Homeland Defense & Security Information Analysis Center

HDIAC TECHNICAL INQUIRY (TI) RESPONSE REPORT

Reactive Skin Decontaminant Lotion With Sarin and Soman and Their Degradation Products

Report Number:

HDIAC-BCO-2022-223

Completed (May/2022)

HDIAC is a U.S. Department of Defense Information Analysis Center

MAIN OFFICE
4695 Millennium Drive
Belcamp, MD 21017-1505
Office: 443-360-4600

REPORT PREPARED BY:
Jeffrey Stiefel, PH.D.
Office: HDIAC

HDIAC is sponsored by the Defense Technical Information Center, with policy oversight provided by the Office of the Under Secretary of Defense for Research and Engineering. HDIAC is operated by the SURVICE Engineering Company.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From – To)*
	Technical Research Report	

4. TITLE AND SUBTITLE

Reactive Skin Decontaminate Lotion With Sarin and Soman and Their Degradation Products

5a. CONTRACT NUMBER
FA8075-21-D-0001

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Dr. Jeffrey Stiefel

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Homeland Defense & Security Information Analysis Center (HDIAC)
SURVICE Engineering Company
4695 Millennium Drive
Belcamp, MD 21017-1505

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

Defense Technical Information Center (DTIC)
8725 John J. Kingman Road
Fort Belvoir, VA 22060-6218

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT

DISTRIBUTION A. Approved for public release: distribution unlimited.

13. SUPPLEMENTARY NOTES

CBRN Defense, Medical, Weapons of Mass Destruction

14. ABSTRACT

Reactive skin decontamination liquid (RSDL) is shown to decontaminate several chemical warfare agents. The process by which RSDL neutralizes is not fully understood. A literature search was performed to determine if any test data exist for the decontamination of nerve agents sarin and soman and the production of hydrolysis products, such as isopropyl methylphosphonate, pinacolyl methylphosphonate, and methyl phosphonate, or any other reaction products identified.

15. SUBJECT TERMS (PROVIDED BY AUTHOR)
Reactive skin decontamination lotion (RSDL), nerve agents, sarin, soman, decontamination, hydrolysis products

16. SECURITY CLASSIFICATION OF: U			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			Ted Welsh, HDIAC Director
U	U	U			**19b. TELEPHONE NUMBER** *(include area code)* 443-360-4600

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

DISTRIBUTION A. Approved for public release: distribution unlimited.

About DTIC and HDIAC

The Defense Technical Information Center (DTIC) preserves, curates, and shares knowledge from the U.S. Department of Defense's (DoD's) annual multibillion dollar investment in science and technology, multiplying the value and accelerating capability to the Warfighter. DTIC amplifies this investment by collecting information and enhancing the digital search, analysis, and collaboration tools that make information widely available to decision makers, researchers, engineers, and scientists across the Department.

DTIC sponsors the DoD Information Analysis Centers (IACs), which provide critical, flexible, and cutting-edge research and analysis to produce relevant and reusable scientific and technical information for acquisition program managers, DoD laboratories, Program Executive Offices, and Combatant Commands. The IACs are staffed by, or have access to, hundreds of scientists, engineers, and information specialists who provide research and analysis to customers with diverse, complex, and challenging requirements.

The Homeland Defense & Security Information Analysis Center (HDIAC) is a DoD IAC sponsored by DTIC to provide expertise in eight technical focus areas: alternative energy; biometrics; chemical, biological, radiological, and nuclear (CBRN) defense; critical infrastructure protection; cultural studies; homeland defense & security; medical; and weapons of mass destruction. HDIAC is operated by SURVICE Engineering Company under contract FA8075-21-D-0001.

A chief service of the DoD IACs is free technical inquiry (TI) research, limited to 4 research hours per inquiry. This TI response report summarizes the research findings of one such inquiry jointly conducted by HDIAC.

Abstract

Reactive skin decontamination liquid (RSDL) is shown to decontaminate several chemical warfare agents. The process by which RSDL neutralizes is not fully understood. A literature search was performed to determine if any test data exist for the decontamination of nerve agents sarin and soman and the production of hydrolysis products, such as isopropyl methylphosphonate, pinacolyl methylphosphonate, and methyl phosphonate, or any other reaction products identified.

Contents

1.0 TI Request

1.1 Inquiry

What data exist on the reaction of reactive skin decontamination lotion (RSDL) with nerve agents sarin (GB) and soman (GD) and the formation of degradation products?

1.2 Description

RSDL has been shown to reduce toxic effects in animals dermally exposed to the nerve agents. The most effective products for skin decontamination are the liquid forms, as they favor rinsing and better extraction of molecules. RSDL contains methoxy polyethylene glycol (MPEG), which imparts hydrophobic properties to the product, and active ingredient Dekon 139, which rapidly neutralizes the vesicant chemical or the organophosphorus (OP) nerve agent. Explanation of the degradation mechanism exerted by RSDL remains undescribed in the literature. However, Dekon 139 has been demonstrated to have a degrading activity. An unclassified literature review on RSDL did not specifically contain information related to mediated degradation of G agent chemical warfare agents (CWAs) and potential byproducts IMPA, PMPA, and MPA.

2.0 TI Response

Provide a brief description of the process and information sources used by the author to complete the inquiry. Also provide a brief description of why this inquiry topic is important to the U.S. Department of Defense/government.

2.1 Skin Decontamination

Rapid decontamination of the skin is the single most important action to prevent dermal absorption of chemical contaminants in persons exposed to CWAs and toxic industrial chemicals (TICs) because of accidental or intentional release [1]. Dermal exposure to low volatile OP compounds (OPCs) may lead to penetration through the skin and uptake in the blood circulation. Organophosphorus nerve agents (OPNAs) are highly toxic compounds inhibiting cholinergic enzymes in the central and autonomic nervous systems and neuromuscular junctions, causing severe intoxications in humans [2]. Skin decontamination of toxic OPCs, such as pesticides and chemical warfare nerve agents, might therefore be crucial for mitigating the systemic toxicity following dermal exposures [3].

OPNAs can be divided into three groups—(1) G-agents (G for German), including GB, cyclosarin, tabun, and GD, which are known as nonpersistent; (2) V-agents (V for venomous, victory, or viscous, depending on the source), such as Venomous Agent X (VX), which are persistent; and (3) compounds belonging to the A-series of agents, or Novichok agents [2].

Recent interest in decontamination systems, which partition contaminants away from the skin and actively neutralize the chemical, has led to the development of several reactive decontamination solutions. RSDL has been shown to reduce toxic effects in animals dermally exposed to the nerve agents [3]; it may have a role in mass human exposure chemical decontamination in both the military and civilian arenas.

Limited studies have focused on the development of solutions that could be used for decontaminating people with the studies focused on developing solutions that could be used for decontaminating people [4].

The following information is based on a 2016 study on decontamination of OP pesticide Paraoxon (POX) with nanometric cerium oxide (CeO_2) [5].

2.1.1 Efficacy of a Skin Decontaminant

An effective skin decontamination product is described as a decontaminant which (1) decreases the quantity of contaminant absorbed into the skin (from the stratum corneum to the receptor fluid) and/or (2) has an ability to degrade the contaminant present on and into the skin. The nonabsorbed fraction (sum of the quantities of POX present on the skin surface and in the first strip) is the fraction considered as removable from the skin. On the contrary, the absorbed fraction (i.e., sum of the quantities from the stratum corneum to receptor fluid [RF]) is the quantity of POX which potentially moves into the blood. Therefore, for each decontamination experiment, the quantities of POX in the nonabsorbed fraction and the absorbed fraction have been compared. The improvement factor of functional prognosis (FP) of each decontaminant system have been compared and calculated as follows:

$$FP = \frac{Q_{2T} + Q_{3T} + Q_{4T}}{Q_2 + Q_3 + Q_4},$$

where:

Q_2 = the amount of POX present on the skin surface immediately after the decontamination process,

Q_{2T} = control samples,

Q_3 = the amount of POX in the skin (i.e., sum of the quantities in stratum corneum, viable epidermis and dermis) at the end of the experiment,

Q_{3T} = control samples,

Q_4 = the amount of POX resorbed (i.e., in RF) at the end of the experiment, and

Q_{4T} = control samples.

The more the FP increases, the more it is improved.

2.1.2 Skin Decontamination With Liquids

The liquid formulations (RSDL and CeO_2-W) were more efficient for eliminating POX on and into the skin than powders. These formulations significantly reduced the fraction of POX quantified in all the compartments except in the receptor fluid. RSDL was the more efficient product (FP = 127). Moreover, RSDL was able to degrade POX into p-nitrophenol (PNT) at a rate of 58% for 24 hr of experiment. The CeO_2-W (FP = 93) was more efficient than CeO_2 in the form of powder (FP was 10× higher). However, its degradation activity has been drastically reduced (production of 0.09 mmol/cm^2 of PNT for CeO_2-W vs. 0.57 mmol/cm^2 for CeO_2 raw particles).

2.1.3 In Vitro Skin Distribution of POX

POX is a lipophilic molecule as revealed by its midrange octanol/ water partition coefficient, logP = 1.95, and its molar mass (MM) is 275 g/mol. It has been demonstrated that chemicals with an MM lower than 500 g/mol and with logP value ranging between 1 and 3 rapidly dissolve into cutaneous lipids and permeate through the stratum corneum. Consequently, POX can be expected to be absorbed quickly into the skin. However, POX was found to be on the skin's surface, and only 3.7% has been absorbed through the skin. It has already been reported that "venomous agent X" or VX, which has similar physicochemical characteristics to POX (MM = 267 g/mol, and log P = 0.7), penetrated faster and earlier (lower lag time) than POX through pig ear skin. Experimental conditions for skin penetration studies often vary, and it is difficult to compare with other studies because all the parameters are not identical (skin nature and thickness, skin surface, exposure time, etc.). Skin penetration studies of POX using Franz cell diffusion are always performed under other conditions. A previous study examined the permeation of POX through a split-thickness pig ear skin. The conditions were not the same as ours—the thickness of the skin samples was 530 ± 5 mm, the applied dose of POX was 5 mg/cm^2, and the membrane area available for diffusion was 1.13 cm^2. The authors used the enzymatic method for the quantification of POX on the skin's surface, in the skin, and in the

receptor fluid. Still, the results were like ours. After 24 hrs of POX skin exposure, 95 ± 8% was recovered on the membrane's surface, 0.20 ± 0.20% of Q0 was quantified in the receptor fluid, and 0.26 ± 0.20% was in the skin.

2.1.4 Liquids

The most effective products for skin decontamination were the liquid forms. When liquids are applied on the skin, they favor rinsing and better extraction of molecules. RSDL contains MPEG, which imparts hydrophobic properties to the product. It allows displacing, retaining, and removing POX from the skin surface. The importance of the polarity of the decontamination product has been demonstrated with Yachau and coworkers [6]. Their study demonstrated that corn oil and a polyglycol-based cleaner were more effective than water or a solution of soap in water in limiting the transfer into the skin of methylene bisphenyl isocyanate, a very lipophilic compound. Another key component of RSDL is the active ingredient Dekon 139, which rapidly neutralizes the vesicant chemical or the OP nerve agent. Explanation of the degradation mechanism exerted by RSDL remains undescribed in the literature. However, we demonstrated that Dekon 139 has a degrading activity. The disadvantage associated with RSDL is that it leaves an oily residue on the skin and can make soldiers uncomfortable while carrying out certain military activities. However, if RSDL leaves a residue, Dekon 139 must certainly remain on the skin's surface and exert its effect over exposure time.

The last compound of RSDL, 2,3-butanedione monoxime (DAM), works on the intoxication by dephosphorylating acetylcholinesterase poisoned with OP. Using a hydrophilic system for the dispersion of CeO_2 did not help the removal of hydrophobic POX from the skin surface. The use of a thickener to avoid the sedimentation of NPs had two drawbacks—(1) after the skin decontamination process, the NPs are conveyed in the suspension and none remained on the skin's surface for degrading the OP compounds, and (2) guar gum does not prevent the accessibility to NPs for the degradation of pesticide. Moreover, the short contact between CeO_2 and POX is not long enough to initiate the degradation of POX. Thus, CeO_2 did not play any part in POX degradation and explain the disappearance of the degradation activity compared to the powder form. The aqueous dispersion of CeO_2 increased the absorbed quantity of POX compared to RSDL. This may be explained by the fact that water is an absorption enhancer. Indeed, it has been found that lipid-soluble compounds, which have a high affinity for the stratum corneum, penetrate the skin less than hydrophilic ones [7]. In general, increased tissue hydration increases transdermal delivery of both hydrophilic and lipophilic compounds [8]. This mechanism is not clearly described in the literature, but water could alter the solubility of the permeant in the stratum corneum and modify the permeation of the chemical through the skin.

Misik et al. have demonstrated that higher permeation rates of POX were observed under wet skin conditions rather than dry ones [9].

References

[1] Schwartz, M. D. "Reactive Skin Decontamination Lotion (RSDL) for the Decontamination of Chemical Warfare Agent (CWA) Dermal Exposure." *Curr. Pharm. Biotechnol.*, pp. 1971–1979, 13 August 2012.

[2] Jacquet, P. "Enzymatic Decontamination of G-Type, V-Type and Novichok Nerve Agents." *IJMS,* p. 8152, 2021.

[3] Thors, S. L. "RSDL Decontamination of Human Skin Contaminated With the Nerve Agent VX." *Toxocology Letters*, pp. 47–54, 5 March 2017.

[4] Jacquet, P., D. Daudé, J. Bzdrenga, P. Masson, M. Elias, and E. Chabrière, E. "Current and Emerging Strategies for Organophosphate Decontamination: Special Focus on Hyperstable Enzymes." *Environ. Sci. Pollut. Res. Int.,* pp. 8200–8218, 2016.

[5] Salerno, A. "In Vitro Skin Decontamination of the Organophosphorus Pesticide Paraoxon With Nanometric Cerium Oxide CeO_2." *Chemico-Biological Interactions,* 2016.

[6] Yachao, C., H. Xiaoying, A. Elmahdy, and H. Maibach. "In Vitro Human Skin Permeation and Decontamination of Diisopropyl Methylphosphonate (DIMP) Using Dermal Decontamination Gel (DDGEL) and Reactive Decontamination Lotion (RSDL) at Different Timepoints." https://www.sciencedirect.com/science/article/pii/S0378427418319441.

[7] El Hussein, S., P. Muret, M. Berard, S. Makki, and P. Humbert. "Assessment of Principal Parabens Used in Cosmetics After Their Passage Through Human Epidermisedermis Layers (Ex-Vivo Study)." *Exp. Dermatol.,* vol. 16, 2007.

[8] Williams, A. C., and B. W. Barry. "Penetration Enhancers." *Adv. Drug Deliv. Rev.,* vol. 56, 2004.

[9] Misik, J., R. Pavlikova, J. Cabal, L. Novotny, and K. Kuca. "Method of Static Diffusion Cells for Assessment of Pesticides in Skin Permeation." *Military Medical Science Letters (Vojenské Zdravotnické Listy),* vol. 80, p. 46–51, 2011.

Biography

Jeffrey Stiefel is a senior executive with deep expertise in the U.S. Department of Defense's and Homeland Security's (DHS's) chemical and biological defense research and development, advanced development, operations and policy, climate change policy, community health resilience, and acquisition/program management. As a program executive, he has managed the National BioWatch Program, health effects of climate change, and the chemical and biological detection acquisition. He is a recognized expert on chemical/biodefense, climate change and health resilience, emergency management, community resilience, disaster health resilience, strategic planning, program management, and cross-functional leadership. He received the DHS Secretary's Silver Medal for Exceptionally Meritorious Service in Program Management. Dr. Stiefel holds a Ph.D. in molecular genetics from Boston College, an M.S. in microbiology from the University of Alabama, Tuscaloosa, and a B.A. in biology from Hood College.

Bibliography

Harri Koskela, M.-L. R.-L. "Determination of Trace Amounts of Chemical Warfare Agent Degradation Products in Decontamination Solutions With NMR Spectroscopy." *Anal. Chem.,* pp. 9098–9106, 2007.

Yachao Cao, X. "In Vitro Human Skin Permeation and Decontamination of diisopropyl methylphosphonate (DIMP) Using Dermal Decontamination Gel (DDGel) and Reactive Skin Decontamination Lotion (RSDL) at Different Timepoints." https://www.sciencedirect.com/science/article/pii/S0378427418319441, accessed 6 June 2022.

Zygfryd Witkiewicz, S. N. "Analysis of the Precursors, Simulants and Degradation Products of Chemical Warfare Agents." *Crit. Rev. Anal. Chem.,* pp. 337–371, 2018.