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SHORT COMMUNICATION

Percutaneous Absorption of Vinyl Chloride

Percutaneous Absorption of Vinyl Chloride. HEFNER, R. E., JR., WATANABE, P. G. AND GEHRING, P. J. (1975). *Toxicol. Appl. Pharmacol.* 34, 529–532. Percutaneous absorption of ^{14}C-labeled vinyl chloride (VC) was examined in male rhesus monkeys. Two monkeys were exposed (whole body, excluding the head) to atmospheres containing 7000 and 800 ppm of VC for 2.0 and 2.5 hr, respectively. The amount of VC absorbed at 7000 and 800 ppm was 0.023 and 0.031 % of the respective total VC available for absorption. The majority of the VC absorbed was eliminated by the lungs.

Vinyl chloride (VC), used widely in the production of polyvinyl chloride and other plastics, has attracted considerable attention recently because it has been associated with the induction of liver disease and neoplasias in industrial workers (Creech and Johnson, 1974; Tabershaw and Cooper, 1974). Because of the potential carcinogenicity of VC, regulations have been enacted to minimize exposures (Anonymous, 1974). These regulations specify certain limitations with respect to the concentration of VC permissible in air to be breathed. However, the question has been posed whether significant quantities of VC may be absorbed through the intact skin. Therefore, the purpose of this study was to elucidate the potential for percutaneous absorption of gaseous VC.

METHODS

Vinyl chloride (99.9 % minimum purity) was purchased from Matheson Gas Products (Joliet, Ill.). For each experiment uniformly labeled [^{14}C]VC was synthesized from 1,2-dichloroethane just prior to use (Wagner and Muelder, 1975).

Male rhesus monkeys (*Macaca mulatta*) weighing 4–5 kg were used. Prior to exposure, 30 mg/kg of sodium pentobarbital was administered iv. An endotracheal catheter with an inflatable collar was inserted into the trachea and connected to a Harvard respiratory pump adjusted to deliver a volume of 20 ml of air at a rate of 28–38 cycles/min. A catheter was placed in the saphenous vein of the leg so that additional sodium pentobarbital could be administered during exposure. The body of the monkey was placed in a 191-liter Plexiglas chamber with the head of the animal protruding outside the chamber through a silastic rubber membrane. To assure an adequate seal around the neck, the hair had been removed with clippers, and the membrane was fitted to the neck and secured to the skin with tape.

To trap VC from the expired air, a polyethylene tube filled with 0.5 g of activated charcoal was placed in the exhaust port of the respiratory pump. A similar tube placed on the intake port of the respirator filtered any VC from the artificially inspired air. The expired air traps were changed at 0.5- or 1-hr intervals while the intake traps were

changed every 2 hr. The VC was eluted from the charcoal with carbon disulfide in a Dry Ice bath (–60°C) and analyzed by gas chromatography (Severs and Skory, 1975).

[^{14}C]VC was metered into the chamber to establish the desired concentration. Chamber concentrations were monitored periodically by recirculating the chamber atmosphere through an infrared spectrophotometer (Miran I, Wilks, 10.9 μm). One monkey was exposed to approximately 7000 ppm of [^{14}C]VC (specific activity, 0.17 μCi/mg) for 2 hr. The other monkey was exposed to approximately 800 ppm of [^{14}C]VC (specific activity, 1.73 μCi/mg) for 2.5 hr. Immediately after exposure the animals were sacrificed by an overdose of pentobarbital.

After exposure, the following tissues were weighed and a sample collected and homogenized in distilled H_2O (50%, w/v): brain, heart, lung, liver, muscle, stomach, duodenum, thymus, spleen, mesenteric fat, testes, and kidney.

Urine was collected from the urinary bladder and bile from the gall bladder. Aliquots of the tissue homogenates were combusted in a biological material oxidizer (Beckman Instruments), and the $^{14}CO_2$ was trapped in a 5 M solution of ethanolamine in 2-methoxyethanol. The resulting solutions, as well as aliquots of urine and bile, were counted in scintillation cocktails in a Nuclear Chicago Mark II liquid scintillation spectrometer. All counts per minute were converted to disintegrations per minute by using an external standard correction for quenching.

RESULTS AND DISCUSSION

Shown in Table 1 are the percentages and total amounts (milligrams) of VC per se found in expired air as detected by gas chromatography or VC equivalents found in

TABLE 1

PERCUTANEOUS ABSORPTION OF [^{14}C]VINYL CHLORIDE EXPRESSED AS A PERCENTAGE OF THE TOTAL AVAILABLE FOR ABSORPTION[a]

Exposure concentration	Duration (hr)	^{14}C activity in tissue (%)	VC in expired air (%)	Total VC equivalents (%)	Equivalents of VC (mg)
7000 ppm (3423 mg of VC)	2.0	0.009[b]	0.014	0.023	0.787
800 ppm (391 mg of VC)	2.5	0.003[c]	0.028	0.031	0.121

[a] The percentages given were calculated by dividing the VC detected in expired air by gas chromatography or the VC equivalents in tissue as determined by ^{14}C activity by the total amount of VC in the chamber. Radioactivity was detected only in those specimens listed.

[b] ^{14}C activity detected in liver, kidney, bile.

[c] ^{14}C activity detected only in the liver.

tissue as determined by ^{14}C activity. To calculate these percentages, the total amount of VC or VC equivalents found in expired air or the indicated tissues, respectively, was divided by the total amount of VC in the chamber. It should be emphasized that the VC equivalents found in tissue represent nonvolatile metabolites of VC, because no

special precautions were made to trap volatile VC from the tissues during preparation for analyses. Past work in this laboratory indicates that VC is metabolized to polar metabolites (Hefner *et al.*, 1975). ^{14}C activity was detected only in the liver, bile and kidney (Table 1). The other tissues examined did not have appreciable counts above background.

The loss of VC from the chamber was determined by recirculating the chamber atmosphere through an infrared spectrophotometer. About 5% of the VC was lost during the experiment. Similar losses from the chamber were noted when equivalent concentrations of VC were maintained in an empty chamber over 2-hr periods. Therefore, the loss was due to leakage rather than to unaccounted for absorption.

Under the conditions of these abbreviated experiments, very little gaseous VC was absorbed through the skin of the monkeys. The proportion of VC absorbed by monkeys exposed to 7000 and 800 ppm was essentially the same when corrected for the duration of exposure. This indicates that, as expected, the amount of VC gas absorbed via the skin is concentration dependent even though it is miniscule in quantity. Since most of the VC absorbed via the skin was expired, analysis of expired air appears to be a meaningful index of exposure.

It is difficult to assess how hair, clothing, and other factors such as skin composition may influence the absorption of VC gas. Whether these factors may contribute to significant species differences is also unknown. However, ignoring these variables and assuming that absorption is related directly to surface area, it may be calculated[1] from the present results that a 6-ft, 90-kg man would absorb 4.75 mg of VC if exposed to 7000 ppm for 2 hr.

Absorption of this amount of VC would be equivalent to being exposed to 0.2 ppm via inhalation for 8 hr assuming that the total amount of air inhaled would be 10 m^3 and that all of the VC inhaled would be absorbed. Many assumptions have been used in making these calculations. However, it seems reasonable to conclude that significant amounts of VC are not absorbed into the body after short-term exposures of the skin to high concentrations of gaseous VC. Furthermore, based on these results, significant percutaneous absorption would not be expected to occur upon exposure to low concentrations of 1 or 5 ppm of VC as encountered in a working environment.

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[1] Monkey: surface area (S, in cm^2) of a 5-kg monkey was calculated according to the following equation (Altman and Dittmer, 1964): $S = 11.8 \times 5000^{2/3}$; $S = 3450\ cm^2 = 0.345\ m^2$. Man: surface area of a 180-cm, 90-kg man is 2.08 m^2 (Altman and Dittmer, 1965). (2.08/0.345) × 0.787 mg equiv of VC = 4.75 mg of VC.

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