INTRODUCTION

1. As a consequence of increasing risk of war and terrorism with chemical or biological warfare agents, it is a challenging issue to develop optimum Protective pharmaceutical dosage forms against various forms of war and terror.
2. For efficient protection, development of pharmaceutical systems providing optimal efficacy, worldwide usage and large-scale production is required.

KEY POINT TO BE CONSIDERED

In order to achieve the development of a proper dosage form with:
1. Optimal efficacy
2. Efficiency
3. Convenience
some key points, other than scientific and technical challenges and considerations, should be considered carefully during the formulation phase.

- Locally-antibiotic and inexpensive material should be used for cost effectiveness and readiness-availability
- Dosage form should be prescribed easily
- Simple and non-problematic administration is necessary, because in most cases we will be either on our own or in small health care centers after an attack while most warfare agents' effects start immediately upon contact
- One should be able to self-administer the dosage form without professional assistance
- A long shelf-life and high stability in various extreme conditions are of great importance for a safe, economic and practical dosage form
- Chemical compatibility within the system is required
- Packaging and transportation of large-scale produced dosage forms should be possible to reach all regions under threat, rapidly

Recent study and advances in defence technology

- Chemical agents for prophylaxis
- Medical countermeasures for vesicant agents
- Advanced antimicrobials
- Low-cost adhesives in order to decontaminate water and natural Resources
- Personal decontamination products

Personal Decontamination Products:

1. Passive and active topical protectants
2. Alcohol based sanitizers
3. Long-lasting formulas that kill infectious germs on contact as well as work to prevent further infections

Passive Skin Protectants

Ointments and creams are preferred pharmaceutical dosage forms as a pre-attack measure against chemical agents (such as extremely lethal vesicants and nerve agents)

- “Barrier Cream” approach
- Goal: To prevent chemical agents’ contact with the skin

RSDL (Reactive Skin Decontamination Lotion)

1. Developed and licensed in Canada
2. Approved by FDA recently
3. For use in military
4. To remove neutralize chemical warfare agents and T-2 fungal toxin from the skin
5. Used by the US military for exposure as soon as possible after exposure to a chemical agent
6. The lotion is impregnated in a sponge pad packaged a single-unit in a heat-sealed foil pouch

SERPACA (Skin Protection Reaction Paste Against Chemical Warfare Agents)

1. Goal: To prevent exposure to both chemical and biological agents
2. The proposed Skin Protectant Technology has been currently approved by the FDA for military use only
3. When used in conjunction with appropriate protective clothing, protects soldiers from skin exposure to chemical warfare agents
4. Topical Skin Protectant (TSP) cream/paste contains polytetrafluoroethylene resin compounds that are similar to the substances that coat non-stick cooking utensils (50-50 mixture of two high molecular weight fluoro containing polymers: polytetrafluoroethylene, PTFE and perfluoropolyether, PFPE)
5. TSP cream/paste functions as a physical barrier between the skin and and chemical warfare agent, the so-called MOOP suit
6. TSP is not a replacement for use of any level of protective gear, but intended to complement and provides a secondary barrier

Advantages
1. Good occlusive property
2. Easy application
3. Large-scale production possible
4. Covering of skin for long duration possible

Disadvantages
1. Must be applied very shortly after exposure
2. Efficacy limited; does not destroy or absorb the chemical agent but only prevent from reaching skin layers
3. Repeated application is necessary for efficient protection

Povidone - Jodine (PJ)

1. Irradiated used product as an antiseptic agent and for the treatment of thermal burns its protective use has been suggested against chemical warfare agents such as potent vesicants and powerful alkylators (Wormser, 1997; 2000)
2. Post-exposure treatment with PJ containing protected against skin ulceration of vesicant agents depending on the interval between exposure and the type of irritant
3. The fact that prototypic activity is involved in inflammatory processes, and lead to skin lesions and necrosis mainly through the separation on the dermo-
epidermal Junction
4. Therefore, the protective effect of iodine may stem, in part, from the reduced skin collagenase activity. In fact, Wormser et al (2002) recently reported the strong inhibitory activity of PJ, or its active ingredient iodine, on three types of collagenase

Active Topical Skin Protectants

1. New active formulations consisting of a base cream and active moiety that act both as protective barrier and an active destructive matrix against chemical warfare agents
2. Base cream: Perfluorinated polymer oil and polytetrafluoroethylene solids (the same as SERPACA)
3. Active moiety: Different reactive ingredients of nanoparticles have been tested by USARICD. Including organic polymers (leading active moieties), enzymes, hybrid organic-inorganic materials, polymeric nanocomposites, inorganic oxides, metal alloys and small organic molecules
4. Active against chemical weapons in pig, rabbit and guinea pig models

Braue et al. “Active Topical Skin Protectant Nearing Transition to Advanced Development” 23rd Army Science Conference, 2-5 December 2002. Orlando, USA

.Active Nanoparticles

2. Demonstrated the potential for highly ‘Reactive Nano Particles’ (RNP) to absorb destructively highly toxic warfare agents such as GA, GB, HD
3. Described RNP as representing a new class of nanoscience of particles of metals and metal oxides that differ from other nanoparticles in reactivity and crystallinity morphology

Reactive Metal Oxide Nanoparticles

1. The potential of monoparticulate oil into a protective barrier skin cream has also been demonstrated
2. Chemical compatibility of nanoparticles in cream and suspension form ensured
3. Nanoparticle oxides synthesized include: aerogel-prepared MgO (AP-MgO) aerogel-prepared Mn3O4 (AP-Mn3O4) Conventional-prepared MgO (CP-MgO) Conventional-prepared CaO (CP-CaO) aerogel-prepared TiO2 (AP-TiO2)
4. Koper et al (2002) also reported formulations of nanoscale powders possessing antimicrobial properties made of simple, nontoxic metal oxides MgO and CaO in nanoscale form, carrying active forms of halogens (Cl2, Br2, I2) when contact with vegetative cells of E.coli, B.cereus, B. globius. 90% were killed within a few minutes, some forms of the Bacillus species were decontaminated within several hours

Disadvantages
1. Sophisticated material- difficult to obtain
2. Expensive chemicals and solvents involved
3. Large-scale production not yet achieved
4. Time-dependent physical stability of nanoparticles still unknown
5. Lack of animal testing

Critical Parameters Concerning the Design of a Pharmaceutical Dosage Form for Potential Use Against Bioterrorism and Chemical Weapons: AN OVERVIEW ON CURRENT CONCEPTS AND FUTURE PROSPECTS

A. Atilla Hincal1, Erem Memişoğlu-Bilensöy1, Sema Çalış1, Filiz Hincal2

Hacettepe University, Fac. of Pharmacy, Deps. of Pharmaceutical Technology1, and Pharmacological Toxicology2, Ankara-Turkey

REFERENCES


