act®,2-Trifluoromethylacrylic acid (TFMAA), Fuller's earth and Itaconic acid (IA). All points are mean ± standard deviation of up to n=6 diffusion cells. Porcine skin was obtained from the dorsum of one animal. Quadrant A shows products which reduced the rate and amount penetrated. Quadrant B shows products that reduced rate, however resulted in no change to amount penetrating at 24 hours. Conversely C shows opposite effects (Reduced amount penetrating at 24 hours, increased rate of penetration). Quadrant D defines products which have increased both rate and amount penetrating the skin. Products delineated by a ring were the five most effective.*

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