Dimethylformamide

CAS: 68-12-2
MF: $HCON(CH_3)_2$
FW: 73.1
Solvent for many hydrophobic organic compounds.

Major uses

N,N-dimethylformamide (DMF) is widely used as an organic solvent in the chemical industry and in laboratories. It is also used in chemical industry for the production of synthetic fibers, synthetic leather, polyuretans and resins, as well as in many other chemical processes [1].

Human toxicity

Acute toxicity of DMF is reported as moderate. It is a hepatotoxin and can cause liver injury.
Acute toxic effects: DMF is mildly irritating to the eyes; gastrointestinal toxicity includes anorexia, vomiting and abdominal pain; skin irritation (contact dermatitis); hypertension (high blood pressure).

Chronic toxic effects: anemia, leucopenia, thrombocytopenia; CNS disorders (e.g. sleep disorders, dizziness); hepatic and kidney damage; testicular cancer; miscarriages in workers in synthetic fiber industry.

Workers can be exposed in industry by inhalation or by skin contact; there are also few cases of the intentional poisoning by DMF. The current threshold limit value for occupational exposure to DMF is 10 ppm (30 mg/m^3) [2].

Maximal blood concentration levels of about 14 mg/l and 8 mg/l were observed for DMF and N-methylformamide, respectively, at 0 and 3 h after a 4 h exposure to 87 ppm of the vapor [2].

Carcinogenicity: According to IARC rating, DMF is "possibly carcinogenic to humans" and it belongs to Group 2B [3].

Kinetic data

Absorption: DMF is well absorbed following inhalation of the vapor, as well as via dermal or oral exposure. The primary target organ following acute or chronic exposure is the liver in both humans and animals. About 15 % of a dose absorbed by the inhalation of DMF was found in urine as AMCC [4]

Elimination half-life of DMF in blood is between 2 and 6 h [2].

Metabolism and excretion

DMF is metabolized in humans by sequential N-demethylation to N-methylformamide and formamide, both of which may undergo conjugation with glutathione [2]. Another metabolite of DMF, found in urine, is N-acetyl-S-(N-methylcarboyl)cysteine (AMCC). Metabolites of DMF are produced in the liver via enzymatic oxidation, in which cytochrome P-450 plays a central role (reviewed in [6]).

Excretion: DMF is mainly excreted in the urine. Metabolites N-methylformamide and formamide were found in urine within 24 h [1]. N-methylformamide is eliminated rapidly via kidney [5].

Toxicological mechanisms

No exact mechanism of toxicity has been determined, but Whitby et al. have found that metabolite of DMF, N-methylformamide, decreases the ability of the liver mitochondria to sequester calcium ions (experiments in rat). The authors proposed that the metabolite affecting the mitochondria calcium pump may be at least part of the toxic mechanism leading to hepatic necrosis [7].

Target organ: liver [7].

References

1. Poisindex, Thomson Micromedex (2005).
2. Baselt, R.C. & Cravey, R.H. (1995) *Disposition of Toxic Drugs and Chemicals in Man*, 4th edn., pp. 254-256. Chemical Toxicology Institute, Foster City, CA, USA.
3. ACGIH: 2004 Threshold Limit Values (TLVs(R)) for Chemical Substances and Physical Agents and Biological Exposure Indices (BEIs(R)), American Conference of Governmental Industrial Hygienists, Cincinnati, OH, 2004.
4. Mraz, J., Cross, H., Gescher, A., Threadgill, M.D., Flek, J. (1989) Differences between rodents and humans in the metabolic toxication of N,N-dimethylformamide. Toxicol Appl Pharmacol 98, 507-516.
5. Kimmerle, G., Eben, A. (1975) Metabolism studies of N,N-dimethylformamide. Int Arch Arbeitsmed 34, 12136.
6. Koh, S.B., Cha, B.S., Park, J.K., Chang, S.H., Chang, S.J. (2002) The metabolism and liver toxicity of N,N-dimethylformamide in the isolated perfused rat liver. Yonsei Med J 43(4), 491-499.
7. Whitby H, Gescher A, Levy L (1984) An investigation of the mechanisms of hepatotoxicity of the antitumor agent N-methylformamide in the rat. Drug Metab Dispos 14:746-749.

Written by Ada Kolman, March 2005; revised March 2007
ada.kolman@telia.com