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Title:

Toxicity of Chemicals Involved in the European Project A-Cute-Tox on the Myeloid Hematopoietic Progenitors

Abstract: (Your abstract must use 10 pt Arial font and must not exceed 250 words)

The European Integrated Project A-Cute-Tox (LSHB-CT-2004-512051) was started up in January 2005. As a partner, our group is responsible for the characterization of the effect of xenobiotics on the hematopoietic tissue. Hematopoietic system displays a wide spectrum of cell populations whose constant proliferation and differentiation give rise to the different lineages of blood cells. Toxicants can cause hematotoxicity by interfering with mature blood cells, committed progenitors or stem cells functions or survival. Neutropenia is an effect which could appear after a cytotoxic insult. CFU-GM assays based on the culture of human mononuclear cord blood cells have been used to characterize the effects of the selected compounds on the myeloid progenitors. Recently, this assay has been approved by ECVAM's Scientific Advisory Committee. The compounds included in the study were Acetaminophen, Acetylsalicylic acid, Atropine sulfate, Caffeina, Carbamazepine, Colchicine, Cycloheximide, Digoxin, Isopropyl alcohol, Malathion, Mercury II chloride, Pentachlorophenol, Phenobarbital, Sodium lauryl sulfate and Sodium valproate. As controls of toxicity on Inmune and Hematopoietic Systems studied in WP4, 5-Fluorouracil, Benzene, Tert-butyl hydroperoxide, Acrolein and Cadmium II chloride pentahydrate were also included. The survival curves of CFU-GMs exposed to different doses of the compounds were obtained and IC values were calculated. CFU-GMs IC_{50} values and acute mouse oral LD50 values from the Registry of Cytotoxicity (RC) were fitted to a linear regression model. The regression equation was: $\log(LD_{50})=0.2724 \times \log(IC_{50})+0.8362$ with a correlation coefficient of 0.61. Outliers in RC regression analysis and chemicals that were not studied previously have been already included into the new regression equation.

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