Determination of Thiodiglycolic Acid in Urine Specimens of Vinyl Chloride Exposed Workers

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Summary. A strong correlation was found between vinyl chloride concentrations at working places and the increased excretion of thiodiglycolic acid of 18 exposed workers. The mean air concentration of vinyl chloride was calculated referring to personal exposure. The values obtained were in the range of 0.14 – 7.0 ppm. The excretion of thiodiglycolic acid – measured by GC-MS analysis – amounted to 0.3 – 4.0 mg/L. It could be demonstrated that significant increases of the metabolite excretion occur even at VC-concentrations below 5 ppm.

Key words: Vinyl chloride – Thiodiglycolic acid – vinyl chloride metabolism in man – Vinyl chloride urine metabolites – Biological exposure control

Today the air concentrations of vinyl chloride at working places are rigorously reduced mainly due to its carcinogenic [5, 14, 16, 19, 20–23, 34] and mutagenic [6, 8, 9, 14, 15, 18, 19, 30] properties. Exposure controls are commonly based on air analyses by means of highly sensitive, but not always strongly specific analytical methods.

Therefore, we emphasized the usefulness of additional biological exposure controls [24, 26].

By animal experiments we could demonstrate the possibility of determining the excretion of thiodiglycolic acid and S-carboxy-methylcysteine, two urine metabolites of vinyl chloride [10, 24, 26, 27, 35]. Data of thiodiglycolic acid in the urine of workers slightly exposed to vinyl chloride and the improved analytical method used for determination are reported here.

Materials and Methods

Chemicals

Thiodiglycolic acid (98 % purity) was purchased from Janssen Pharmaceutica, Dept. Aldrich Europe, B-2340 Beerse, Belgium. Diazomethane was generated from N-methyl-N-nitroso-p-toluene-sulfonamide according to de Boer and Backer [3]. All other substances were purchased at analytical grade from E. Merck AG, D-6100 Darmstadt.
Procedures

Determinations of Individual Exposure by Personal Air Sampling

Sampling

Sampling Tube. Traces of organic pollutants (among which vinyl chloride) in the factory air were collected by glass tube samplers with a length of 12 cm and an internal diameter of 3 mm, filled with 35-50 mesh charcoal [7]. These charcoal tubes had a breakthrough volume, for vinyl chloride at 20°C, of about 5 liters [33].

Pump. To draw the air through the tube samplers we used a small pump named personal sampler manufactured by Anatole J. Sipin Co. The sampled air volume can be calculated from the number of pistonplays of the pump, registered by a built in counter.

As the amount of charcoal and the density of packing varied from sampling tube to sampling tube, we had to calibrate the pump before each experiment. The relationship between pistonplays and normal gas volume was easily measured with a gasbubble meter and a stopwatch.

Analysis

Analytical Conditions. A special injection port that allows for direct introduction of the total sample, cartridge included, was used for the thermal desorption of the trapped vinyl chloride [1, 29]. The vaporized vinyl chloride was routed to a gaschromatographic column. To separate the vinyl chloride from other sampled organic vapor pollutants we used a 25 m wall coated carbowax 20 M capillary at 80°C. The detector used was, of course, a flame ionization detector.

The surface of the vinyl chloride peak was measured by an integrating computer.

Calibration. A calibration gas was dynamically prepared by passing a known gasstream over a teflon permeation tube filled with liquid vinyl chloride [28, 31]. The concentration of vinyl chloride was calculated by the loss of weight of the permeation tube over several days. A known volume of this gas was drawn through a charcoal tube and this tube was analyzed as described above. The gaschromatographic results were reported as the amount of µg absorbed by the charcoal tube sampler.

Evaluation of the Personal Exposure Data. The mean concentration of vinyl chloride in the air during the experiment was calculated from the amount of absorbed vinyl chloride analyzed by gaschromatography and from the sampled air volume calculated from the number of pistonplays of the pump during sampling.

VC-Determination in the Air of Working Places. The measurements were performed using multipoint flame ionisation detectors (FID), type RADFISH, spread in the working area. Total hydrocarbons in the air of each sampling point were analyzed once a minute. It has been shown by GC-measurements that approximately 2 ppm of the total hydrocarbons in this working area are not VCM. Considering this amount of 2 ppm not - VCM - hydrocarbons the true air concentration of vinyl chloride monomer was calculated. The personal exposure of each worker was evaluated. Thus, from registrations based on the duration of stay at different working places, all values of VCM air concentrations given in this paper, which are not obtained by personal air sampling, refer also to personal exposure.

Determination of Thiodiglycolic Acid by GC-MS-Analysis. In a 10 ml glass tube 1 ml of urine and 0.3 ml of conc. HCl were evaporated to dryness in vacuo at room temperature. The residue was suspended in methanol and the suspension was completely methylated by means of diazomethane in ethyl ether [3]. After 15 minutes 500 mg dry cation exchange resign (Dowex 50 WX 8; H⁺) were added. Thiodiglycolic acid dimethyl ester was determined by gaschromatographic separation and single ion detection of the mass fragment M 146. It is necessary to use the standard addition technique to obtain exact measurements.