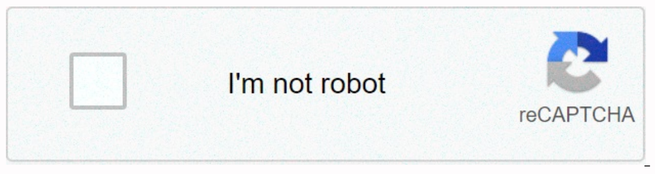

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Ethyl chloroformate hydrolysis

Groups of five males and five female Charles River albino rats were exposed to methyl chloroformate fumes for 1 h at 0, 145, 173, 233 or 274 ppm (nominal concentrations) followed by a 14-day observation period (IBT 1975). The vapor was created by a bubble of pure, dry air through an unreached methyl chloroformate in a gas-mre bottle. An air vapour mixture was then introduced into the exposure chamber. The 1-h LC50 was set at 163 ppm and the calculated BMCL05 was 74 ppm. Rats are more sensitive than females. Hypoactivity, ptosis, taut fur, enophthaalamus and dyspnoea were observed during exposure in all rats. Evidence of acute bronchiolitis, followed by pulmonary parenhima fibrosis, was observed in animals killed on 14 March 2015. Data from this study are summarised in Table 2-7.In in the second study, the Sprague Dawley 10 rat group was exposed to methylchloroformate at 735, 2947, 9610 or 66,235 ppm (nominal concentrations) for 1 h (Warf Institute, Inc. 1972). A semi-portable exposure chamber containing an exhaust fan for adjustable air flow has been used. Methyl chloroformate was given into the in-doted airflow before entering the chamber port and the exposure concentrations were calculated by dividing the total quantity dispersed into the chamber by the total cubic legs of the air circulating through the chamber. All animals died within 18 hours of exposure (see Table 2-8). Groups of five males and five females Fischer 344 rats (main group) were exposed to methylchloroformate vapour at 0, 26, 110, 133, 159 or 192 ppm for 1 h in a 3-ft wide chamber of Hinner style (Fisher et al. 1981a). Chamber concentrations were accompanied by infrared photospectrometry of variable length in real time. In addition, 10, 10 and 20 rats/sexes (satellite rats) were co-exposed to methyl chloroformate at 26, 110 or 133 ppm. One male and one satellite rat in each exposure group and two females and two rats in three groups with lower exposure were killed 4 h, 24 h, 9 days or 10 days after exposure. All other surviving animals were killed 14 days after exposure. LC50 values were 100 ppm for females and 92-123 ppm for males at 14 days after exposure. Respiratory distress occurred in all rats of the main group exposed at 110, 133, 159 and 192 ppm during the first 24 h after exposure. Respiratory distress was resolved within 24 h in the 110 ppm group; however, the effect lasted for day 14 in other exposure groups and was accompanied by lethargy, weakness and inactivity. In rats exposed to 110, 133, 159 and 192 ppm, concentration-related red or clear eyes and nasal discharge and gross pulmonary lesions were observed. The controls and rats in the 26 ppm group were clinically normal. The rats in the satellite group responded similarly to the corresponding rats in the main group. In the main group weight and weight gain 110-, 133-, 159-, and 192-ppm rats and associated with poor clinical condition before death or termination of the study. No effect on body weight was observed in rats exposed to 26 ppm. The injuries found in satellite rats exposed at 110 and 133 ppm were comparable at all three times of sacrifice and included severe degeneration, necrosis, erosion and nasal turbinate ulcer and trachea epithelial epithelial; alveolar haemorrhage; and erosion of the bronchial and bronchiolar epithelials. The effects were similar. On day 9 or 10, the effects of the nasal turbine were eliminated, but the regeneration was incomplete and purulent rhinitis persisted. Other respiratory and pulmonary lesions seen at 4 and 24 hours resolved after 9 or 10 days. Pulmonary edema was observed in the 110-, 133-, 159-, and 192-ppm groups. Pulmonary oedema was not observed in the controls or in the 26 ppm group. Vernot et al. (1977) reported 1-h LC50 of 88 ppm (64-123 ppm) for men and 103 ppm (90-118 ppm) for Sprague-Dawley rats. The experiments were carried out in bottles using groups of five rats per concentration; concentrations have been analytically determined. No further experimental details were available. Groups of five males and five female SPF Wistar rats were exposed to methyl chloroformate for 4 h at 35, 45, 57 or 73 ppm (analytical concentrations) followed by a 14-day observation period (Hollander et al. 1986). All-body exposure was performed in an exposure chamber of 2,25 m3 operating under dynamic flow conditions. The concentrations of methyl chloroformate were measured every 15 minutes during exposure using a single beam photometer and analytically measured every 120 min using gas chromatography. Clinical signs observed in all concentration-related treatment groups included a constipated or closed palpebral fissure; increased care; the holding for the ation; accelerated, irregular and jerky breathing; the daming; sleepiness; sealed movements; sounds for fading and squeam; sneezing; and piloerektion. Weight gain was reduced in both sexes after exposure, but animals that survived the study study regained their initial body weight. There were no severe treatment-related effects in non-cropsy in animals that survived the study. A rough search of the animals that died during the study revealed dark red to black lungs, foam fluid in the lungs, red water fluid in the thoracic cavity and distinctive gastrointestinal tracts. Histopathological examination showed increased alveolar septa and adequate damage to the bronchial epithelium; this effect was observed in all treatment groups. Four-hour LC50 values of 51 ppm and 53 ppm respectively were calculated for males and females. The combined male and female BMCL05 were calculated with 42.4 ppm and combined male and female BMC01 with 47.8 ppm. Mortality data are summarised in 2-9.Groups of 10 males and 10 female Sprague-Dawley rats were exposed to methyl chloroformate at nominal nominal 16, 65, 96 or 127 ppm (analytical concentrations were 1.5, 13,7, 33.6 and 31.0 ppm respectively) for 4 h, followed by a 14-day observation period (BASF 1980a). Exposure to the whole body was performed in a glass inhalation chamber 200 L. Analytical concentrations were measured by gas chromatography. Clinical signs in the 65-96-, i 127-ppm group of su included dyspnoea, stinging, blistering in front of the nose, red and nasal roasting i encrustations, tense and stump fur, tightening, dytenten, abdomen general condition, attempts to escape, collapsed coordination, salivation, i štip striving. Animals in the 16-ppm group exhibited jerky breathing and eyelid closure. Weight gain initially decreased in the three highest concentration groups; this effect was resolved in surviving animals 14. A combined male and female LC50 value of 15 ppm was also calculated. Data from this study are summarised in Table 2-10. The LC50 values calculated from this study are 3-4 times lower than those found in the Hoechst study (Hollander et al. 1986) and are not in line with other data (see Table 2-12). Death occurred in 12/12 rats exposed to methyl chloroformate vapour (20 °C) at 37,500 pp/min (BASF 1981a). Clinical signs included severe escape behaviour, severe mucosal irritation and sathyroid disease. Pulmonary emphysema from petehial haemorrhage and drug treatment on the right side of the heart were observed in necropsy. Death occurred in 11/12, 5/6 and 6/6 rats exposed to the atmosphere enriched or saturated with methyl chloroformate vapours (20 °C) for 3, 10 and 30 min (BASF 1978, respectively). Clinical signs included severe escape behaviour, severe mucosal irritation, corneal opacity, dyspnoea and convulsions. Pulmonary edema and emphysema and bilateral heart dilation were found in necropsy. Death occurred in 10/10 rats exposed to the atmosphere enriched or saturated with methyl chloroformate vapours (20 °C) for 3 min (Hollander and Weigand 1985). Clinical signs included breathing, extreme excitement and severe corneal opacity. Pleural hemorrhaging was found in necropsy. The following oral LD50 values for methyl chloroformate have been reported: 190 mg/kg for male Sprague-Dawley rats (Vernot et al. 1977); 110 mg/kg for female Sprague-Dawley rats (Vernot et al. 1977); 313 mg/kg for male and female Sprague-Dawley rats (BASF 1981b); and 220 mg/kg (Warf Institute Inc. 1972). Dermal LD50 LD50 at 894 mg/kg was reported in Sprague-Dawley rats (BASF 1981c). In the second study, dermal LD50 was reported to be more than 2 ml/kg for male rats (Warf Institute, Inc. 1972). A four-week multiple exposure study (BASF 1993) described fatal and non-annual effects in rats (see section 2.3.2 [Multiple exposure]) for details of the study). After a 10-minute period of fresh air control, groups of four men mice were exposed only to methyl chloroformate aerosol at nominal concentrations of 0, 16,5, 25, 35, 50, 75 or 125 ppm for 30 min (Carpenter 1982a). The mice were then removed and exposed to fresh air for a 10-minute recovery period, and respiratory rates were continuously monitored during the exposure and recovery period. The unmained methyl chloroformate was delivered to the Pitt aerosol generator No. 1 via a 2-cc syringe driven by a pump at a known speed. The aerosol was directed at the 9-L stainless steel chamber, which was continuously evacuated at a rate of 20 L/min. RD50 (concentration that reduced respiratory rate by 50%) 52.4 ppm. The results of this study are summarised in Table 2-11.Gurova et al. (1977) reported 2-h LC50 of 47 ppm for mice. No other experimental details were available. Available.