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OBSERVATIONS ON THE ORAL ADMINISTRATION AND TOXICITY OF VINYL CHLORIDE IN RATS*

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Abstract—Various possibilities were studied for administering vinyl chloride monomer (VCM) orally to rats. Upon storage, solutions of VCM in soya-bean oil appeared to be stable with respect to their VCM content and the fatty acid composition of the oil. In addition no oligomers of vinyl chloride or reaction products of VCM with components of the oil were detected. Stomach intubation of such solutions was considered an acceptable method of oral administration of VCM to rats in short-term toxicity studies. Within a period of 4 hr following intragastric intubation of VCM in soya-bean oil (300 mg VCM/kg body weight) over 92% of the VCM administered was recovered from the gases excreted (mainly exhaled) by the animals. Eructation did not appear to be involved in the excretion of VCM.

VCM dissolved in soya-bean oil was administered by gavage to male and female rats at levels of 0 (controls), 30, 100 and 300 mg/kg body weight, once daily on 6 days/wk for a period of 13 wk. Several haematological, biochemical and organ weight values differed to a statistically significant degree from those of the controls, but these differences were considered to have only minor, if any, toxicological significance. A slight increase in liver-to-body weight ratio occurred in males and females on the highest dose level. This increase was not accompanied by liver damage, as was evident from histological examination, enzyme histochemistry and electron microscopy. The no-effect level in this 90-day study was conservatively placed at 30 mg VCM/kg body weight, but was probably higher since the effects occurring at 100 and 300 mg/kg body weight were of doubtful toxicological significance.

Indications were obtained that the feeding of rats on diets containing polyvinyl chloride (PVC) powder with a high VCM content is a more practical method for the long-term oral exposure of rats to VCM than is stomach intubation of VCM in oil. VCM was almost completely released from PVC powder during passage through the digestive tract.

INTRODUCTION

Vinyl chloride monomer (VCM) is used in the manufacture of the resin, polyvinyl chloride (PVC). Industrial exposure to VCM has been associated with several disorders, including acro-osteolysis (Dinman, Cook, Whitehouse, Magnuson & Ditchek, 1971; Harris & Adams, 1967; Lange, Jühe, Stein & Veltman, 1974; Markowitz, McDonald, Fethiere & Kerzner, 1972) and non-malignant liver diseases (Kramer & Mutchler, 1972; Marsteller, Leibach, Müller, Jühe, Lange, Rohmer & Veltman, 1973; Suciu, Dreyman & Valaskai, 1967) and, only recently, also with angiosarcoma of the liver (Block, 1974; Creech & Johnson, 1974; Lee & Harry, 1974) and tumours of the brain and lungs (Monson, Peters & Johnson, 1974). Degenerative changes in the liver, kidneys, bone and brain were detected in rats and rabbits following exposure to VCM inhalation (Baskakov, Vazin & Kochetkov, 1972; Jaeger, Reynolds, Conolly, Mosden, Szabo & Murphy, 1974; Torkelson, Oyen & Rowe, 1961; Viola, 1970). Moreover, VCM inhalation was found to induce tumours in both rats and mice (Maltoni & Lefemine, 1974; Viola, Bigotti & Caputo, 1971).

Certain formulations of PVC are used widely as food-packaging materials. Residual VCM present in the extruded polymeric product was shown to be liable to migration into PVC-packed foods and drinks, especially distilled spirits (Randolph, 1973). Since no data on the oral toxicity of VCM appeared to be available, studies were initiated to examine the subacute toxic properties of this compound when administered orally to rats. Oral administration is greatly hampered by the fact that VCM is a gas at room temperature (b.p. c. −13·8°C) and therefore preliminary experiments were carried out to find an acceptable way of administering the compound orally to rats.

Administration in the drinking-water was considered in this respect but was rejected because of the rather poor solubility of VCM in water (Hardie, 1964) and, more significantly, because of the difficulties to be expected in handling the solutions and in estimating the quantities of VCM actually ingested by the animals.

As VCM is lipophilic, we investigated the possibility of administering VCM as a solution in edible oil either by gastric intubation or by incorporation into the diet. Another possibility studied was the addition to the diet of a PVC powder containing an unusually high concentration of VCM.

The present report describes tentative experiments on the oral administration of VCM and presents some observations on the fate of VCM in rats. In addition, the results are given of a subacute toxicity

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