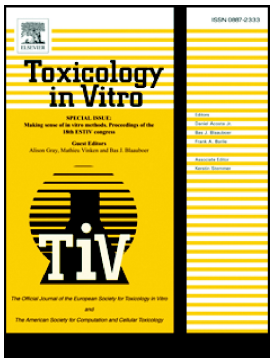

Further studies of the efficacy of military, commercial and novel skin decontaminants against the chemical warfare agents sulphur Mustard, Soman and VX

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Further Studies of the Efficacy of Military, Commercial and Novel Skin Decontaminants Against the Chemical Warfare Agents Sulphur Mustard, Soman and VX

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Running head: Skin decontaminants against sulphur mustard, soman and VX

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Abstract

Background/Aims: Following an incident involving toxic chemicals, deployment of countermeasures before the arrival of specialised services at the scene may provide a "therapeutic" window in which to mitigate skin absorption. ***Methods:*** Five potential candidates (itaconic acid, N,N′-methylenebisacrylamide, 2-trifluoromethylacrylic acid, fuller's earth and Fast-Act®) previously found effective against a simulant (methyl salicylate) were evaluated against a 10 µL droplet of ^{14}C-sulphur mustard (HD), soman (GD) or VX applied to the surface of porcine skin mounted on static skin diffusion cells. ***Results:*** All the decontaminants applied to the skin 5 minutes post exposure achieved a marked reduction in the amount of ^{14}C contaminant remaining within the skin at 24 hours. Itaconic acid significantly (p<0.05) reduced the amount of ^{14}C-HD, GD and VX remaining in the skin at 24 hours. Additionally, 2-trifluoromethylacrylic acid significantly reduced the amount of ^{14}C-HD, whilst fuller's earth significantly reduced the amounts of ^{14}C-HD and VX recovered within the skin at 24 hours. ***Conclusion:*** All of the products evaluated in this study performed well in reducing the dermal absorption of all the chemical warfare agents tested.

1. Introduction

Decontamination can be defined as "the process of removing hazardous material(s) both on or available to the external surfaces of the body in order to reduce local or systemic exposure to a contaminant and thus minimise the risk of subsequent adverse health effects" (Chilcott, 2014). It is well established that a major route of exposure to chemical warfare (CW) agents is via contact with the skin (Evison, 2002). The deliberate release of chemical warfare agents targeting civilian populations, exemplified by the sarin attacks in Tokyo (1995) and Syria (2014) (Eisenkraft, 2014; Okumura, 1996), has led to the continued development of more effective decontamination strategies focused on dealing with civilian mass-casualty incidents (Amlot, 2010; Amlôt, 2017; Kassouf, 2017; Matar, 2016).

Typically, decontamination strategies include physical removal or chemical neutralisation. Physical removal methodologies aim to remove contaminants, whereas chemical neutralisation aims to modify the structure of the contaminant in order to reduce or eliminate toxicity by hydrolysis, oxidation or metabolism (Chan, 2013). The issue surrounding chemical neutralising agents is the lack of a single substance capable of neutralising compounds with a wide range of physiochemical properties and a potential for skin or eye irritation. Furthermore, it has been demonstrated that some neutralising products (e.g. bioscavengers) undergo stoichiometric reactions that result in rapid saturation (Nachon, 2013). In certain cases, there is the potential to inadvertently produce toxic breakdown products, as observed with the degradation of VX (Munro, 1999). A wide range of products have been evaluated for decontamination of surfaces (Capoun, 2014; Yang, 1992); however, few of these are suitable for skin decontamination (Salerno, 2016; Schwartz, 2012; Thors, 2017), especially if the skin is damaged (Dalton, 2017; Lydon, 2017). Given the lack of medical treatments for some chemical contaminants, such as sulphur mustard, decontamination can be used to mitigate toxic effects by reducing the contaminant and

removing it from skin, thus preventing or at least ameliorating the subsequent lesion severity (Chilcott, 2007; Hall, 2017).

The objective of this current study was to extend the evaluation of five candidate products identified from a previous study (Matar, 2016) for the decontamination of chemical warfare agents. The rationale behind this work was to discover alternative products that could be used at the scene of an incident, prior to the deployment of specialised services, in conjunction with or in lieu of showering. A recent study demonstrated the effectiveness of using any absorptive material for decontamination (Kassouf, 2017). However, the ability to retain these contaminants should be evaluated to prevent secondary contamination.

2. Materials and Methods

2.1. Chemicals

The storage and use of chemical warfare agents (CWA) was performed in full compliance with the chemical weapons conventions. CWA soman (GD), sulphur mustard (HD), VX and their (^{14}C) radiolabelled analogues were custom synthesised by TNO Defense, Security and Safety (Rijswijk, Netherlands) and were reported to be >97% pure. Radiolabelled ^{14}C-Soman (23.5 mCi mmol^{-1}), ^{14}C-sulphur mustard (56 mCi mmol^{-1}) and ^{14}C-VX (31 mCi mmol^{-1}) were mixed with their corresponding unlabelled analogues to provide a stock solution with a nominal activity of ~1 mCi g^{-1} that was stored for up to six months at 4°C. Aliquots of each stock solution were diluted with their respective unlabelled CW agent immediately prior to each experiment to provide a working solution with a nominal activity of ~0.5 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 (FE) (Sigma Aldrich, Poole, UK) and the Fast-Act® chemical containment and neutralisation system (NanoScale, Manhattan, USA). Novel polymers itaconic acid (IA), N,N′-methylenebisacrylamide (MBA) and 2-trifluoromethylacrylic acid (TFMAA) were prepared by the University of Cranfield (Cranfield, UK) as described in the patent (Chilcott, 2013).

2.2. Skin Samples

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 -20°C for up to 3 months before use. Prior to the commencement of each experiment, a skin sample from a single animal was removed from cold storage and thawed in a refrigerator (4ºC) 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 × 3 cm) in preparation for mounting on to diffusion cells.

2.3. Diffusion Cells

Static skin diffusion cells were purchased from PermeGear (Chicago, Illinois, USA) and were based upon the design of the Franz diffusion cell (Franz, 1975). Each diffusion cell comprises 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, with the epidermal surface facing the donor chamber, and the ensemble was securely clamped. The receptor chambers were filled with 50% (v/v) aqueous ethanol (14 ± 0.8 mL). Each diffusion cell was placed in a Perspex™ holder above a magnetic stirrer which

constantly mixed the receptor fluid via a (12 × 6 mm) Teflon™-coated iron bar placed within the receptor chamber. The receptor chambers were equipped with a jacket, 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 six treatment groups each comprising n=6 diffusion cells.

2.4. Experimental Procedure

Each experiment was initiated by the addition of either 10 µL ^{14}C-radiolabelled soman (GD), sulphur mustard (HD) or VX (0.5 µCi µL^{-1}) to the skin surface of each diffusion cell. Samples of receptor fluid (250 µL) were withdrawn from each diffusion cell at 3-hour intervals up to 24 h post exposure and were placed into vials containing 5 mL of LSC fluid. Each receptor chamber was replenished 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 200 mg test product to each contaminated skin surface (where appropriate). Each product remained in situ for 24 hours, at which point they were removed and placed into 20 mL glass vials containing 20 mL LSC fluid. The contents of each receptor chamber were also removed and placed into 20 mL glass vials. Each skin surface was then swabbed with a dry gauze pad that was subsequently placed in 20 mL isopropanol. Finally, the skin samples from all diffusion cells were removed and placed into pre-weighed vials. The difference between 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 soman, sulphur mustard or VX 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, in which 250 μL aliquots were placed 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-GD, HD or VX to 990 μL of fresh receptor fluid (50% aqueous ethanol), from which a range of triplicate samples (25, 50, 75 and 100 μL) 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 LSC fluid prior to measurements.

2.5. Liquid Scintillation Counting

The radioactivity in each sample was quantified using a PerkinElmer 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 LSC fluid (Ultima Gold™). The amounts of radioactivity in each sample were converted to quantities of ^{14}C-radiolabelled chemical warfare agent by comparison with the corresponding standards (measured simultaneously). Quantification of the amounts of CWA 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 ($\mu g\ cm^{-2}$) against time for each experiment.

2.6. Data Analysis

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

$$\%CD_{24} = (QT_{24}/QC_{24}) \times 100 \quad \text{Eq. (1)}$$

where $\%CD_{24}$ is the percentage of the control dose penetrating the skin, QT24 is the quantity of contaminant penetrating the skin at 24 hours following treatment (decontamination) and QC_{24} is the quantity of contaminant penetrating control (untreated) skin at 24 hours.

The maximum rate of penetration (J_{max}) was calculated from the amount penetrated against time, which was averaged across the number of replicates. The time at which J_{max} was achieved (T_{max}) was also averaged across all cells.

2.7. Statistical Analysis

A test for normality (Kolmogorov–Smirnov) was conducted on all data (per group) acquired from the in vitro studies: the data were found to be not normally distributed (non-Gaussian) and so were analysed using non-parametric statistical tests. Treatment effects were analysed using the non-parametric equivalent of one-way analysis of variance (ANOVA; Kruskal-Wallis) followed by Dunn's post-test, allowing comparisons of each group against a control group. A probability level of $p < 0.05$ was the criterion for statistical significance throughout.

3. Results

All of the products evaluated (IA, TFMAA, MBA, FE and Fast-Act®) reduced the penetration of ^{14}C-GD, HD and VX compared to their respective controls (Figure 1). With respect to ^{14}C-GD penetration, FE, IA and TFMAA achieved a significant ($p < 0.05$) reduction compared to controls at 24 hours. FE, TFMAA, IA and Fast-Act® all significantly

decreased the amount of ^{14}C-HD compared to controls at 24 hours ($p < 0.05$). The same was true for ^{14}C-VX (Figure 1).

Similarly, all treatments greatly reduced the flux over 24 hours (Figure 2). TFMAA, IA and FE were the only three products to significantly ($p < 0.05$) reduce J_{max} of ^{14}C-GD. Additionally, TFMAA, FE and FA significantly reduced J_{max} of ^{14}C-HD, whilst FE, FA and IA significantly reduced J_{max} of ^{14}C-VX over 24 hours.

No significant effects on T_{max} were observed for any of the products with respect to ^{14}C-GD (Figure 2, A). All of the products employed against ^{14}C-HD significantly ($p < 0.05$) reduced T_{max}, whilst IA, FE and MBA significantly reduced T_{max} with respect to ^{14}C-VX (Figure 2, B & C).

Among the three contaminants, there was a large variation in the percentage dose recovered, with the least recovery from HD (2%) and the greatest from VX (70%) (Tables 1-4). All of the decontaminants applied to the skin 5 minutes post exposure achieved a marked reduction in the amount of ^{14}C contaminant remaining within the skin at 24 hours. IA significantly ($p < 0.05$) reduced the amount of ^{14}C-HD, GD and VX remaining in the skin at 24 hours (Table 1). Additionally, TFMAA significantly reduced the amount of ^{14}C-HD, whilst FE and FA significantly reduced the amounts of ^{14}C-HD and VX recovered within the skin at 24 hours (Table 1).

The amounts remaining on the skin surface at 24 hours were not significantly reduced by any of the decontaminants when compared to their respective controls (Table 2). TFMAA, MBA and FA resulted in increased amounts of ^{14}C-GD remaining on the skin surface compared to controls, though the differences were not statistically significant.

There was no statistical difference between the amounts of ^{14}C-GD, HD or VX retained by each of the tested products when compared to FE (Table 3).

4. Discussion

Based upon the penetration profiles for each experiment in this study, it was difficult to discriminate between the products in terms of amount and rate of penetration of CWA. However, some differences were apparent among the five remaining products: MBA did not significantly reduce J_{max} or overall absorbed dose compared to any of the agents, and neither TFMAA nor Fast-Act® performed as well as FE or IA against ^{14}C-GD. Thus, the products that showed all round efficacy against all three CWA (soman, sulphur mustard and VX) and methyl salicylate (Matar, 2016) in terms of reduced J_{max} and total amount penetrated were IA, FE, and TFMAA.

The main mechanism of action for the test products is absorption, with the exception of Fast-Act®, which combines absorption with the capability to neutralise chemical warfare agents via hydrolysis and or dehydrohalogenation (Lanz and Allen, 2004). The molecularly imprinted polymers were designed to bind a range of chemicals with a relatively high affinity. However, further work is required to characterise any additional abilities, such as neutralisation.

One of the advantages of identifying an effective synthetic product is the ability to molecularly imprint these polymers into sponges or textiles. In recent years, there has been some scepticism over the suitability of aqueous-based decontamination systems, due to the phenomenon of a "wash-in" effect that can enhance chemical penetration through the skin (Idson, 1978; Moody and Nadeau, 1997; Zhai, 2002). Studies comparing the effectiveness of washing the skin or using absorbent materials resulted in better efficacy when absorbent materials were employed (Amlôt, 2017; Kassouf, 2017; Lademann, 2011). A further reason for developing a sponge or textile formulation is to mitigate possible issues surrounding the use of powder decontaminants, such as methods of application to the skin, containment and clear-up, in light of the dispersive properties of powders as well as their potential to be

inhaled (Waysbort, 2009). Furthermore, sponges may be more suitable for applications where the skin barrier is damaged or there are penetrating wounds, as studies have shown that reactive skin decontamination lotion is contraindicated for use on damaged skin (Walters, 2007), while granular products such as fuller's earth are unsuitable for intra-wound use because of the risk of an inflammatory response and neurovascular injury (Gerlach, 2010).

The methodology employed in this study requires some consideration. Although it is highly unlikely that a decontamination product could be administered 5 minutes post exposure in a mass-casualty incident, the authors wished to observe the efficacy of the decontamination agents under optimum conditions. In addition, the products were left on the skin surface for a relatively long duration (24 hours), in order to further evaluate their ability to retain the contaminant. Off-gassing and secondary hazards are serious issues in this type of CWA scenario, posing a potential risk to emergency workers and the general public after such events as the sarin attacks in the Tokyo subway, as well as the possible contamination of hospital staff who have to treat victims (Okumura, 1996). A further limitation of this study was the use of radiolabelled chemicals without further chemical analysis to assess whether the agents were intact or a neutralised by-product. However, this represents a highly conservative approach to determining decontamination efficiency, as all measured radioactivity was assumed to be representative of the original toxic agent, rather than of any less toxic breakdown products.

5. Conclusions

All of the products evaluated in this study performed well in reducing the dermal absorption of all three chemical warfare agents. Further studies will evaluate more realistic exposure scenarios and decontamination efficacy investigated up to 6 hours post exposure, progressing to in vivo and human volunteer trials.

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Declaration of Interest

The authors have declared a potential conflict of interest to highlight the fact that two of them are named inventors of the products evaluated in this study (Patent WO2013150317A1). The authors do not deem this a major conflict of interest, as this patent is not held by the authors and is currently the intellectual property of the UK Secretary of State for Health.

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Fig. 1. Cumulative amount of ^{14}C-radiolabelled soman (GD, A), sulphur mustard (HD, B) and VX (C) penetrating untreated (control) or decontaminated pig skin over a 24 hour period. 10 µL of ^{14}C-GD, HD or VX (5 µCi total per cell) was applied to the skin surface. Skin surface decontamination was conducted five minutes post exposure using itaconic acid (IA), fuller's earth (FE), Fast-Act®, N,N′-methylenebisacrylamide (MBA) and 2-trifluoromethylacrylic acid (TFMAA). Asterisk (*) indicates significant ($p < 0.05$) reductions in amount penetrated at 24 hours compared to control. All points are mean ± standard deviation of n=6 diffusion cells. Porcine skin was obtained from the dorsum of a single animal.

Fig. 2. Flux profile of ^{14}C-Radiolabelled soman (GD, A), sulphur mustard (HD, B) and VX (C) penetrating untreated (control) or decontaminated pig skin over a 24 hour period. 10 µL of ^{14}C-GD, HD or VX (5 µCi total per cell) was applied to the skin surface. Skin surface decontamination was conducted five minutes post exposure using itaconic acid (IA), fuller's earth (FE), Fast-Act®, N,N′-methylenebisacrylamide (MBA) and 2-trifluoromethylacrylic acid (TFMAA). Asterisk (*) indicates significant ($p < 0.05$) reductions in J_{max} compared to control. Hash (#) indicates significant ($p < 0.05$) reductions in T_{max} compared to control. All points are mean ± standard deviation of n=6 diffusion cells. Porcine skin was obtained from the dorsum of a single animal.

Table 1. Dose distribution as a percentage of the applied dose of ^{14}C-radiolabelled soman (GD), sulphur mustard (HD) or VX penetrating untreated (control) or decontaminated pig skin over a 24 hour period.

	Amount (% of applied dose) absorbed in the skin		
	GD	**HD**	**VX**
Control	9.1 ± 1.7	1.0 ± 0.1	65.1 ± 2.8
IA	0.4 ± 0.6*	0.2 ± 0.1*	3.6 ± 1.5*
TFMAA	6.6 ± 3.9	0.1 ± 0.0*	7.5 ± 2.7
MBA	4.0 ± 5.2	0.6 ± 1.0	6.3 ± 5.0
Fast-Act®	4.4 ± 2.7	0.2 ± 0.1*	6.3 ± 4.1*
Fuller's earth	2.1 ± 2.5	0.2 ± 0.0*	3.7 ± 7.1*

Skin surface decontamination was conducted five minutes post exposure using itaconic acid (IA), 2-trifluoromethylacrylic acid (TFMAA), N,N-methylenebisacrylamide (MBA), Fast-Act® and fuller's earth. All values are mean ± standard deviation of n=6 diffusion cells. Porcine skin was obtained from the dorsum of a single animal. Asterisk symbol (*) indicates significant reductions ($p < 0.05$) in the amount of ^{14}C-GD, HD or VX remaining within the skin at 24 hours compared to control.

Table 2. Dose distribution as a percentage of the applied dose of ^{14}C-radiolabelled soman (GD), sulphur mustard (HD) or VX remaining on the skin surface of untreated (control) or decontaminated pig skin over a 24 hour period.

Amount (% of applied dose) recovered on the skin surface			
	GD	**HD**	**VX**
Control	0.9 ± 0.5	0.1 ± 0.0	0.5 ± 0.3
IA	0.1 ± 0.1	0.2 ± 0.1	0.3 ± 0.2
TFMAA	1.6 ± 0.1	0.2 ± 0.0	0.5 ± 0.2
MBA	4.6 ± 2.0	0.2 ± 0.1	0.3 ± 0.5
Fast-Act	1.7 ± 1.1	0.1 ± 0.1	1.5 ± 0.1
Fuller's earth	0.1 ± 0.5	0.1 ± 0.0	0.3 ± 0.2

Skin surface decontamination was conducted five minutes post exposure using itaconic acid (IA), 2-trifluoromethylacrylic acid (TFMAA), N,N'-methylenebisacrylamide (MBA), Fast-Act® and fuller's earth. All values are mean ± standard deviation of n=6 diffusion cells. Porcine skin was obtained from the dorsum of a single animal.

Table 3. Dose distribution as a percentage of the applied dose of ^{14}C-radiolabelled soman (GD), sulphur mustard (HD) or VX retained within the decontaminants over a 24 hour period.

Amount (% of applied dose) retained within the decontaminants			
	GD	**HD**	**VX**
Control	N/A	N/A	N/A
IA	83.0 ± 10.9	84.9 ± 20.8	51.2 ± 21.5
TFMAA	1.8 ± 11.6	91.3 ± 34.5	50.1 ± 11.0
MBA	22.7 ± 35.2	25.2 ± 38.7	56.7 ± 28.5
Fast-Act®	68.6 ± 23.5	45.9 ± 24.6	24.6 ± 19.2
Fuller's earth	28.0 ± 1.6	69.5 ± 28.1	29.0 ± 12.9

Skin surface decontamination was conducted five minutes post exposure using itaconic acid (IA), 2-trifluoromethylacrylic acid (TFMAA), N,N'-methylenebisacrylamide (MBA), Fast-Act® and fuller's earth. All values are mean ± standard deviation of n=6 diffusion cells. Porcine skin was obtained from the dorsum of a single animal.

Highlights:

- Five decontaminants were tested against chemical warfare agents applied to porcine skin.
- All achieved a marked reduction in the amount of contaminant within the skin.
- Early deployment of countermeasures may help mitigate skin absorption.

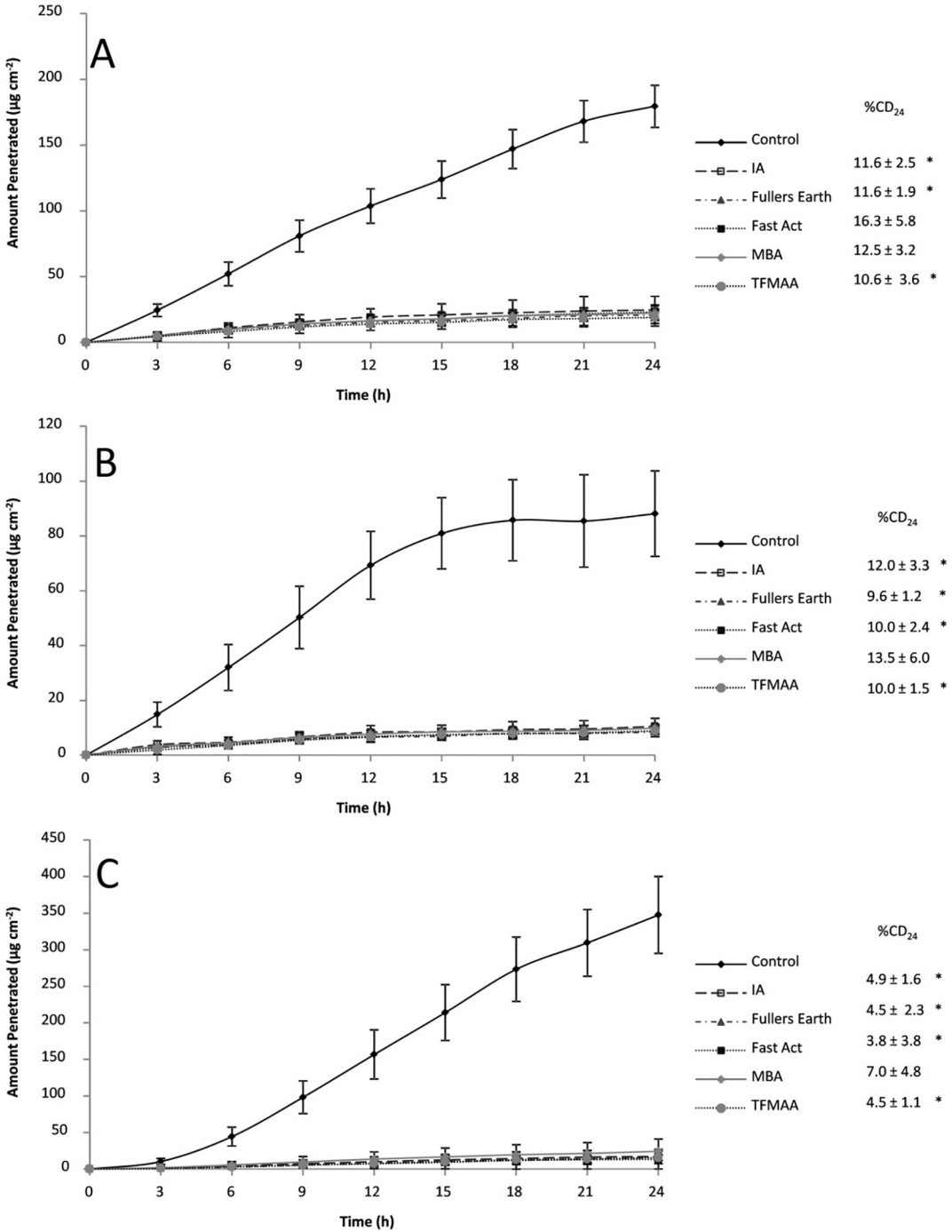
A
Amount Penetrated (µg cm-2)
Time (h)
%CD24
Control
IA 11.6 ± 2.5 *
Fullers Earth 11.6 ± 1.9 *
Fast Act 16.3 ± 5.8
MBA 12.5 ± 3.2
TFMAA 10.6 ± 3.6 *
B
Amount Penetrated (µg cm-2)
Time (h)
%CD24
Control
IA 12.0 ± 3.3 *
Fullers Earth 9.6 ± 1.2 *
Fast Act 10.0 ± 2.4 *
MBA 13.5 ± 6.0
TFMAA 10.0 ± 1.5 *
C
Amount Penetrated (µg cm-2)
Time (h)
%CD24
Control
IA 4.9 ± 1.6 *
Fullers Earth 4.5 ± 2.3 *
Fast Act 3.8 ± 3.8 *
MBA 7.0 ± 4.8
TFMAA 4.5 ± 1.1 *

Figure 1

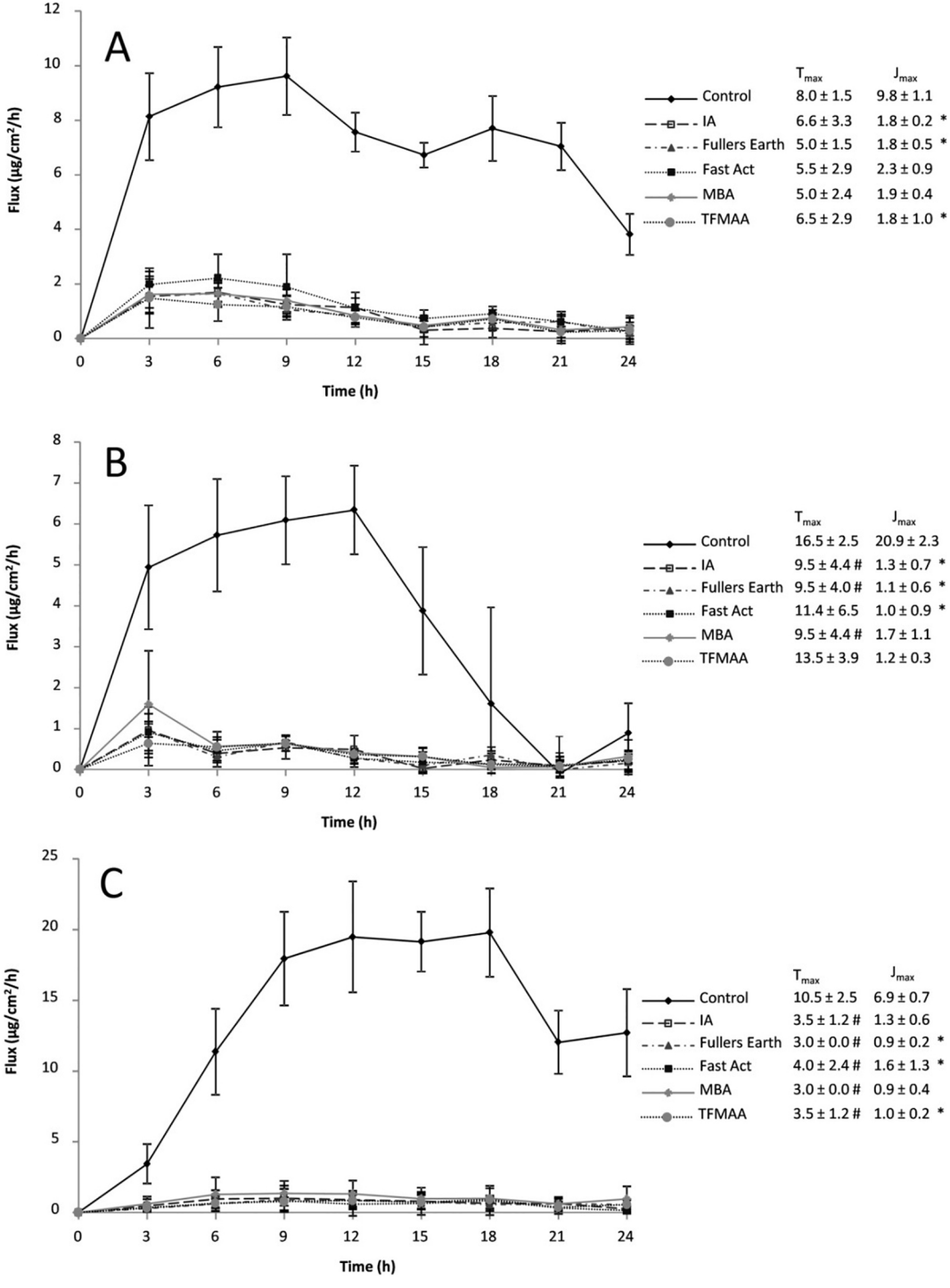
A
Flux (µg/cm²/h)
Time (h)
Control 8.0 ± 1.5 9.8 ± 1.1
IA 6.6 ± 3.3 1.8 ± 0.2 *
Fullers Earth 5.0 ± 1.5 1.8 ± 0.5 *
Fast Act 5.5 ± 2.9 2.3 ± 0.9
MBA 5.0 ± 2.4 1.9 ± 0.4
TFMAA 6.5 ± 2.9 1.8 ± 1.0 *
B
Flux (µg/cm²/h)
Time (h)
Control 16.5 ± 2.5 20.9 ± 2.3
IA 9.5 ± 4.4 # 1.3 ± 0.7 *
Fullers Earth 9.5 ± 4.0 # 1.1 ± 0.6 *
Fast Act 11.4 ± 6.5 1.0 ± 0.9 *
MBA 9.5 ± 4.4 # 1.7 ± 1.1
TFMAA 13.5 ± 3.9 1.2 ± 0.3
C
Flux (µg/cm²/h)
Time (h)
Control 10.5 ± 2.5 6.9 ± 0.7
IA 3.5 ± 1.2 # 1.3 ± 0.6
Fullers Earth 3.0 ± 0.0 # 0.9 ± 0.2 *
Fast Act 4.0 ± 2.4 # 1.6 ± 1.3 *
MBA 3.0 ± 0.0 # 0.9 ± 0.4
TFMAA 3.5 ± 1.2 # 1.0 ± 0.2 *

Figure 2