DEVELOPMENT OF MEANS FOR THE DECONTAMINATION OF SUPERTOXIC LETHAL CHEMICAL WARFARE AGENTS ON HUMAN SKIN

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Abstract

Main features of the R&D resulting in the new mean for primary decontamination based on the sorption--mechanical principle introduced into the Czech Army´s individual decon packet IPB-80 and into the Czech Civil Protection first aid kit ZPJ-80, and in the upgrading of sets for secondary decontamination PCHB-60-P and PCHP-60-P are presented. First results of research on universal solution for decontamination of human skin are shown.

1. Introduction

To the most important rescue measures after contamination of the body surface with the supertoxic lethal chemical warfare agents belongs decontamination on the lowest tactical level, i.e. at individual. Possible contamination of skin by toxic agents with extreme high percutaneous toxicity and high penetration rate, such as VX, V-gaz, GF, GP and like stresses the urgency and effectiveness of *primary decontamination* which is to be considered as a *medical measure of life-saving importance*. In some cases, depending on the extent of contaminated skin, this primary decontamination might be decisive and more important than the antidote administration.

The **first post-WW-II generation** of modern means for personal decontamination on the lowest tactical level, i.e. at individual, for that what we call „primary decontamination" within the framework of the first aid, was the two-solutions system manufactured in Czechoslovakia according to the Soviet-originated model IPP-51. It was introduced under the depiction **IPB-60** into the Czechoslovak Army and under more simple modification in the first aid kit **OZB** into the Czechoslovak Civil Defence in the early 1960s. The same system has been used for the „secondary decontamination" within the facilities of the medical evacuation chain in the means used at the medium and higher tactical levels, known as **PCHB-60-P** and **PCHP-60-P**. This system is based on the subsequent use of two solutions, i.e.

- **Solution No 1**–15 per cent (w/v) of sodium cresolate in 96 per cent ethyl alcohol and
- **Solution No 2**–20 per cent (w/v) of sodium benzene sulphochloroamide (chloramine B) in 82 per cent (v/v) ethyl alcohol in water with 11.6 per cent (w/v) of zinc(II)chloride.

After appearance of new agents with high percutaneous toxicity (V-agents) in the 1960s, it was necessary to test this two-solutions system on the effectiveness in decontaminating V-agents. The chemical formula of VX was published in 1974, but our suspicion on the possible structure of this agent led us to start R&D works on all problems of physical and medical protection (detection, decontamination, first aid, therapy, means of personal protection etc.) against V-agents using a model substance, i.e. the N,N-dimethyl analogue of VX, depicted later as Medemo. I initiated this research in the Czechoslovak NBC-Defence R&D Establishment (at present known as Military Technical Institute of Protection in Brno) with synthesis and determination of principal chemical, physical an toxic properties of the group of O-alkyl S-n-(N,N-dialkyl)aminoalkyl methylphosphonothiolates in 1963–1964.

To the first tasks belonged testing of impact of these agents on then introduced means of protection and laboratory decontamination in order to assure workplace safety of personnel. It is obvious that it was necessary to begin with synthesis of agents with highest possible and standard purity including development of standard analytical methods for testing contents of active agent and impurities.

The works on the problems of medical protection performed mainly at the Purkyne Military Medical Institute (nowadays known again as Military Medical Academy) in Hradec Králové started with already standard compounds by exact toxicometrics in the late 1960s continuing with works on the first aid and experimental therapy of intoxication.

I started the research on the decontamination problems within first aid and medical evacuation system in 1971. This research commenced with the above mentioned testing of efficiency of then introduced two-solutions system as the point of outcome for any further development.

Experimental works proceeded using biological objects. General toxicity testing (with various ways of administration) was carried out in mice, rats and guinea pigs, testing of percutaneous toxicity and of decontamination efficiency was performed mainly on rats, some experiments were made also on guinea pigs and rabbits. For this reason, standard methods of percutaneous contamination and standard methods of decontamination for both liquid and solid decontaminants were developed in the first line.

I have found that the best way to express the decontamination efficiency is the **Decontamination Index DI_{50}**. This expression corresponds to the ratio of LD_{50} p.c. (mg/kg) *with decontamination* (under standard conditions) to the LD_{50} p.c. (mg/kg) *without decontamination*. It is obvious that the higher the value of DI_{50}, the higher the decontamination efficiency. $DI_{50} = 1$ means zero decontamination effect.

Testing of the decontamination efficiency of the two-solutions system with acceptable effectiveness in case of GB, GD and HD showed insufficient decontamination effectiveness in case of Medemo (later confirmed also on actual VX). This was the main impetus to start extensive R&D of the quite new mean for primary decontamination and at least of upgrading the means for secondary decontamination.

Our research followed three main directions:
- Decontamination solutions and emulsions
- Decontamination ointments, gels and pastes
- Decontamination by means of adsorption and chemisorption powders.

2. Experimental part

2.1 Chemical agents

Main types of supertoxic lethal chemical warfare agents, i.e. HD, GB, GD, Medemo and VX, as described in [1], used undiluted.

2.2 Experimental animals

Mice, albino rats, guinea pigs and rabbits, as described in [1].

2.3 Standard method of percutaneous administration

Undiluted agents were put in the form of small droplets on prior sheared skin on *dorsal thorax* using specially calibrated platinum wires or loops, as described in [1] in detail.

2.4 Standard method of decontamination

If it was not necessary to determine the influence of time between contamination and decontamination on the decontamination efficiency (significantly decreasing in time), the decontamination was provided uniformly 2 min after animal had been intoxicated. The whole prior sheared area (i.e. 15 sq.cm) was treated:

- In case of sorbent, 0.3 g of powder was uniformly spread over the whole area. Then the powder was softly rubbed on the whole area for 30 seconds, using twisted sections of cotton wool 42x45 mm (together 0.50 g), held with tweezers, as described in [2].
- In case of liquid, standard wicked gauze tampons (about 0.330 g) held with tweezers were soaked with standard contents of liquid mean (1.6 ml) by dipping into solution and the whole area was whipped for 30 seconds. In case of two solutions, the second was applied 1°min after the first one.

2.5 Evaluation of experiments

Determined percutaneous toxicities (LD_{50}) both without and with decontamination were calculated statistically using the probit-numerical method by means of elaborated programme on the computer HEWLETT-PACKARD 9830-A. Individual doses were applied to the groups of 5–10 experimental animals and at least five points with the mortality between 5–95 per cent were necessary to be found.

3. Results and discussion

3.1 Percutaneous toxicities of used chemical warfare agents

Percutaneous toxicities of supertoxic lethal chemical warfare agents in tested experimental animals are summarized in table 1.

Table 1

Percutaneous toxicity of tested agents LD_{50} p.c. mg/kg [2]
/standard deviation/ (lower - upper confidence limit)

Agent	Albino rat	Guinea pig	Rabbit
HD	15.82 /3.28/	---	---
GB	128.40 /84.90/	98.49 (63.54–152.7)	---
GD	15.77 /4.23/	22.73 /4.98/	5.868
Medemo	0.0630 /0.0222/	0.809 (0.521–1.824)	0.0572 (0.0408–0.804)
VX	0.0132 /0.0073/	0.246 (0.196–0.321)	0.0514 (0.0210–0.115)

3.2 Decontamination efficiency of the two-solutions system

The carefully determined decontamination efficiency of the above mentioned first post-WW-II generation of means based on the subsequent use of two solutions, i.e. IPB-60, OZB,PCHB-60-P and PCHP-60-P used as reference standard to compare all R&D results, achieved later is shown in table 2.

Table 2

Decontamination efficiency of IPB, OZB, PCHB-60-P and PCHP-60-P [2]
(DI_{50}, albino rats)

Agent	HD	GB	GD	Medemo	VX
DI_{50}	11.4	8.1	23.5	71.7	147

The decontamination efficiency of VX seems high on the first view. But it is quite opposite. Let us only confront the toxicity data vs. contamination density on the skin surface in mg/sq.cm [2]. Moreover, the non-sufficient rate of the decontaminating reaction even diminishes the protective properties of clothing [1] in case of decontamination on man [3]. Also irritancy of human skin contributed to the commencement of R&D of the new means.

3.3 Upgrading of the two-solutions system

It may be understood that the two-solutions system where the subsequent use of both solutions is necessary in case of primary decontamination because of lacking knowledge which agent the person has been contaminated with, contains solutions, otherwise relatively effective when used alone in case of exact knowledge on the agent to be decontaminated (Solution No 1 - GB, GD, Solution No 2 - HD, VX) which might occur in case of secondary decontamination. This was the reason of relatively cheap upgrading of this system to utilise the results for innovations of PCHB-60-P and PCHP-60-P in order to find substitution for the Solution No 2. while retains the Solution No 1 unchanged due to its excellent efficiency against GB and GD and low irritancy.

In these research works, the main stress was laid on various oxidating agents offering the possibility of being stable in solution, low toxic and low irritant. Good results were obtained with hydroperoxy compounds of various structures, compounds with active iodine with combined detergent effects, such as polyvinylpyrrolidone and like and with other chlorinating agents. The most promising results, utilising *inter alia* developed industrial production of chlorinated derivatives of trichloroisocyanuric acid in Czechoslovakia, were obtained with upgraded Solution No 2, where 15 g of trichloroisocynuric acid and 10 g zinc(II)chloride was dissolved in 100 ml of acetone [7]. The decontamination efficiency is presented in table 3.

Table 3

Decontamination efficiency of the upgraded two-solutions system [4]
(No 1 as in IPB, No 2 trichloroisocyanuric acid in acetone)

Agent	HD	GB	GD	Medemo	VX
DI_{50} (rats)	6.1	5.1	11.3	345	949

Even the toxicity profile of this solution is more advantageous, as seen from table 4.

Table 4

Toxicity of some decontamination solutions (LD_{50} ml/kg in mice)[4]

Solution	i.m.	p.o.
No 1 (IPB)	1.42 (0.94–2.10)	2.17 (1.68–2.65)
No 2 (IPB)	2.05 (1.60–2.57)	1.85 (1.36–2.85)
No 2 (TCICA)	6.73 (3.57–9.61)	2.03 (1.23–3.77)

Also the skin irritancy is significantly lower at the upgraded solution No 2 containing trichloroisocyanuric acid (TCICA). This decreases to only 40 per cent of cases, observed at the original Solution No 2, while only slight irritancy occurs and no case of heavy skin corrosion can be observed.

3.4 Decontamination with the sorption-mechanical mean

In the search for simple, cheap and universal mean, we have tested up to hundred various materials with sorption (chemisorption respectively) properties. Very promising results were obtained in a group of specially treated montmorillonites of domestic origin. The final solution was acidically treated bentonite (i.e. with active H-centre) enabling to manufacture a simple mean for primary decontamination that we have depicted according to the principle of employment as „sorption-mechanical"[5]. It is based on chemisorption and for optimal result of decontamination some rubbing of the fine powder on the skin surface is recommended. This material, known under acronym „DESPRACH" during development (reflecting the Czech for *des*activation and fine powder *prach*), was introduced into the new mean for individual decontamination **IPB-80** [6] in the Czechoslovak Army and as the substantial part of the set in the new kit for the first aid **ZPJ-80** [6] in the Czechoslovak Civil Defence. For some details on this mean see [2].

What is the most important, the new mean meets all principal requirements, mainly:

- effectiveness against all main types of chemical warfare agents, i.e. universality,
- speed of decontamination effect,
- non-irritancy on skin,
- non-aggressivity on clothing material,
- simplicity of manipulation,
- readiness to use,
- low weight,
- use within a wide temperature range,
- mechanical resistance,
- extreme stability on storage,
- simplicity of manufacturing enabling mass production,
- accessibility of raw materials,
- extremely low costs.

The mean is actually very simple for production and use [6]. The powder is placed in a hand-operated PE bottle (in the form of quadrangular prism) with small orifice for oriented spreading of powder on the contaminated area. The bottleneck contains a screw cap. It is interesting that this R&D resulted in an atypically cheaper innovation: The price of the new IPB-80 was less than one third as compared with the old IPB-60 introduced twenty years ago.

The most important property is the decontamination efficiency, as shown in table 5.

Table 5

Decontamination efficiency DI50 of the new method for primary decontamination (DESPRACH) based on sorption-mechanical principle [4]
Decontamination 2 minutes after contamination

Agent	HD	GB	GD	Medemo	VX
DI_{50} (rats)	12.56	3.73	19.03	968	1200

3.5 Research of efficient universal decontamination solutions

Even if our mean for primary decontamination possesses beside universality and high cost-effectiveness also other exploitation properties as required for the mean of primary decontamination, it seems that the use of this principle would not be the best solution under *all* circumstances, mainly in the case of secondary decontamination at the facilities of the medical evacuation chain where the use of solutions (emulsions) for decontamination of wounded personnel is felt to significantly enhance productivity in preparing prior intoxicated patients (where the decontamination of skin, adjacent parts of clothing, as well as of dressing materials is necessary) for further medical especially surgical interventions.

This research that has been proceeding for several decades seems to be something like a never finished agenda due to necessary compromises among several contradictory requirements. During this research works, having learned lessons from previous works, we have laid stress on following methodical points and basic requirements:

- *In vivo* experiments (standard experimental animals - albino rats)
- Standard method of contamination (preparation of skin, p.c. intoxication techniques),
- Standard method of decontamination (volume, materials, techniques)
- Standard testing compounds (HD, GB, GD, VX, group approach for screening: GD, VX)
- Toxicity of decontaminants (mice, i.m., p.o.)
- Irritancy (human volunteers)
- Impact on textile materials
- Impact on other relevant materials (including environmental impact)
- Stability of solution (stability of components)
- Temperature range of use
- Accessibility of components
- Simple use
- Cost-effectiveness.

Because of different chemical nature and thus also ability of principal groups of supertoxic lethal chemical warfare agents to undergo basic types of reactions (electrophilic and nucleophilic), it is obvious how difficult is to find one simple universal reactant for agents with high affinity to nucleophilic reactions (such as G-agents) with similar decontamination efficiency for agents possessing high affinity to electrophilic reactions (such as HD and V--agents). If we take into consideration also requirements regarding toxicity, irritancy and corrosion, not to speak on other desired properties, it is clear how uneasy task is to suggest a solution based on one universal chemical principle, or to be quite realistic, how to find acceptable compromise among all requirements.

Nevertheless, it seems according to our results that it would be possible to find efficient chemical decontaminants among some nucleophilic agents (taking into consideration limitations due to toxicity and irritancy) and among combination of oxidation principle and enhancement of solubility of toxic agent, if possible in one complex agent and last but not least utilising catalysis. Anyway, only reaction principles offering high reaction rate are valuable.

Due to the limited extent of this chapter, we mention only some positive results achieved in the orientation to oxidative principles (see e.g. [8]), involving use of compounds with active chlorine, active iodine, peroxo-compounds, various mixtures of these compounds, as well as the use of oxidative agents and enhancement of decontamination efficiency due to simultaneous addition of detergents. It can be concluded that e.g. iodophores of various origin, although effective on VX, were generally insufficiently effective on GD. Similar results were achieved in case of various compositions of chloro--derivatives of isocyanuric acid. On the other hand, some promising results were achieved combining sodium peroxide with commercially accessible detergents, as shown in one example in table 6 [4].

Table 6

Decontamination efficiency (DI50) of the sodium peroxide solution of detergents

Agent	HD	GB	GD	Medemo	VX
DI_{50} (rats)	3.9	3.9	22.6	4115	2658

The emulsion contains 12.5 per cent (w/v) of sodium peroxide, 0.5 per cent (w/v) of Slovanion, 0.5 per cent (w/v) of of Slovafol and 0.5 per cent (w/v) of Alkon in water.

Another very promising direction of ongoing research is the orientation on alkaline alcoholate solutions in a very cautiously selected mixture of aprotic solvents, taking into consideration the actual danger of skin irritancy and corrosivity (See e.g. [9]).

4. Conclusions

As a result of our R&D, a new mean for primary decontamination of human skin and adjacent parts of clothing in the variations for armed forces (IPB--80) and for civil protection (ZPJ-80) has been introduced recently and a cheap and efficient mood of partial upgrading of the means for secondary decontamination (PCHB-60-P and PCHP-60-P) has been suggested. First results on universal solution (emulsion) for decontamination of human skin (including adjacent parts of clothing or/and dressing in case of wounded personnel) using e.g. sodium

peroxide emulsion of detergents are described and the possibility of use of alkaline alcoholate solutions of cautiously selected mixtures of aprotic solvents is mentioned.

References

1. MATOUSEK, J.: Protective properties of standard combat clothing against skin penetration of supertoxic lethal chemical warfare agents. In Sohns, T., Voicu, VA. (Eds.): *NBC Risks: Current Capabilities and Future Perspectives for Protection.* Kluwer Academic Publishers Dordrecht - Boston - London, 1999, p.. 303-310.
2. MATOUSEK, J.: Sorption-mechanical principle in skin decontamination. In Sohns, T., Voicu, VA. (Eds.): *NBC Risks: Current Capabilities and Future Perspectives for Protection.* Kluwer Academic Publishers Dordrecht - Boston - London, 1999, p. 265-269.
3. MATOUSEK, J.: Problem of decontamination of clothing on man. *6th International Sympos. on Protection against CBW Agents.* Stockholm, 1998. *Proceedings, vol. 1*, NDRC, Dept. of NBC Defence Umea, 1998, p. 255-256.
4. MATOUSEK, J.: Means for decontamination of supertoxic lethal chemicals on human skin. *Symposium on Nuclear, Biological and Chemical Threats in the 21st Century, NBC-2000,* Helsinki-Espoo 2000. *Symposium Proceedings, Research Report, No 75,* University of Jyvaskyla, 2000, p. 216-221.
5. MATOUSEK, J.: Universal mean for primary decontamination on the body surface (in Czech) CS Pat.1403/T (1974).
6. MATOUSEK, J., HODBOD, J., SEBESTIK, M.: Sorption--mechanical mean for decontamination of CW agents for multiple use (in Czech).CS Pat. 1931/T (1981).
7. MATOUSEK, J., ELSNEROVA, I.: Liquid mean for decontamination of CW agents on the body surface (in Czech). CS Pat. 1409/T (1974).
8. MATOUSEK, J.: Universal solution for decontamination on body surface based on oxidation principle (in Czech). CS Pat. 1951/T (1981).
9. MATOUSEK, J.: Non-irritant non-corrosive suspension for decontamination of CW agents (in Czech). CS Pat. 1952/T (1981).

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