

Dose Response Relationships Between Furan Induced Cytotoxicity and Liver Cancer.

T. L. Goldsworthy, R. Goodwin, M. Burnett, P. King, H. El-Sourady, G. Moser, J. Foley, and R. R. Maronpot. Integrated Laboratory Systems, Inc., Research Triangle Park, NC, and NIEHS, Research Triangle Park, NC.

Furan is hepatocarcinogenic and hepatotoxic, and thus is considered a model agent for studying the dose response characteristics and mechanisms of action of cytotoxic carcinogens. In mice, furan, at doses levels >4.0 mg/kg, has been shown to increase cell replication. The current study tested the hypothesis that furan-induced hepatic cancer only occurs at doses that produce cytotoxicity and compensatory cell growth. Furan was administered in corn oil to female B6C3F1 mice (n=50-100/group) 5 days per week for 2 years at doses of 0, 0.5, 1.0, 2.0, 4.0, or 8.0 mg/kg. Survival was somewhat decreased in the 8.0 mg/kg furan-exposed mice, but otherwise did not appear to be dose-dependent. Mean relative liver weights (% body weight) at terminal sacrifice were significantly greater in the 4.0 and 8.0 mg/kg furan-exposed mice than in mice at lower doses. Necropsy and microscopic evaluations demonstrated an increase hepatic tumor incidence and multiplicity, as well as decreased tumor latency in the 4.0 and 8.0 mg/kg furan-exposed mice but not in mice at lower doses. These two high dose groups also exhibited an increase in hepatic parenchymal inflammation/degeneration upon histopathology evaluation. This study provides new experimental evidence for the demonstration of the relationship between dose, cytotoxicity, and tumor induction for a model cytotoxic hepatocarcinogen. (This work was sponsored by NIEHS [N01-ES-95434].)

Presented at Society of Toxicologic Pathology (STP) 2001 Annual Conference, Orlando, Florida