780 11-24-67

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mtw

Chemical Name: Sodium Methyldithio carbamate

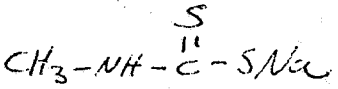
Trade Name:

1)	Chem Sect Brand Chem Vape USDA Reg. No. 1439-123	31%
2)	Stauffer Vapam Soil Fumigant Solution USDA Reg. No. 476-859	32.7% (ANH)
3)	DuPont VPM Soil Fumigant USDA Reg. No. 352-225	32.7% (ANH)

Use: Soil Fumigant to be applied by sprinkling can, Hose Proportioner, Irrigation or Sprinkler, Soil Injection on dosage range of 1/2 to 1 1/2 quarts per 100 ft^2.

Empirical Formula: CH_3 NH CSS Na $2H_2O$

Chemical Structure:



Molecular Weight: 165.22

Physical State: White crystalline solid
Unpleasant odor

Solubility: Water 72.2 gm/100 ml
MS in alcohol

Non-Flammable

Deadline: 3 weeks from 10/25-10/27

PR 230: Included

1/13

Data Summary

I Acute Mouse Oral	:	LD_{50} 285 mg/Kg No effect level - 100 mg/Kg Demonstrated ↓ respiration + peripheral vaso-dilitation
II Acute Rat Oral	:	LD_{50} = 820 mg/Kg No effect level - 600 mg/Kg Demonstrated ↓ respiration and depression.
III Acute Rabbit Dermal	:	LD_{50} ∿ 1.0 gm/Kg No effect level as high as 0.25 gm/Kg. Severe dermal irritation produced at all levels: Systemic effects only at 1 gm/Kg level
IV Subacute Rabbit Dermal (10 days)	:	Severe dermal irritation again noted. No sensitization claimed. No deaths recorded.
V Acute Inhalation (6 hr Exposure)	:	
Guinea Pig		3/7 ↓
Rat		2/7 ↓
Mouse		4/5 ↓
		All animals demonstrated ↓ respiration and eye irritation. Air concentration not calculated. LC_{50} not calculated.

Summary

Evaluation of the data in our possession reveal sodium methyl dithio carbamate to fall within the slightly toxic class by the oral route and probably within the slightly toxic class by the dermal route according to Lykken & within Class II according to USDA.

Acute Inhalation studies reveal the compound to have a respiratory hazard, on both an irritative and a pharmacologic basis. Also noted is its primary irritant effect on the skin.

Further studies should include:

1) More accurate acute inhalation studies with LC_{50}.
2) Acute Rabbit Eye Irritation with aqueous solution
3) Sub-acute rat feeding studies
4) Any additional sub-acute or chronic data available.
5) Reports of human exposure and/or poisoning

HBerry:deg
November 17, 1967

Sodium Methyldithiocarbamate

The material use in these studies was received from Stauffer Chemical Company. It is coarsely granular, white and solid with a sharp irritating odor. The 1.0 and 5.0 weight/volume aqueous solutions used in some of these studies contained a small quantity of particulate matter, probably due to the presence of water-insoluble impurities.

I Acute Mouse Oral

Procedure

Groups of 13 male albino mice each were given single doses of Sodium Methyldithiocarbamate by stomach tube at the following levels: 100, 200, 300, and 400 mg/Kg. A 5.0 weight/volume aqueous solution was used. Following oral administration the animals were observed for a period of one week. Surviving animals were sacrificed at autopsy.

Results

Immediately following oral administration the animals were depressed and exhibited lacrimation, squinting, slow respiration, and also redness of the nose, mouth, feet and ears, probably due to peripheral vasodilation. During the observation period the surviving animals at the two lower dosage levels appeared essentially normal. Depression and squinting eyes were observed at the two higher dosage levels for several days following administration and prior to death, if it occurred. In addition, at the highest dosage level, the surviving animals appeared bloated and showed irregular labored respiration 24 hours following administration.

The acute oral LD_{50} calculated according to the method of Litchfield and Wilcoxon is 285 mg/Kg with confidence limits from 228 to 356 mg/Kg. Significant gross pathological findinds observed at autopsy of the animals that died were hemorrhagic lungs, small quantities of fluid in the pleural cavity and slight irritation of the pyloric portion of the stomach and small intestine. The surviving animals sacrificed at the end of the observation period showed no significant gross pathology.

II Acute Rat Oral

Procedure

Groups of seven male albino rats were given the following dosages by stomach tube: 400, 600, 800, 900, 1000, and 1200 mg/Kg. A 5.0% weight/volume aqueous solution was used for all dosage levels. Gross autopsies were performed upon all animals that died and after an observation period of seven to eight days the surviving animals were sacrificed and autopsied.

Results

Immediately following oral administration, animals at all dosage levels exhibited depression, preening, salivation, and lacrimation. In addition, the animals at the higher dosage levels showed squinting, labored respiration, and sporadic hyperactivity prior to death or recovery. During the remainder of the observation period the surviving animals appeared essentially normal. The acute oral LD_{50} is 820 mg/Kg with confidence limits from 756 to 889 mg/Kg. Gross autopsies performed upon the animals

that died revealed the following pathology: hemorrhagic lungs, extreme dilatation of the vessels of the stomach, slight irritation of the small intestine, hemorrhagic adrenals, and congested kidneys and testes. The only significant gross pathological findings observed upon autopsy of the surviving animals was a thickening of the wall of the cardiac portion of the stomach, with resultant adhesions involving the stomach, dorsal body wall, spleen, and adjoining portions of the liver. This condition was observed in the majority of animals that survived the seven day observation period and probably resulted from severe gastric irritation produced by the experimental compound.

III Acute Rabbit Dermal
Procedure

Albino rabbits were used to evaluate the acute dermal toxicity and irritative properties of the test compound following the single exposure and later to establish a tolerable level for repeated dermal applications. The following doses were administered: 1 gm/Kg group included one rabbit. Material applied was dry diluted with 4.0 gm of Attapulgus clay. Three rabbits at the same dosage level had dry material undiluted applied and three more rabbits at the same dosage level had dry material moistened with sufficient distilled water to form a paste applied. At the 0.25 gm/Kg level three rabbits had the dry material diluted with 1.0 gm of Attapulgus clay appied and three other rabbits had dry material moistened with water

to form a paste applied. At the 0.10 gm/Kg level three animals had the dry material plus one gram of Attapulgus clay applied and three other animals had the dry material plus water to form a paste applied. At the 0.05 gm/Kg level two rabbits had 5% weight/volume aqueous solution applied and two rabbits had 5% weight/weight test compound in Attapulgus clay applied. At the 0.01 gm/Kg dosage level two rabbits had 1% weight/volume aqueous solution applied and two rabbits had 1% weight/weight in Attapulgus clay applied. The dry or paste applications were spread evenly on non-absorbent paper backing, applied to the closely clipped abdominal skin, and secured with gauze and adhesive tape. At each of the 0.05 and 0.01 gm/Kg dosage levels, the fluid application was administered to one animal under rubber damming, which was secured with gauze and adhesive tape. The second animal at each of these two dosage levels received the fluid application by inunction; in order to prevent oral ingestion of the compound, cardboard collars were placed around the neck. The material remained in contact with the skin for 24 hours. After the exposure period the binders were removed and the animals were observed for dermal irritation and signs of systemic toxicity. Autopsies were performed upon the animals that died and after an observation period of three to seven days the surviving animals were sacrificed and autopsied. Throughout the study the animals were housed individually.

Results

At dosage levels of 1.0, 0.25, and 0.1 gm/Kg, both the dry and paste applications of the test compound produced severe dermal irritation characterized by moderate to marked erythema, edema, necrosis, fissures, atonia, desquamation, and coriaccousness. When undiluted material was applied the animals immediately showed increased activity as if the compound caused a burning sensation. At the 0.05 gm/Kg dosage level, the animals receiving the dry material in Attapulgus clay exhibited a moderate degree of erythema, edema, hemorrhagic areas, necrosis, and coriaccousness, while the animals receiving a similar dose as a 5.0% solution exhibited mild erythema, and one showed corrosion and slight necrosis. At the 0.01 gm/Kg level, the dry application of the test compound in Attapulgus clay produced slight erythema, edema, desquamation and atonia; animals at this level receiving the 1.0% aqueous solution exhibited no dermal irritation. All animals at the 1.0 gm/Kg level appeared depressed within 24 hours following dermal exposure, and after 24 to 48 hours, four of the six animals at this level were dead. Prior to death these animals exhibited weight loss, tremors, dilated pupils with no response to light, slow respiration, gasping, and mild clonic convulsions; all reflexes were depressed or absent. Several survivors at all dosage levels showed a loss in body weight. No other signs of systemic toxicity were observed and no deaths occurred at any of the other dosage levels tested. The animals that died had hyperamic or hemorrhagic lungs and irritation of

the gastrointestinal tract at the time of autopsy. The surviving animals at the 1.0 gm/Kg dosage level exhibited the following significant gross pathology: subcutaneous hemorrhage and edema and irritation of the gastrointestinal tract and peritoneum. There were no significant gross pathological findins in any other animal examined.

IV Subacute Rabbit Dermal (10 Days)

Procedure

Groups of albino rabbits were used to evaluate the dermal toxicity and irritative properties of the test compound following repeated exposure. The dosage levels tested were selected on the basis of the information provided by the acute dermal study. Since Attapulgus clay was used as a diluent at one of the experimental dosage levels, a control group of animals received repeated applications of Attapulgus clay; no control applications of distilled water were used. Three rabbits were at the dosage level of 1½ grams per day. Material applied was undiluted Attapulgus clay. Number of applications were ten. At the .05 gm/Kg level six rabbits received 5% weight/volume aqueous solution for a total of two applications. At the 0.01 gm/Kg level six rabbits received 1% weight/volume aqueous solution for ten doses. At the 0.005 gm/Kg level six rabbits received 1% weight/weight in Attapulgus clay for ten doses. The first, third, and fourth groups also received challenge doses. The fluid applications were administered under rubber damming and the dry material was spread evenly on non-absorbent paper backing.

The paper or damming was applied to the closely clipped abdominal skin and secured by gauze and adhesive tape. Each exposure period was approximately 24 hours. After daily removal of the binders, the animals were observed for dermal irritation and signs of systemic toxicity before reapplication of the material. Throughout the study the animals were housed individually with food and water available at all times. At a dosage level of 0.05 gm/Kg the animals exhibited marked dermal irritation following the second application. Administration was therefore discontinued. The remainder of the control and experimental groups received the full course of ten exposures. There was a two day rest period between the fifth and sixth applications. The animals were observed for ten days following the tenth application and then given a challenge dose to determine whether sensitization had been produced. The animals were then observed for an additional period of 72 hours, then sacrificed and autopsied.

Results

The control animals receiving undiluted Attapulgus clay exhibited a transient mild erythema, atonia, desquamation, dryness of the skin, and poor fur regeneration during the second week of the exposure period. After the fourth application the lower abdomens of two animals became irritated and during the second week of the exposure period, indurated, necrotic areas and scab formations were observed in this region. These changes were undoubtedly exaggerated by the binders and to some extent by the abrasive effect of the clay. Two applications of 0.05 gm/Kg as

a 5.0% aqueous solution produced a moderate degree of erythema, edema, and hemorrhagic blanched and necrotic areas which continued into the observation period following the discontinuation of the compound. The skin of three of the six animals became coriaceous and all animals showed rather extensive scab formations. Ten applications of 0.01 gm/Kg as a 1.0% aqueous solution produced a mild to marked degree of erythema, edema, atonia, desquamation, dryness of the skin, and poor fur regeneration. following the fourth, fifth, or seventh application, necrosis was noted in five animals. This condition progressed to induration and scab formation. Ten applications of 0.005 mg/Kg produced a mild to moderate degree of erythema, atonia, desquamation, dryness of the skin, and poor fur regeneration. Following the fourth, fifth, and seventh application, four animals showed necrotic areas on the lower abdomen; this condition progressed to induration and scab formation. Prior to the administration of the challenge dose to evaluate sensitization, all evidence of skin irritation had subsided except for eschars observed in a few animald from each group. After 24 to 48 hours following administration of the challenge dose, the control animals exhibited no erythema while several animals in each experimental group exhibited a mild erythema and atonia. At 72 hours the skin of all control and experimental animals appeared normal. There appeared to be a normal amount of fur regeneration in all animals at the time of sacrifice. Throughout the experimental period all animals exhibited normal behavior and no

signs of systemic toxicity were observed. No mortality occurred in the control or any experimental group. At the time of sacrifice several animals at the 0.05 gm/Kg dosage level exhibited a decrease from their initial body weight but in the control and remaining experimental level groups all animals showed an increase in body weight. The response to the challenge dose indicates that the compound is a primary irritant but it does not produce sensitization. The control animals revealed no significant gross pathological findings on autopsy. Among the experimental groups an occasional animal exhibited pale kidneys and slight irritation of the small intestine.

V Acute Inhalation Exposure (6 Hours)

Procedure

Seven guinea pigs, seven rats, and five mice were exposed the dust compound for six hours. These animals were housed in a 500 liter chamber equipped with a 500 liter dusting tower into which the dust was fed by means of a Wright dust-feed mechanism. The chamber was operated at slight negative pressure with an air flow of 35 liters per minute. During the six hours exposure a total of 30 gm was dusted into the chamber. In the absence of a working chemical detection procedure, no attempt was made to determine the atmospheric content of the test compound and estimation of air concentration is unreliable according to the report.

Results

Within five minutes after the beginning of operation the rats began preaning and after about one hour's operation evidence of eye irritation developed. At this time all animals appeared somewhat depressed. After approximately four hours operation all animals showed definite respiratory embarrassment and shortly thereafter one mouse died. At the end of five hours the rats and guinea pigs both showed lacrimation and salivation in addition to the previously existing dyspnea. When the six hour exposure was terminated, four mice, three guinea pigs, and two rats had succumbed and the remaining animals displayed the toxic signs previously described. The survivors were sacrificed and the organs examined for gross pathology. The lungs of all three species were hyperemic and edematous and the intestinal tracts of the guinea pigs and mice were markedly distended with gas. These data indicate that the test compound is a severe mucous membrane irritant under the conditions of the study and it is at least moderately toxic by the inhalation route. LC_{50} was of course not calculated.