

CHEMOPROPHYLAXIS TO REDUCE THE EFFECTS OF
IONIZING RADIATION ON PERSONNEL

1. Introduction

The U.S. Army has an approved requirement to develop a chemoprophylactic agent that will reduce or offset the harmful effects of ionizing radiation on personnel. (Please refer to the attached "Department of the Army Approved Qualitative Materiel Development Objective (QMDO) for Prophylaxis and Therapy to Offset the Effects of Ionizing Radiation").

Ideally, such an agent would be easily administered, provide continuous effective protection at low doses without harmful side effects, be easily obtainable in large quantities and stable in expected battlefield environments.

2. History

Since 1949 chemoprophylaxis in experimental animals has been reported in the literature. In May 1959 the U.S. Army Medical Department initiated a drug development program based on the demonstrated protection afforded by aminothiols and related chemicals. This program has continued at a modest level of effort as an Exploratory Development RDT&E Project. At present, the approved interim objectives for this program are as follows:

- a. Dose Reduction Factor: 2 to 3*
- b. Drug Dose: 50 mg/kg body weight
- c. Safety Factor: 6-8
- d. Oral Administration
- e. Duration of Action: 8 hours
- f. Incidence of side effects requiring hospitalization: 5/100,000

These objectives apply to the hematopoietic, gastrointestinal and central nervous system levels of ionizing radiation injury.

* The dose reduction factor (DRF) used herein is expressed as the ratio of the dose of radiation producing and LD 50/30 (radiation dose lethal to 50% of animals in 30 days) in the protected animal to the dose of radiation producing an LD 50/30 in the unprotected animal. The LD50 is determined by probit analysis from several points including high and low ranges of ionizing radiation dosage.

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3. Current Status of the Program

The agents under development have been established as offering effective protection against all three levels of radiation injury. Animal experiments have shown that the toxic effects can be appreciably diminished with a retention of protective effect. Several drugs have been evaluated for tolerance in man. The Investigational New Drug Application for an additional chemical compound is being reviewed by the appropriate authorities. This chemical has the possibility of offering significant protection in man at anticipated tolerance levels.

The aminothiols and related compounds remain the only significant lead; however, other chemical families are being continuously tested for their radioprotective effect.

The scientists involved believe that it is now technically feasible to attain the above interim objectives and that a major effort should be undertaken at the next higher level, i.e., "Advanced Development."

4. Operational Concepts

These agents would be readily available for administration to troops when ordered by the Commander. Medical officers would advise the Commander in regard to drug limitations. Obvious advantages would occur under the following situations:

- a. When troops are knowingly exposed to moderate or emergency risk levels of radiation resulting from Command Guidance.
- b. When exposure to supralethal prompt radiation doses can be anticipated, the protection against immediate incapacitating effects could allow mission completion.
- c. When personnel must survive in, exit from or maneuver through fall-out fields, the reduction in harmful effect would significantly reduce the risks involved.