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Scientific paper

PERCUTANEOUS TOXICITY AND DECONTAMINATION OF SOMAN, VX, AND PARAOXON IN RATS USING DETERGENTS

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Highly toxic organophosphorus compounds (OPs) were originally developed for warfare or as agricultural pesticides. Today, OPs represent a serious threat to military personnel and civilians. This study investigates the *in vivo* decontamination of male Wistar rats percutaneously exposed to paraoxon and two potent nerve agents - soman (GD) and VX. Four commercial detergents were tested as decontaminants – Neodekont™, Argos™, Dermogel™, and FloraFree™. Decontamination performed 2 min after exposure resulted in a higher survival rate in comparison with non-decontaminated controls. The decontamination effectiveness was expressed as protective ratio (PR, median lethal dose of agent in decontaminated animals divided by the median lethal dose of agent in untreated animals). The highest decontamination effectiveness was consistently achieved with Argos™ (PR=2.3 to 64.8), followed by Dermogel™ (PR=2.4 to 46.1). Neodekont™ and FloraFree™ provided the lowest decontamination effectiveness, equivalent to distilled water (PR=1.0 to 43.2).

KEY WORDS: *Argos™, chemical warfare agent, Dermogel™, FloraFree™, mass decontamination, military toxicology, Neodekont™, protective ratio*

Chemical warfare agents (CWAs) are compounds with the potential to be used as weapons of mass destruction. Among them, organophosphorus nerve agents are the most toxic (1). Although they were developed over 70 years ago (before and during World War II), CWAs still pose a threat. Nerve agents, as well as the somewhat less toxic organophosphorus pesticides, could be misused by terrorist groups as cheap and easily obtainable chemical weapons (1, 2). Thus, mass decontamination is often discussed in order to establish an optimal decontamination procedure. Compared to military decontamination, mass decontamination requires a different approach, since victims are mainly unskilled to adequately respond and are without the necessary decontamination equipment.

The main approach to preventing the harmful effects of CWAs is to decrease systemic absorption (3). For this purpose, the military uses protective clothes and gas masks, which are not available to civilians during mass casualty scenarios. Therefore, unprotected civilians are under a greater risk of becoming contaminated (mostly through the skin and respiratory system). Thus, an effective decontamination method to counteract the impact of pollutants needs to be made part of the onsite first aid procedure. Many different decontamination methods have been developed (4-6). The most common one for mass casualties is wet type decontamination using detergents (7, 8).

In this study, four commercial detergents (Neodekont™, Argos™, Dermogel™ and FloraFree™)

were tested and compared for their decontamination effectiveness in rats pre-exposed to topical nerve agents soman and VX, as well as to an active metabolite of the OP pesticide parathion - paraoxon (Figure 1). The protective ratios (PR) of detergents were determined against the PR of distilled water using a standard *in vivo* decontamination test (6, 9).

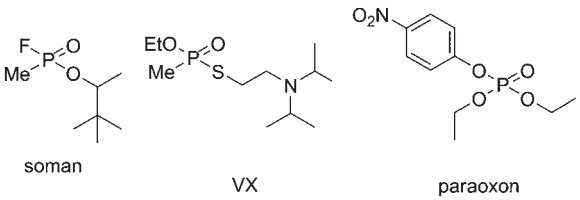

Figure 1 *The chemical structure of soman, VX, and paraoxon.*

MATERIALS AND METHODS

Decontaminants and other chemicals

The nerve agents soman (O-pinakolyl methylphosphonofluoridate) and VX {*O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothioate} were obtained from Zemianske Kostolany military laboratory (Slovak Republic) and had a purity of 97 % and 90 %, respectively. Paraoxon (diethyl 4-nitrophenyl phosphate, 97 %) was purchased from Sigma Aldrich, Ltd. (Czech Republic). The application of VX required small doses due to its high toxicity; hence dilution was done before administration to animals (2). Accordingly, VX was administrated as a 0.01 % hexane (Sigma Aldrich, Ltd.) solution. The detergents FloraFree™ (Deb Ltd., United Kingdom), Dermogel™ (KAO Corporation España, Spain), and Argos™ (Argos Hygiene Ltd., France) were obtained from the Health Protection Agency (United Kingdom). Neodekont™ was produced by the ChemProtect corp. (Czech Republic). Argos™ consists mainly of surfactants (e.g., sodium alkylethersulphate, sodium alkylbenzensulphonate, cocamide diethanol amine, etc.) and other compounds (methylchloroisothiazolinone), while the remaining three detergents contain other compounds such as potassium tallate, isopropyl alcohol, sodium citrate, triclosan, sodium laureth sulphate, triethanolamine lauryl sulphate, glycerin, alkylamide betaine triethanolamine-dodecylbenzene sulphonate, bentonite, etc. All of the detergents were pre-mixed with distilled water (5.0 %).

Animals

A total of 327 adult male Wistar rats (b.w. from 180 g to 210 g) were obtained from the Velaz corp. (Czech Republic) and placed at an approved animal facility at the Faculty of Military Health Sciences (FMH). The animals were housed in standard boxes in groups of six and received standard food and drinking water *ad libitum*. The handling and treatment of the experimental animals were done under the supervision of the Ethics Committee of the FMH and in full accordance with laws and regulations.

Methods

The acute percutaneous toxicity of the selected OPs was established using a conventional acute toxicity test (10) prior to skin decontamination. Undiluted toxic agents (soman, paraoxon) or hexane diluted VX were topically administered onto clipped dorsal skin (5 cm x 7 cm) using a pipette. Clipping was performed on the day before the experiment to avoid post-clipping irritation. The animals were placed in a fume hood and restrained on plastic platters during agent application/decontamination. Each experimental group consisted of four to six animals. Four to five different doses of the agent were applied. Decontamination was initiated 2 min after exposure by swabbing the dose site manually by 10 strokes in a head-to-tail direction using a cotton swab (2.5 cm x 2.5 cm) moistened in a 5 % aqueous solution of a single detergent type and finally dried by another swab. The temperature of the decontamination fluid was maintained at 25°C. The control group was decontaminated with distilled water instead of a detergent solution following the same protocol. Blank controls (n=5) were fixed, clipped, and "decontaminated" with distilled water without pre-exposure to toxic agents. The animals that survived for 24 h were euthanized by CO_2.

Data analysis

Acute toxicity was evaluated by assessing the median lethal dose (LD_{50}, mg kg^{-1}) and its 95 % confidence limits, calculated by a probit analysis of deaths occurring within 2 h (soman) and 24 h (VX, paraoxon). The effectiveness of decontamination was expressed as the protective ratio (PR); i.e., the ratio between LD_{50} in decontaminated animals and LD_{50} in untreated animals (9). The statistical significance of the difference between decontaminated and non-decontaminated LD_{50} was assessed on the basis of

non-overlapping confidence limits. Other results are shown as a mean±standard deviation (SD).

RESULTS

The rats percutaneously poisoned by OPs showed dose-dependent signs of intoxication. In soman poisoned groups, the local fasciculation of dorsal muscles started usually several (from 3 min to 7 min) after application and expanded gradually. The animals that received supra-lethal doses of soman (from 10 mg kg^{-1} to 40 mg kg^{-1}) suffered from strong central convulsions terminated by respiratory crisis (apnoea) and death. When 30 mg kg^{-1} was administered, convulsions occurred within (5.3±1.9) min. Mastication, salivation, and piloerection were also observed. Dermal LD_{50} of soman assessed 2 h after exposure was 9.83 mg kg^{-1} (from 5.87 mg kg^{-1} to 13.63 mg kg^{-1}), and it remained the same after 24 h. Compared to soman, VX-poisoned animals showed signs of a cholinergic crisis later on. Local and central convulsions started (91.8±6.1) min after VX administration at a dose of 0.1 mg kg^{-1}. Hyper-salivation, lacrimation, and pilo-erection also occurred as signs of intoxication. Dermal LD_{50} of diluted VX observed 24 h after exposure was 0.085 mg kg^{-1} (from 0.027 mg kg^{-1} to 0.102 mg kg^{-1}). In paraoxon-treated animals, the first signs of intoxication were apparent approx. 4 h after application (local fasciculation) with 24 h LD_{50} of 4.37 mg kg^{-1} (from 1.59 mg kg^{-1} to 8.84 mg kg^{-1}). There were no cholinergic signs or deaths within 2 h and 24 h in blank controls.

Animals subjected to decontamination suffered less from cholinergic symptoms compared to non-treated. In all cases, the survival of decontaminated animals increased and deaths were usually related to higher agent doses. In general, the most promising decontamination effectiveness was achieved with Argos™, followed by Dermogel™. Lower decontamination effectiveness was found with FloraFree™ and Neodekont™ solutions (Table 1, 2, and 3).

DISCUSSION

Acute toxicity of OPs

The toxic effect of OPs is caused mainly by the irreversible inhibition of the enzyme acetylcholineseterase (AChE, EC 3.1.1.7), which leads to the accumulation of the neurotransmitter acetylcholine in the central and peripheral nervous systems and ultimately to a fatal impact on neuromuscular transmission (2, 11, 12). Thus, typical signs of cholinergic crisis were observed in percutaneously intoxicated rats (fasciculation, salivation, etc.). In this study, VX was the most toxic

Table 1 *Decontamination effectiveness of detergents against soman*

Decontamination effectiveness	Decontaminant *vs.* soman										Acute toxicity of soman	
	Ar		De		Fl		Ne		water		D	M
	D	M	D	M	D	M	D	M	D	M		
	20	1/4	20	1/4	20	1/4	20	1/4	20	0/4	5.0	0/6
	40	2/4	40	3/4	40	3/4	30	3/4	30	3/4	10.0	3/6
	60	3/4	60	3/4	60	3/4	40	3/4	40	4/4	15.0	5/6
	80	4/4	80	4/4	80	4/4	60	4/4	60	4/4	20.0	6/6
											30.0	6/6
LD_{50} / mg kg^{-1}	35.85		30.70		30.70		25.83		26.72		9.83	
LCL / %	-		-		-		-		5.98		5.87	
UCL / %	-		-		-		-		38.50		13.63	
PR	3.6		3.1		3.1		2.6		2.7			

The effectiveness is shown as protective ratio (PR; median lethal dose in decontaminated animals divided by median lethal dose in untreated animals). Mortality (M) is shown as the number of deaths versus the number of animals in the experimental group.
D – dose in mg kg^{-1}
Ar - Argos™; De - Dermogel™; Fl - FloraFree™; Ne - Neodekont™;
LCL - lower confidence limit; UCL - upper confidence limit
Significant difference ($p<0.05$) between decontaminated LD_{50} and non-treated LD_{50} is marked with an asterisk.

Table 2 *Decontamination effectiveness of detergents against VX*

Decontamination effectiveness	Decontaminant *vs.* VX										Acute toxicity of VX	
	Ar		De		Fl		Ne		water		D	M
	D	M	D	M	D	M	D	M	D	M		
	2.0	0/4	2.0	0/4	0.5	0/4	2.0	0/4	1.0	0/4	0.079	2/6
	3.0	1/4	3.0	2/4	1.0	3/4	3.0	1/4	2.0	1/4	0.1	5/6
	5.0	0/4	5.0	2/4	2.0	4/4	5.0	4/4	5.0	3/4	0.126	6/6
	8.0 10.0	3/4 4/4	8.0	4/4	3.0	4/4	8.0	4/4	10.0 15.0	3/4 4/4	0.159	6/6
LD_{50} / mg kg^{-1}	5.51		3.92		0.846		3.45		3.67		0.085	
LCL / %	3.00		-		0.003		2.10		0.82		0.027	
UCL / %	17.95		-		1.889		33.32		9.52		0.102	
PR	64.8*		46.1		10.0		40.6*		43.2*			

See Table 1 for a more detailed explanation.

Table 3 *Decontamination effectiveness of detergents against paraoxon*

Decontamination effectiveness	Decontaminant *vs.* paraoxon										Acute toxicity of paraoxon	
	Ar		De		Fl		Ne		water		D	M
	D	M	D	M	D	M	D	M	D	M		
	5.0	0/4	5.0	0/4	2.5	0/4	2.5	0/4	2.0	0/4	2.0	0/5
	10.0	2/4	10.0	1/4	5.0	1/4	5.0	0/4	4.0	2/4	5.0	3/5
	15.0	2/4	15.0	4/4	10.0	4/4	10.0	4/4	8.0	3/4	10.0	5/5
	20.0	4/4	20.0	4/4	15.0	4/4	15.0	4/4	12.0	4/4	20.0	5/5
LD_{50} / mg kg^{-1}	11.34		10.62		9.91		7.07		4.52		4.37	
LCL / %	-		-		2.65		-		0.52		1.59	
UCL / %	-		-		18.16		-		10.52		8.84	
PR	2.6		2.4		2.3		1.6		1.0			

See Table 1 for a more detailed explanation.

agent with LD_{50} being less than 0.1 mg kg^{-1}, which is in concordance with established data on VX (2), even though it was diluted. In some studies, dilution was found to elevate skin permeation *in vitro* (13, 14), which could possibly lead to an earlier manifestation of cholinergic signs and higher VX toxicity *in vivo*. On the other hand, Hamilton et al. (15) found little or no effect of dilution on VX absorption. The extreme toxicity of agent VX is caused by a preferential reaction with AChE, contrary to G-agents which are more willing to be hydrolyzed by other ChE (2). Although VX was the most toxic, cholinergic signs occurred relatively late (1.5 h) compared to soman. When high doses of soman were applied, a rapid manifestation of AChE inhibition occurred in several minutes (fasciculation, central convulsions). In supra-lethal doses, other cholinergic signs such as hyper-salivation or mastication usually did not firmly manifest because of an early onset of central symptoms followed by rapid death. Muscarinic signs were observed mainly in sub-lethal (mainly miosis, hyper-salivation, and piloerection) and lethal doses (all of the mentioned signs). The rapidity of soman's effect can be explained by its high lipophilicity, which supports easy passage through the blood-brain barrier (16). Animals surviving 2 h also survived a 24 h exposure in all cases. In paraoxon, mild cholinergic symptoms (fasciculation) started 1.5 h under a high dose (20 mg kg^{-1}) and several hours after lower doses (from 2 mg kg^{-1} to 5 mg kg^{-1}). Finally, even when the onset of signs was mild, the LD_{50} of paraoxon was approximately 50 % lower than the LD_{50} of nerve agent soman after 24 h of exposure.

Decontamination of OP

Wet type decontamination using detergents reduced the symptoms of OP toxicity. Deaths were either fewer or associated with higher doses of OPs.

All of the detergents provided a low or modest level of protection, which was attributed to their low detoxification potency (17, 18) and the low solubility of lipophilic OPs in water solutions (2, 17). The lowest decontamination effectiveness was achieved against paraoxon (PR=1.6 to 2.6), followed by soman (PR=2.6 to 3.6). A more effective decontamination was achieved against VX (PR=10.0 to 64.8) which penetrated tissue slowly (15) and was not significantly absorbed during 2 min of exposure. Moreover, a low dose of VX was easily removed by a moistened cotton swab during decontamination. Argos™ and Dermogel™ were more effective in OP decontamination, whereas Neodekont™ and FloraFree™ provided lower decontamination effectiveness corresponding to that of distilled water or even lower. As for VX decontamination, both Neodekont™ and FloraFree™ were less effective than distilled water, suggesting the enhancement of skin permeation after washing with detergent solutions, as demonstrated *in vitro* (14, 19, 20). Although the chemical composition of the tested detergents was similar, the highest decontamination effectiveness against all of the tested OPs was consistently achieved with Argos™, which was also the most effective in the decontamination of sulphur mustard (9). The slight difference in the chemical composition of detergents apparently went in favour of Argos™, which is a relatively simple mixture of two primary and one secondary surfactant with a minor additive content to reduce the detergency effect of the surfactants (9).

Several more effective reactive and non-reactive decontamination methods or special preventatives as barrier creams were evaluated as countermeasures against CWAs (e.g., 6, 18, 21, 22). Most of them require skilled or prophylactic application and are appropriate only in the military domain. On the other hand, non-reactive detergents and soapy water are useful in mass decontamination facilities because of their availability, low health risk, and low skill requirements. Despite the fact that none of the studied detergents were able to effectively eliminate OPs from the skin, their use in emergencies could delay a fatal impact on victims. They could provide precious time for transport and subsequent medication of victims by pharmaceuticals such as anticholinergics (atropine) and AChE reactivators (23, 24).

Mass casualty decontamination requires a certain amount of time for technical implementation, which usually delays treatment. The response time is an important factor which influences the effectiveness of the decontamination (15, 17, 25, 26). In this study, decontamination was performed 2 min after exposure and the effectiveness would have certainly been decreased had the treatment been delayed. Another *in vivo* study (27) showed a good effectiveness for detergents used in the delayed decontamination of VX; however, as demonstrated, VX is a relatively slow-acting agent. Thus, further investigation is needed to evaluate the effectiveness of delayed decontamination against more rapid G-agents.

CONCLUSIONS

The harmful effect of OPs could be counteracted prior to systemic absorption using an appropriate decontamination method. In this study, wet type decontamination using four commercial detergents originally developed for cleaning and decontamination purposes were tested against OPs. All of the detergents generally provided modest protection against soman and paraoxon (PR=1.6 to 3.6). Higher protection was achieved against VX (PR=10.0 to 64.8). According to the obtained results, Argos™ (PR=2.3 to 64.8) should be investigated as a possible decontaminant in mass casualty scenarios. Moreover, the search for more effective alternatives should be considered.

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Conflict of Interest Declaration

The authors report no conflicts of interest. The authors alone are responsible for the content of the paper.

REFERENCES

1. Greenfield RA, Brown BR, Hutchins JB, Iandolo JJ, Jackson R, Slater LN, Bronze MS. Microbiological, biological, and chemical weapons of warfare and terrorism. Am J Med Sci 2002;323:326-40.
2. Munro NB, Ambrose KR, Watson AP. Toxicity of the organophosphate chemical warfare agents GA, GB and VX: implications for public protection. Environ Health Perspect 1994;102:18-38.
3. Gupta RC, editor. Handbook of Toxicology of Chemical Warfare Agents. 1st ed. London: Elsevier Inc; 2009.

4. Yang YC, Baker JA, Ward JR. Decontamination of chemical warfare agents. Chem Rev 1992;92:1729-43. doi: 10.1021/cr00016a003
5. Tiwari S, Ghosh KK, Marek J, Kuca K. Functionalized surfactant mediated reactions of carboxylate, phosphate and sulphonate esters. J Phys Org Chem 2010;23:519-25. doi: 10.1002/poc.1635
6. Cabal J, Kassa J, Severa J. A comparison of the decontamination efficacy of foam-making blends based on cationic and nonionic tensides against organophosphorus compounds determined *in vitro* and *in vivo*. Hum Exp Toxicol 2003;22:507-14. doi: 10.1191/0960327103ht377oa
7. Amlôt R, Larner J, Matar H, Jones DR, Carter H, Turner EA, Price SC, Chilcott RP. Comparative analysis of showering protocols for mass-casualty decontamination. Prehos Disaster Med 2010;25:435-39. doi: 10.1017/S1049023X00008529
8. Zilker T. Medical management of incidents with chemical warfare agents. Toxicology 2005;214:221-31. doi: 10.1016/j.tox.2005.06.028
9. Misik J, Pavlikova R, Cabal J, Vodakova E, Kuca K. A comparison of decontamination effects of commercially available detergents in rats preexposed to topical sulphur mustard. Cutan Ocul Toxicol 2013;32:135-9. doi: 10.3109/15569527.2012.730087
10. Lipnick RL, Cotruvo JA, Hill RN, Bruce RD, Stitzel KA, Walker AP, Chus I, Goddards M, Segal L, Springer JA, Myers RC. Comparison of the up-and-down, conventional LD50, and fixed-dose acute toxicity procedures. Food Chem Toxicol 1995;33:223-31.
11. Maxwell DM, Brecht KM, Koplovitz I, Sweeney RE. Acetylcholinesterase inhibition: does it explain the toxicity of organophosphorus compounds? Arch Toxicol 2006;80:756-60. doi: 10.1007/s00204-006-01
12. Bajgar J. Organophosphates/nerve agent poisoning: mechanism of action, diagnosis, prophylaxis, and treatment. Adv Clin Chem 2004;38:151-216.
13. Dalton CH, Hattersley IJ, Rutter SJ, Chilcott RP. Absorption of the nerve agent VX (O-ethyl-S-[2(di-isopropylamino)ethyl] methyl phosphonothioate) through pig, human and guinea pig skin *in vitro*. Toxicol In Vitro 2006;20:1532-6. doi: 10.1016/j.tiv.2006.06.009
14. Moody RP, Maibach HI. Skin decontamination: Importance of the wash-in effect. Food Chem Toxicol 2006;44:1783-8. doi: 10.1016/j.fct.2006.05.020
15. Hamilton MG, Hill I, Conley J, Sawyer TW, Caneva DC, Lundy PM. Clinical aspects of percutaneous poisoning by the chemical warfare agent VX. Effects of application site and decontamination. Mil Med 2004;169:856-62.
16. Joosen MJ, van den Boom JE, Kuijpers TM, Smit WC, Lucassen AB, van Helden HP. Long-term cognitive deficits accompanied by reduced neurogenesis after soman poisoning. Neurotoxicology 2009;30:72-80. doi: 10.1016/j.neuro.2008.11.010
17. Bjarnason S, Mikler J, Hill I, Tenn C, Garrett M, Caddy N, Sawyer TW. Comparison of selected skin decontaminant products and regimens against VX in domestic swine. Hum Exp Toxicol 2008;27:253-61. doi: 10.1177/0960327108090269
18. Braue EH Jr, Smith KH, Doxzon BF, Lumpkin HL, Clarkson ED. Efficacy studies of reactive skin decontamination lotion, M291 skin decontamination kit, 0.5% bleach, 1% soapy water, and skin exposure reduction paste against chemical warfare agents, Part 2: Guinea pigs challenged with soman. Cutan Ocul Toxicol 2011;30:29-37. doi: 10.3109/15569527.2010.515281
19. Loke WK, Lau SK, Lim JS, Tay GS, Koh CH. Wet decontamination-induced stratum corneum hydration: effects on the barrier function to diethylmalonate. J Appl Toxicol 1999;19:285-90. doi: 10.1002/(SICI)1099-1263(199907/08)19:4<275::AID-JAT578>3.0.CO;2-B
20. Misik J, Pavlikova R, Josse D, Cabal J, Kuca K. *In vitro* skin permeation and decontamination of the organophosphorus pesticide paraoxon under various physical conditions – evidence for a wash-in effect. Toxicol Mech Methods 2012;22:520-5. doi: 10.3109/15376516.2012.686535
21. Chilcott RP, Dalton CH, Hill I, Davison CM, Blohm KL, Clarkson ED, Hamilton MG. Evaluation of a barrier cream against the chemical warfare agent VX using the domestic white pig. Basic Clin Pharmacol Toxicol 2005;97:35-8.
22. Taysse L, Daulon S, Delamanche S, Bellier B, Breton P. Skin decontamination of mustards and oranophosphates: comparative efficiency of RSDL and Fuller's earth in domestic swine. Hum Exp Toxicol 2007;26:135-41. doi: 10.1177/0960327107071866
23. Kuca K, Jun D, Musilek K. Structural requirements of acetylcholinesterase reactivators. Mini Rev Med Chem 2006;6:269-77.
24. Kuca K, Jun D, Bajgar J. Currently used cholinesterase reactivators against nerve agent intoxication: comparison of their effectivity *in vitro*. Drug Chem Toxicol 2007;30:31-40.
25. Knezevic D, Tadic V, Katic S. Combined decontamination and parenteral therapy improve the chances of survival in rats percutaneously poisoned with organophosphorus insecticides. Acta Veterinaria (Beograd) 2001;51:187-95.
26. Dorandeu F, Taysse L, Boudry I, Foquin A, Hérodin F, Mathieu J, Daulon S, Cruz C, Lallement G. Cutaneous challenge with chemical warfare agents in the SKH-1 hairless mouse. (I) Development of a model for screening studies in skin decontamination and protection. Hum Exp Toxicol 2011;30:470-90. doi: 10.1177/0960327110373615
27. Misik J, Pavlik M, Novotny L, Pavlikova R, Chilcott RP, Cabal J, Kuca K. *In vivo* decontamination of the nerve agent VX using the domestic swine model. Clin Toxicol 2012;50:807-11. doi: 10.3109/15563650.2012.720986

Sažetak

PERKUTANA TOKSIČNOST I DEKONTAMINACIJA SOMANA, VX-A I PARAOKSONA U ŠTAKORA DETERDŽENTIMA

Visokotoksični organofosforni spojevi (krat. OP) prvotno su se proizvodili za ratovanje i uporabi u poljoprivredi kao pesticidi. Danas su nepobitno iznimna prijetnja vojnom osoblju i civilima. Ova studija istražuje *in vivo* dekontaminaciju muških štakora Wistar perkutano izloženih paraoksonu i dvama snažnim nervnim agensima – somanu (GD) i VX-u. Četiri komercijalna deterdženta ispitana su kao sredstva dekontaminacije - *Neodekont*, *Argos*, *Dermogel* i *FloraFree*. Dekontaminacija dvije minute nakon izlaganja rezultirala je višom stopom preživljavanja u usporedbi s nedekontaminiranom kontrolnom skupinom. Učinkovitost dekontaminacije izražena je kao zaštitni omjer (PR, medijan smrtonosne doze agenta u dekontaminiranih životinja podijeljen s medijanom smrtonosne doze agenta u nedekontaminiranih životinja). Najveća konzistentna učinkovitost postignuta je *Argosom* (PR=2.3 do 64.8) i *Dermogelom* (PR=2.4 do 46.1). Deterdženti *Neodekont* i *FloraFree* bili su najmanje učinkoviti i imali jednak učinak kao destilirana voda (PR=1.0 do 43.2).

KLJUČNE RIJEČI: *Argos, Dermogel, FloraFree kemijski ratni agens, masovna dekontaminacija, Neodekont, vojna toksikologija, zaštitni odnos*

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