METABOLISM OF VINYL CHLORIDE MONOMER IN THE LIVER OF RATS

J. M. WIŚNIEWSKA-KNYPL, S. TARKOWSKI and W. DRAMIŃSKI
Institute of Occupational Medicine, Łódź, Poland

Vinyl chloride monomer (VCM) undergoes biotransformation in the liver via oxidation by microsomal enzymes and/or conjugation with non-protein thiols catalysed by sulfotransferases (cf. Hefner et al., 1975; Green and Hathway, 1977).

In this experiment the following aspects of VCM metabolism have been assessed: (1) conjugation – on the basis of a decrease of -SH groups level in the liver and excretion of thiodiglycollic acid (TDGA) in the urine; (2) microsomes--mediated oxidation – on the basis of efficiency of the reaction of conjugation in phenobarbital and cobaltous chloride-pretreated rats.

Male Wistar rats were exposed by inhalation in dynamic chambers to VCM at concentrations of 50, 500 and 20,000 ppm 5 hours daily, for different periods of time.

It has been found within an hour after the end of exposure a marked decrease (by 19 and 54%) of -SH group content in the liver in rats exposed to 500 and 20,000 ppm of VCM, respectively. The level of the -SH group within 5–7 hours progressively recovered, reaching significantly higher values after 19 hours, than in the concurrent control.

Excretion of TDGA in the urine was dependent on the concentration of VCM but not on the duration of exposure.

Induction of synthesis of cytochrome P-450 in the liver of rats prior to the exposure to VCM resulted in much more pronounced decrease of -SH groups level in the liver immediately after exposure and increase of excretion of TDGA with urine. None of the decrease of the -SH group's content and deeply decreased level of TDGA were found in analysed materials from rats pretreated with the inhibitor of synthesis of cytochrome P-450.

It may be concluded that VCM first undergoes oxidation by cytochrome P-450 and only metabolites are conjugated.

REFERENCES

Hefner, R. J., Jr., Watanabe, P. G. and Gehring, P. J., (1975). *Ann. N. Y. Acad. Sci.*, 246, 135.
Green, T., and Hathway, D. E. (1977). *Chem. Biol. Interact.* 17, 137.