MICA FLAKES

Single Inhalation Exposures

Male CRCD Rats

MR-582 - H-2937, 38, 40, 64 - P-62-156

Necropsy findings were reported on 5-31-61, and attention was directed to minor lung changes whose significance could not be properly assessed because of coexistent pneumonitis in the rat colony, lack of controls, variability of dosage, and temporal disparities of the component studies. Mica being a fibrous mineral also may cause delayed lung injury if retained to a significant degree.

Histologic interpretation did, however, elucidate some differences between the pulmonary responses to the four types of mica (Table 1). Comparison could also be made with the results obtained from a study of coated mica flakes (H-2978) which contained 2 per cent antimony trioxide (Report P-112 of 11-17-61).

In the present group of tests, all reactions which could be attributed to the inhaled substances were limited to the lungs. In this respect, this group of agents differs sharply from that which received the Sb_2O_3-charged pigment. The latter agent, it will be recalled, caused reactions in the brain, liver, spleen and kidneys, as well as in the lungs. A further distinction between the effect of the Sb_2O_3-charged mica flake pigment and the flake pigment of

the present series is furnished by the persistent pulmonary edema, the bronchitis and bronchiolitis seen in the former group but not in the latter.

The differences between the titanium coated, carbon coated and uncoated mica of the present experiment are interesting and perhaps important. The underlying murine pneumonitis was not modified by the four types of inhaled mica. The lack of retention of the calcined titanium coated mica contrasts decisively with the phagocytosis of the carbon coated product. In the former group, there also was a decisive tendency to alveolar mural hyperemia and petechiae, whereas perivascular accumulation of macrophages and plasma cells, and mural catarrh was more noticeable in the latter group. Invasion of the lymphoid system by macrophages was fostered by titanium coating of the mica flakes.

— exposure conc 1/3

COMMENT

Assessment of relative biologic activities of the five mica flake pigments, which is inferable from these studies, is governed by the known fact that mica per se is pathogenic for lung tissue if exposure is continued for protracted periods. It seems permissible to infer, however, that the presence of antimony trioxide in the flake coating has an adverse influence, both because the antimony is absorbed and exerts an effect on other organs and because

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of the persistent pulmonary edema and bronchiolitis.

The calcined titanium dioxide coating is next in order of pathogenicity, especially when cognisance is taken of the fact that the exposure with this type of mica flake was conducted at relatively lower aerosol concentration than those used in the experiments with the other agents.

The granulomatous type of lesion seen in the experiment with the carbon coated mica suggests, however, that this variety of flake mica must also be viewed with suspicion.

It is strongly urged that if prolonged human exposures to these micaceous agents are at all likely, long-term inhalation studies be instituted.

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1-11-62

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TABLE 1 - MR-582
H-2837,38,40,64
P-62-156

MICA FLAKES

Single Inhalation Exposures

Male CRCD Rats

Residual Histopathology

Coating on Mica Flakes	Exposure mg/L	H-No.	Animal No.	LUNGS: Pneumonitis	Mica Flakes: Phagocytosed	Mica Flakes: Unphagocytosed	LUNGS: Pigment	Alveolar Catarrh	Hyperemia (Alveolar)	Petechiae	Focal Emphysema	Perivascular Reaction	Macrophage Infiltration, Lymphoid Medulla	HEART - Hypertrophy Right Ventricle	BRAIN, LIVER, KIDNEYS, SPLEEN, ENDOCRINES, GONADS, STOMACH, DUODENUM, BONE MARROW
Hydrous TiO_2 25%	8.1	2837	45830	+	-	+	-	-	-	+	-	-	+	- +	
			45831	+	-	++	-	-	-	-	++	-	+	-	
			45832	++	-	++	-	-	+	++	+++	-	++	+ -	
			45833	+	-	+	-	-	-	+	-	-	+	-	
Calcined TiO_2 30%	6.6	2838	45838	+	-	-	+	++	++	++	+	-	+	+	
			45839	+	-	-	+	++	+	+	-	-	+	-	
			45844	-	-	-	-	+	+	+	+	+	+	+	
			45845	+	-	-	-	+	++	++	++	+	+	+	
Carbon 2%	23.34	2864	46559	+	++*	+	++	++	-	-	-	+	-	+	
			46569	+	+	+	+	++	-	-	+	+	-	+	
			46584	+	+	+	+	++	-	-	-	+	-	-	
			46586	+	+	+	-	++	-	-	+	+	-	+	
None	24.38	2840	46516	+	+	+	-	++	-	-	-	+	-	-	
			46517	+	-	+	-	+	-	-	+	-	-	-	
			46524	+	+	+	-	+	-	-	++	-	-	+	
			46524	++	-	+	-	+	-	-	-	-	-	+	

--No Abnormality Detected(**)---

* Pigmented granulomatous foci around phagocytosed mica. (**) Attributable to inhaled mica or pigment.
\+ = Slight reaction ++ = Moderate reaction +++ = Extreme reaction.

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COATED MICA FLAKE PIGMENTS

MR-382

Comments:

In both exposures the rate of administration of the material is the highest which can be acheived by the Wright-Dust-Feed Mechanism. The concentrations, in mg. of compound per liter air, to which the rats were exposed, are similar to those found for previous exposures of other mica flake pigments (Report No. 68-61).

Histopathological examination of rats exposed to the Sb_2O_3 coated flakes revealed slight to moderately severe residual pulmonary response. Particles characteristic of mica were found in all the phagocytes, and pulmonary edema, hyperemia, petechial hemorrhages, and focal emphysema were noted. Reactions were also found in the brain and liver. The damage may be due to the antimony in the compound. Less pronounced residual lung reactions were found in rats exposed to mica flakes coated with Cr_2O_3. This produced, in addition, interstitial cellular infiltration and lipophage clusters in the lung. Tissue reactions in brain, pancreas, thymus and adrenal glands were found in rats exposed to this compound. The changes in the brain were more marked than those observed from Sb_2O_3 coated mica. Deposits characteristic of mica were found in the spleen which was otherwise unaffected.

Histopathological studies of mica flake preparations cited in Haskell Laboratory Report No. 68-61 demonstrated lung changes roughly similar to those found with the present samples, but no extra-pulmonary change. The TiO_2 coated flakes (hydrous and calcined) differed from

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all other samples in showing no phagocytised mica flakes in the lung, but the exposures to these flakes were at approximately one-third the concentration of the exposures to the other samples.

Summary:

The tests conducted on the various samples of coated mica flakes indicate a low order of acute inhalation toxicity in that the highest concentrations possible did not cause death to rats. However, all the materials are capable of producing at least lung changes on one exposure. A tentative estimate of ranking order of severity of reaction might be: H-2978, 2979, 2864, 2838 and 2837, in descending order. Mica flakes coated with Sb_2O_3 and Cr_2O_3 caused detectable tissue reaction at other sites. Prolonged exposure of man to significant inhalation of these dusts is contraindicated. Guidance on safe atmospheric levels of mica flakes coated with Sb_2O_3 and Cr_2O_3 may be had from the concentrations in air considered safe for Sb_2O_3 and Cr_2O_3, viz., 0.1 mg/M3 and 0.5 mg/M3 respectively.

JWC:ljm
Jan.26, 1962

DUP050041432