TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
MAY 80   A W SINGER
UNCLASSIFIED   USAEHA-75-51-0854-80
UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT A13-36016
PHENETHYL 2-FUROATE
STUDY NO. 75-51-0854-80
MARCH 1976 - MARCH 1980

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REPORT DOCUMENTATION PAGE

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Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-36016, Phenethyl 2-Furoate

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6. PERFORMING ORG. REPORT NUMBER

7. AUTHOR(S)

ALLEN W. SINGER CPT, VC

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US Army Environmental Hygiene Agency
Aberdeen Proving Ground, MD 21010

9. SUMMARY

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US Army Health Services Command
Fort Sam Houston, TX 78234

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19. ABSTRACT (limit abstract to 200 words)

A preliminary hazard evaluation of AI3-36016 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild primary skin irritation and proved to be moderately toxic if ingested. It did not cause eye or phototreaction and did not sensitize guinea pigs. It was recommended that AI3-36016, phenethyl 2-furoate, not be approved for further testing as a candidate insect repellent.

20. KEYWORDS (Continue on reverse side if necessary and identify by block number)

AI3-36016
Phenethyl 2-Furoate
Candidate Repellent
Eye Irritation
Skin Irritation
Acute Ingestion Hazard
Topical Hazard Evaluation
USDA Proprietary Compound

21. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A preliminary hazard evaluation of AI3-36016 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild primary skin irritation and proved to be moderately toxic if ingested. It did not cause eye or phototreaction and did not sensitize guinea pigs. It was recommended that AI3-36016, phenethyl 2-furoate, not be approved for further testing as a candidate insect repellent.
HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent A13-36016, Phenethyl 2-Furoate, Study No. 75-51-0854-80, March 1976 to March 1980

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

A preliminary hazard evaluation of A13-36016 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild primary skin irritation and proved to be moderately toxic if ingested. It did not cause eye or photoirritation and did not sensitize guinea pigs. It was recommended that A13-36016, phenethyl 2-furoate, not be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

JOHN F. MAZUR
MAJ, MSC
Director, Laboratory Services

1 Incl
as (5 cy)

CF:
HQDA (DASG-PSP)
Cdr, MSC (HSPA-P)
Dir, Advisory Ctr on Tox, NRC
Supt, AHS (HSA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region
1. AUTHORITY.
   

   b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations; titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.


3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent A13-36016.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent A13-36016, phenethyl 2-furoate, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1978.
† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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TABLE. PRESENTATION OF DATA

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SKIN IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
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<tr>
<td>Single 24-hour application</td>
<td>Compound A13-36016 caused a mild irritation of the intact skin and the skin surrounding an abrasion.</td>
<td>USAEHA Category II (ref Appendix).</td>
</tr>
<tr>
<td>to intact and abraded skin</td>
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<tr>
<td>of New Zealand White rabbits.</td>
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<tr>
<td>0.5 mL technical grade</td>
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<tr>
<td>compound applied to each</td>
<td></td>
<td></td>
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<tr>
<td>of six rabbits.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EYE IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application</td>
<td>Compound A13-36016 did not cause irritation of cornea or conjunctiva in any rabbits.</td>
<td>USAEHA Category A (ref Appendix).</td>
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<tr>
<td>of 0.1 mL technical grade</td>
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<tr>
<td>compound to one eye of</td>
<td></td>
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<tr>
<td>each of six New Zealand</td>
<td></td>
<td></td>
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<tr>
<td>White rabbits.</td>
<td></td>
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<tr>
<td><strong>APPROXIMATE LETHAL DOSE (ALD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td></td>
<td></td>
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<tr>
<td>Rats (male) - no diluent</td>
<td>ALD = 216 μg/kg</td>
<td>May be fatal if accidentally ingested.</td>
</tr>
</tbody>
</table>

2
PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single 0.05 mL application of a 25 percent (w/v) solution of the compound and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm. The ethanol solution of AI3-36016 caused a moderate primary irritation on all sites. A13-36016 did not cause a photochemical irritation in rabbits and is not expected to cause such a reaction in humans. It did, however, cause a moderate primary irritation as applied.

Control

Following UV exposures of the rabbits, 0.05 mL of test compound, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours. Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.
**SENSITIZATION STUDIES**

**Guinea Pigs (Male)**

Intrademal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-36016 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ten test guinea pigs were given 10 sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of test compound.</td>
<td>Challenge dose of AI3-36016 did not produce a sensitization reaction.</td>
<td>Compound AI3-36016 did not produce a sensitization reaction under test conditions and is not expected to produce a sensitization reaction in man.</td>
</tr>
<tr>
<td>Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.</td>
<td>Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.</td>
<td>DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.</td>
</tr>
</tbody>
</table>

* A known skin sensitizer
5. CONCLUSION. Technical grade compound AI3-36016 caused mild skin irritation and is acutely toxic by ingestion. Due to the inherent oral toxicity, this compound does not qualify as a nonhazardous repellent.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36016, Phenethyl 2-furoate, not be approved for further testing as a candidate insect repellent.

ALLEN W. SINGER
CPT, VC
Veterinary Animal Laboratory Officer
Toxicology Division

APPROVED:

ARTHUR H. McCREEESH, Ph.D.
Chief, Toxicology Division
TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.