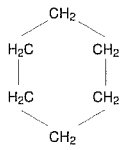
Recommendation of the Scientific Committee on Occupational Exposure Limits for Cyclohexane

Eight-hour TWA: 200 ppm (700 mg/m³)
STEL (15 minutes):
Additional classification: —

Substance identification

Cyclohexane



Synonyms: Hexahydrobenzene, hexamethylene
Einecs No: 203-806-2
EEC No: 601-017-00-1
Classification: F; R11
CAS No: 110-82-7
MWt: 84.18
Conversion factor (20 °C, 101 kPa): 3.50 mg/m³ = 1 ppm

Occurrence/use

Cyclohexane is a colourless liquid with a melting point of 6.5 °C and a boiling point of 80.7 °C. It is highly flammable and has a pungent odour similar to that of petrol, with an odour threshold of approximately 50 ppm (175 mg/m³). The vapour pressure is 12.7 kPa at 20 °C.

Cyclohexane occurs naturally in all crude oils in concentrations of 0.1–1.0 %. It is manufactured in closed system by hydrogenation of benzene. Current EU capacity for cyclohexane production is 835 000–925 000 tonnes per annum. The majority of cyclohexane is used for production of nylon, with lesser amounts used as a solvent and as a chemical intermediate. Occupational exposure to cyclohexane is in combination with other solvents. A mixture of solvents including n-hexane and cyclohexane, known as 'commercial hexane', is widely used as a solvent in shoe factories. Exposure levels of up to 360 ppm (1 260 mg/m³) have been measured. Analysis is by gas chromatography or Drager tube and it should be noted that other solvents may interfere.

Health significance

Data on the effects of pure cyclohexane are limited. Studies on 'commercial hexane' are not adequate for setting an OEL for cyclohexane, as the observed effects may be due to n-hexane.

Cyclohexane is well absorbed in animals and humans by the lungs and readily exhaled in breath of all species studied. Metabolism involves mostly hydroxylated derivatives which are excreted after glucuronide conjugation in the urine. Urinary metabolites include cyclohexanol and cyclohexanone (ACGIH 1997).

A recent study in volunteers after eight-hour periods of inhalation exposure at a concentration of 1 010 mg/m³ (290 ppm) showed that 1.2 and 1.4 cyclohexandiol were the major metabolites, accounting for 23.4 % and 11.3 % respectively for the dose (Mraz et al. 1998).

Cyclohexane is of low acute toxicity by oral, inhalation or dermal routes. A short-term inhalation (one hour) concentration in rabbits of 29 190 ppm was lethal to all of the animals; for mice, the lowest lethal concentration exceeded 17 460 ppm (two-hour exposure). The oral LD_{50} was found to be 6 200 to 30 000 mg/kg body for the rat (DECOS 1990).

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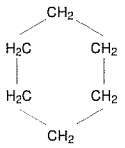

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tological alterations in the sexual organs were seen after four months' exposure to a cyclohexanone concentration of 1 000 ppm. At this concentration the rats were exposed to cyclohexanol concentrations of at least 120–180 mg/kg bw (Greim 1996). It is probable that application by bolus or i.p. produces peak concentrations that cannot be achieved in the case of inhalation, and that consequently no spermatotoxic effects were seen after inhalation.

In humans, an experimental study has been reported in which 12 healthy male volunteers were exposed using a double blind, two-way cross-over design to 250 ppm for four hours. As a control condition an exposure of the same subjects to 25 ppm was established. The two test conditions were spaced seven days apart. Cognitive functioning was assessed using selected tests from the neurobehavioural evaluation system (NES). In addition a computer-administered questionnaire designed to assess changes in mood and effect was also included. Measurements were normally carried out before, during (twice) and following exposure. There were no significant effects of inhalatory exposure to 250 ppm cyclohexane on any of the 20 variables measured. An analysis of self-reported symptoms showed that 7 out of 12 volunteers reported headache at 250 ppm cyclohexane, compared with one person out of 12 at 25 ppm (Hoogendiik and Emmen 1998). It cannot be ruled out that the persons that reported having headache may have felt slightly unwell. But this finding cannot be regarded as a consistent and significant adverse effect.

Exposure to cyclohexane (geometric mean 27 ppm and highest concentration 274 ppm; reference period was not given, but supposedly it is an eight-hour TWA) did not induce in the exposed workers any significant rise in the prevalence of subjective symptoms or in haematological and serum biochemical parameters of liver and kidney functions (Yasugi et al. 1994).

A study on 18 workers exposed to a glue containing 75.6 % cyclohexane, 12 % toluene and 0.9 % n-hexane showed that concentrations of airborne cyclohexane ranging from 5 to 211 ppm (reference period was not given but presumably it is an eight-hour TWA) did not have any adverse effects on the peripheral nervous system. No differences were found in nerve conduction velocities between workers exposed to cyclohexane and age and sex matched controls (Yuasa et al. 1996).

Recommendation

The data on behavioural effects of cyclohexane in human volunteers suggest that headache can occur at 250 ppm. Exposure of four hours to 250 ppm cyclohexane caused headache complaints in 7 out of the 12 exposed volunteers. This finding, however, is not regarded as a consistent and significant adverse effect; in fact on the same volunteers no significant effect of exposure was found on cognitive performance (Hoogendijk and Emmen 1998). In addition animal data established a NOAEL of 500 ppm and a LOAEL of 2 000 ppm for narcotic effects in rats and mice (Malley et al. in press). The human data suggest that the NOAEL is about 250 ppm; taking this into account a recommended eight-hour TWA of 200 ppm can be established.

At the level recommended, no measurement difficulties are foreseen.

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