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SKIN ABSORPTION AND SENSITIZATION TESTS WITH PAINTS CONTAINING PHENYLMERCURY OLEATE

Medical Research Project No. MR-353

Report No. 6-57

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The toxicity tests were performed by Regina Neher, Richard Gant, and Ardis Hinkle. The biochemical tests were performed by Katherine Ranta and Dr. J. R. Barnes. The pathological examinations were made by Drs. Douglas M. Gay and A. R. Borgmann.

SKIN ABSORPTION AND SENSITIZATION TESTS WITH PAINTS

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INTRODUCTION

In order to determine whether phenylmercury oleate (PMO) in paint can be absorbed through the skin or can cause skin irritation, tests were conducted on samples submitted by Marshall Laboratory. The skin absorption studies were carried out on four types of paint containing PMO and on control samples of each type that contained no PMO. The test for skin irritation was made on one of the paints containing the highest concentration of PMO. In addition an Approximate Lethal Dose (ALD) of PMO in linseed oil containing 1.8 per cent mineral spirits was determined to establish the relative oral toxicity of the compound in a paint vehicle.

SAMPLES

The samples received from Marshall Laboratory were as follows:

Paint	F & F Code No.	Type Vehicle	% PMO by Wt	Haskell No.
"Dulux" Trim and Shutter	87-894	Alkyd resin	0.2	1699
" " " "			0.0	1700
Vinyl Masonry	387-301	Polyvinyl acetate	0.02	1701
" "			0.0	1702
Light Cream House	301-920	Linseed oil	0.075	1703
" " "			0.0	1704
Experimental Emulsion House	389-016	Alkyd resin, modified polyvinyl acetate	0.2	1705
			0.0	1706
PMO in 1.8% Mineral Spirits, 98% Linseed Oil	VO-E-61870	--	0.2	1698

ACUTE ORAL TOXICITY

The 0.2 per cent solution of phenylmercury oleate in linseed oil containing 1.8 per cent mineral spirits was administered by stomach tube to male albino rats. The ALD was found to be 75 mg of active ingredient per kilo of body weight. The lethal dose produced weight loss, anuria and diarrhea. Death occurred on the third day after the dose was administered. Pathological findings showed rather severe tubular nephritis which was presumed to be the cause of death.

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Sublethal doses produced a temporary weight loss and polyuria which lasted two to seven days after the compound was administered. When the animals were sacrificed three weeks after treatment, autopsies revealed enlarged kidneys and evidence of residual nephritis in the animals receiving doses of 50, 35 and 15 mg/kg, but the kidneys of the animal receiving 22 mg/kg were essentially normal.

Comparison of these results with the results of an earlier acute oral toxicity test of phenylmercury oleate carried out at Haskell Laboratory showed that linseed oil did not lessen the toxic effects of the mercurial. In the earlier test a 2.0 per cent solution of phenylmercury oleate containing 18 per cent mineral spirits and 80 per cent peanut oil was used. The oral ALD was found to be 133 mg/kg.

SKIN ABSORPTION

The paint containing PMO and the control paint containing no PMO were applied to the clipped backs of male albino rabbits. The animals were restrained in metal stocks during treatment and until the paint had dried. The animals were then returned to their cages. The cages of the animals receiving the paint containing PMO were isolated from those of the controls. Daily one-milliliter applications of the paint were made serially down the back of each rabbit on each of five successive days. Within four to five hours following the fifth treatment the animals were sacrificed. The liver and kidneys were excised and weighed, and samples were taken for microscopic and chemical analysis.

On the mornings following treatment, the Vinyl Masonry paint and Experimental Emulsion paint were observed to have cracked and peeled from the rabbits' backs. Since this introduced the possibility of the animals ingesting some of the paint a second test was made using a single five-milliliter application. The animals were restrained in stocks until the paint was dry. The painted area was then wrapped with cellophane, gauze and adhesive and the rabbits returned to their cages. They were then sacrificed twenty-six hours after treatment. There were no clinical signs of toxicity in any of the animals nor were there any significant pathological changes that could be attributed to the effects of the treatment. The results of the chemical analysis are shown in Table I.

The mercury content of the liver and kidney was measured by the colorimetric method of Laug and Nelson[1] and expressed as micrograms of mercury per gram of wet tissue. The amounts of mercury found in the livers and kidneys of the rabbits treated with paints containing no PMO were negligible in all cases. Mercury appeared in the kidneys and in the livers of all the animals treated with paints containing PMO but the kidneys contained much more mercury than the livers. More mercury was recovered from

[1] Edwin P. Laug and Kenneth W. Nelson: Micromethod for Determination of Mercury - Assoc. of Off. Agri. Chem. J. 25:399-403 (1942)

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kidneys after large single applications of paint than after repeated small applications, with the exception of the Vinyl Masonry paint containing 0.02 per cent PMO. This exception may have been due to ingestion of some of the dried paint since the animals were left unwrapped after the small daily applications. The greatest percentage of applied mercury was retained in the kidneys of rabbits treated with the Light Cream House paint, in which the vehicle is linseed oil, and the least in the kidneys of rabbits treated with the Experimental Emulsion House paint, in which the vehicle is a modified alkyd resin-polyvinyl acetate emulsion.

HUMAN PATCH TEST

"Dulux" Trim and Shutter White (Code No. 87-894, Haskell No. 1699, 0.2 per cent PMO) was selected for evaluating the primary irritation and sensitization potential. Patches were prepared by applying five drops of test paint to the gauze on plastic "Band-Aids" and allowing them to dry thoroughly at room temperature. Control patches of the same paint without PMO were prepared in a similar fashion. The patches of dried paint which covered about 2 square centimeters of skin were applied to the arms or legs of five men and five women. Two of the individuals had no history of exposure to mercury, the other eight had exposure in varying degree; one test subject was known to have become sensitized to "Merthiolate." The patches were removed after twenty-four hours of exposure, and the reactions to the paint observed at 24, 72, and 96 hours.

Two subjects showed no reaction to either paint. Six of the ten subjects showed reactions to both control and test paint at 24 hours. These reactions were considered to be primary irritation. In two of these subjects the reaction to the control paint subsided at the end of 72 hours while the reaction to the test paint persisted for 96 hours; one of these subjects was the person known to be sensitized to "Merthiolate." The other two subjects were irritated by the test paint, but not by the control paint.

These results showed that sufficient mercurial compound could escape from a 2 sq. cm. panel of dry paint to elicit dermatitis. Since this was the case, one must consider that contact with the dry paint can be a potential means of producing primary irritation and of inducing sensitization, since PMO is known to be a skin sensitizer. For this reason it was considered unwise and unnecessary to run a large scale patch test with 200 persons.

SUMMARY AND CONCLUSIONS

Phenylmercury oleate in linseed oil was found to be lethal to male albino rats, when administered orally, at a concentration of 75 mg/kg. Concentrations as low as 15 mg/kg caused residual tubular nephritis. These results showed that PMO in linseed oil was at least as toxic as PMO in the previously tested solvent system of 18 per cent mineral spirits and 80 per cent peanut oil. In the latter case the ALD was 133 mg/kg.

The mercury from paint containing phenylmercury oleate was found to be absorbed through the skin of rabbits and concentrated in the liver and kidneys. The amount of mercury absorbed was apparently a function of the paint vehicle as well as the amount applied, for more mercury was deposited in the kidneys from linseed oil and alkyd resin base paints than from polyvinyl acetate emulsions.

The patch test on ten human subjects indicated that phenylmercury oleate in dry paint penetrated the skin in sufficient quantities to produce contact dermatitis reactions. This suggested that contact with dry paint containing phenylmercury oleate might be a potential means of producing skin sensitization. For this reason it was considered unwise to attempt the usual irritation and allergic sensitization skin test on 200 human subjects where the risk of sensitizing some of them would be great.

The results of these tests have shown that phenylmercury oleate in wet paint can be absorbed through the skin and deposited in the liver and kidneys. Since mercury is eliminated very slowly, long continued exposure to such paint might result in concentrations great enough to produce kidney damage. Sufficient PMO from dry paint can also penetrate the skin of humans to elicit a contact dermatitis reaction.

These tests show that PMO in wet or dry paint is not immobilized by the other ingredients. Persons exposed to either wet or dry paint are, therefore, exposed to PMO with the attendant risk of mercurial dermatitis and of systemic mercury poisoning.

HASKELL LABORATORY FOR TOXICOLOGY
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Table I

ANALYSES OF RABBIT KIDNEY AND LIVER TISSUES FOR MERCURY CONTENT

Haskell No.	Code	Paint	PMO %	Treatment	µg Hg per Gm Wet Tissue Liver	Kidney
1699	87-894	"Dulux" Trim & Shutter	0.2	5 x 1 ml	2.0	21.0
			0.2	1 x 5 ml	1.8	28.3
1700		" " " "	0.0	5 x 1 ml	0.0	0.11
1701	387-301	Vinyl Masonry	0.02	5 x 1 ml	<0.1	1.33
			0.02	1 x 5 ml	<0.1	0.63
1702		" "	0.0	5 x 1 ml	<0.1	0.12
1703	301-920	Light Cream House	0.075	5 x 1 ml	0.65	8.8
			0.075	1 x 5 ml	1.30	25.2
1704		" " "	0.0	5 x 1 ml	0.0	<0.1
1705	389-016	Experimental Emulsion House	0.2	5 x 1 ml	0.60	8.4
			0.2	1 x 5 ml	0.90	12.4
1706		" "	0.0	5 x 1 ml	0.0	<0.1

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