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# PHARMACODYNAMICS AND UPTAKE OF VINYL CHLORIDE MONOMER ADMINISTERED BY VARIOUS ROUTES TO RATS

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*Finding at least 2–3 ppm and occasionally as much as 10–20 ppm of vinyl chloride monomer in a wide range of foodstuffs has prompted concern for a possible human health hazard. The recognition of vinyl chloride as a carcinogen to humans in April 1974, following the discovery of angiosarcoma as the cause of death in at least 25 workers who had been engaged in the manufacture of polyvinyl chloride, enhanced this concern with respect to the presence of vinyl chloride monomer in foods.*

*To assess the hazard presented by the oral ingestion of vinyl chloride monomer, rats that had been surgically prepared with an indwelling jugular cannula were dosed by intragastric intubation with aqueous solutions containing up to 2.0 mg/ml vinyl chloride. Time–concentration curves were obtained from sequential samples of blood. The uptake of vinyl chloride by this route was found to be extremely rapid; peak concentrations were achieved less than 10 min after administration of the dose. Elimination from the blood compartment appeared to be biexponential.*

*Studies with the same animal model in a single restraint cage that allowed a "head only" exposure to concentrations of vinyl chloride up to 7,000 ppm in the gas phase have shown a similar rapid uptake followed by a plateau blood concentration during several hours of exposure. On removal from the vinyl chloride atmosphere, blood levels fell rapidly to barely detectable concentrations after 2 hr.*

*The precise kinetic coefficients that describe the distribution and elimination rates of vinyl chloride from the blood compartment were also determined from the blood concentration data after the administration of an intravenous dose of aqueous or vegetable oil solution.*

## INTRODUCTION

Prior to the discovery of a connection between the induction of angiosarcoma in humans and the exposure to vinyl chloride monomer (VCM) in January 1974 (Falk et al., 1974; Thomas et al., 1975), the U.S. Food and Drug Administration had already withdrawn their prior sanctioned use of

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It is a pleasure to acknowledge the technical assistance of Mr. Peter Collins in this work. The interest, skill, and dedication of Mr. Henry James, who surgically prepared the animals used in this study, is also appreciated.

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