

Common Solvent Toxicity: Autoxidation of Respiratory Redox-Cyclers Enforced by Membrane Derangement

Thomas R. Garbe and Hideaki Yukawa*

Research Institute of Innovative Technology for the Earth (RITE), 9-2, Kizugawadai, Kizu-cho, Soraku-gun, Kyoto, 619-0292 Japan.

Fax: +81 774 75 2321. E-mail address: yukawa@rite.or.jp

* Author for correspondence and reprint requests

Z. Naturforsch. **56c**, 483-491 (2001); received February 13/March 16, 2001

Respiration, Lipophilicity, Prooxidants

Unspecific biological effects of chemically diverse solvents strikingly reveal the unifying motif of oxidant toxicity both in higher organisms and in aerobic bacteria. In a few spectacular cases, solvent metabolites with oxidant properties were demonstrated, which however cannot explain extrahepatic toxicity, e.g. in muscle and nerve cells. A common source of solvent-inducible oxidants, by contrast, is suggested to be located in mitochondria or, more general, in membranes where the respiratory chain operates. Orderly respiration depends on membrane integrity, which is invariably compromised by exposure to most solvents and many other lipophils. In rat mitochondria, toluene-induced membrane derangement has been directly implicated with superoxide production, resulting from autoxidation of the membrane-located respiratory redox-cycler ubiquinone. A related mechanism may occur in bacteria: Exposure of *Escherichia coli* to lipophils such as ethanol, tetralin, indole, chlorpromazine and procaine, or to heat shock, induces anti-oxidant proteins, which are reliable indicators of increased oxidant levels. Although many molecular details remain to be elucidated, this review documents that oxidant toxicity of lipophilic compounds is a common physiological phenomenon correlated with derangement of membranes where respiratory processes take place. Subjective consequences of acute oxidant injury are probably the hangover from alcohol and nicotine consumption, and the sudden death from recreational solvent abuse. Suggestions concerning oxidants as major contributors to ageing remain unchallenged.