

tion. The mortality rate for each of the three B dose groups was 8.3% with contributing factors being hypothermia, ataxia, prolonged QT intervals, and partially inverted T waves. These results suggest that both B and S may have adverse physiological effects and that B may have more significant effects on blood pressure than an equivalent dose of S.

1444 D-RIBOSE HAS NON-SIGNIFICANT TOXICITY IN BOTH SHORT AND LONG TERM SUPPLEMENTATION.

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D-Ribose (DR), a pentose carbohydrate, has repeatedly demonstrated its beneficial properties in replenishing cellular high energy phosphate compounds with an accompanying functional improvement following ischemic or hypoxic stressful situations without obvious significant toxicity. Food ingredients and dietary supplements (including DR) must clearly show safety-in-use. To that end, DR has been tested for toxicity in both animal and human investigations. Adult female rodent experiments analyzing both embryotoxicity and teratogenicity revealed no effects at an oral DR dose at 5% of the diet (a daily dose of ~4 gms/kg body weight/day). Findings revealed no developmental defects in the fetus, including visceral malformations or anomalies. When adult male and female rodents were fed 5% DR in the diet for 13 weeks (3.6 and 4.4 gms/kg body weight/day) in a standardized OECD Guideline 408 protocol, no abnormal measured hematological or biochemical parameters were found. Human studies have also reflected similar findings. In an acute evaluation, using escalating single oral doses of DR (0, 2, 5, 10 gms/dose) in young and older adult humans, there were no significant biochemical or purine abnormalities except for mild asymptomatic, hypoglycemia and a slight elevation in uric acid concentrations. When providing DR (20 gm/dose) for 14 days to healthy adult subjects, similar findings were also observed. There were no long-term significant changes in hematological or biochemical parameters; however, an acute elevation in uric acid and aspartate aminotransferase levels occurred at day 7 with normalization to baseline in both measurements by day 14. A clinically, asymptomatic hypoglycemia was found throughout the 14 day trial. The data from these investigations give further support for the safety of DR in both an acute and chronic setting.

1445 GENETIC TOXICOLOGY ASSESSMENT OF A NOVEL OXYGEN-COORDINATED NIACIN-BOUND CHROMIUM(III) (NBC) COMPLEX.

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Chromium (III) is a novel micronutrient essential for normal protein, fat and carbohydrate metabolism. NBC is a unique form of bioavailable chromium. We have previously assessed the acute oral toxicity, acute dermal toxicity, primary dermal and eye irritation, Ames' bacterial reverse mutation assay, mouse lymphoma test, and 90-day subchronic toxicity of NBC, and demonstrated its safety [J. Inorg. Biochem. 99 (2005) 2161-2183]. Recently, we demonstrated the long term (52-weeks) safety of NBC by administering either 0 or 25 ppm [1,000 mg elemental Cr(III) HED] doses of NBC in diet for 52 consecutive weeks to Sprague-Dawley rats (Eurotox 2006). In this study, we examined the genetic toxicology profile of NBC in a mouse micronucleus (MN) assay model, using young, healthy adult male and female Cr1:CD1(ICR) mice. NBC was administered to mice in corn oil by single dose oral gavage at doses of 1000, 2000 and 3000 mg NBC/kg body weight. Cyclophosphamide (70 mg/kg body weight) was used as a positive control. Mice were sacrificed at 24 and 48-hr post-treatment, and marrow aspirated from both femurs of each animal into a tube of fetal bovine serum. Following centrifugation, the resulting pellets were resuspended in serum. The slides were prepared from the suspensions and stained with Giemsa. A minimum of 2000 polychromatic erythrocytes (PCEs) per animal or 10,000 per treatment group were scored for micronuclei using 1000X brightfield microscopy. The number of PCEs among 500 total erythrocytes (expressed as the PCE fraction) was determined for each animal. No adverse clinical events or reduction in body weight gain were observed in the NBC treated animals. Numbers of MN-PCEs were not increased in any group treated with NBC compared to the corresponding negative control groups, while the positive control groups displayed strong increase in MN-PCEs. The results of the micronucleus test are in agreement with and further extend our previous findings with regards to the safety of NBC.

1446 ASSESSMENT OF POTENTIAL HUMAN HEALTH RISKS POSED BY BENZENE IN A COMMERCIAL BEVERAGE.

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A recent study by the Center for Food Safety and Nutrition (CFSAN) provided limited data regarding the concentration of benzene in a selection of commercial beverages. A reaction between sodium benzoate and vitamin C appears to give rise

to benzene in some drinks under certain conditions. CFSAN reported that several beverages contained levels of benzene which exceeded the EPA drinking water standard of 5 ppb. One of the beverages, Crystal Light Sunrise Classic Orange (CLSCO), was reported to have concentrations as high as 87.9 ppb, though a newer formulation registered levels <1 ppb in CFSAN testing. Due to limited testing by CFSAN, a more robust study was conducted to better characterize the levels of benzene in CLSCO. Samples of the beverage were obtained from retail outlets in the Houston Texas area, following a statistically-based sampling strategy. Three formulations were obtained during sampling: 16 oz old and new formulations, and 32 oz. formulation. Analysis of the samples revealed mean benzene concentrations of 90 ppb in 16 oz old formulation bottles, and undetectable levels in the 16 oz new formulation product. The 64 oz product was determined to contain a mean concentration of 3.38 ppb benzene, though sodium benzoate is not listed as an ingredient. Upper bound point estimates of cancer risk for exposure to these two products were calculated as 5.22×10^{-6} for teens and 2.76×10^{-7} for adults. Hazard indices for teens and adults were calculated at 0.277 and 0.0002 respectively. Monte Carlo analysis, utilizing distributions for consumption rate, benzene concentration, and body weight, resulted in a 95th percentile excess cancer risk of 7.94×10^{-6} for teens and 3.52×10^{-7} for adults. Non-cancer risk for teens and adults at the 95th percentile was estimated at 0.575 and 0.0022 respectively. These calculations indicate that cancer and non-cancer risks due to exposure to benzene in CLSCO are below levels of concern.

1447 CYTOTOXICITY OF PYRROCIDINES IN HEPG2 HEPATOCYTES AND PK15 RENAL CELLS.

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Pyrocidines are newly reported polyketide-amino acid-derived antibiotics produced by *Acremonium zeae*, a prevalent seed-borne endophyte of corn. Pyrocidines exhibit potent activity against Gram-positive bacteria, including drug resistant strains, and displayed significant activity against *Candida albicans*, as well as fumonisin and aflatoxin producing fungi. In this study, we evaluated the effect of pyrocidines in two mammalian cell lines, HepG2 cells (a cell line derived from a human hepatocellular carcinoma) and PK15 cells (a cell line derived from a normal pig kidney). The HepG2 and PK15 cells were incubated overnight to form monolayers and treated with 0 to 100 μ M of pyrocidine A and B for 24 hours. Cytotoxicity was evaluated by the MTT assay. Pyrocidine A and B were cytotoxic to both HepG2 and PK15 cells after 24 hours of treatment. ED₅₀ of pyrocidine A to HepG2 cells was $0.66 \pm 0.16 \mu\text{g/mL}$ and to PK15 cells was $1.03 \pm 0.37 \mu\text{g/mL}$. Pyrocidine B was less potent than pyrocidine A. ED₅₀ of pyrocidine B to HepG2 was $15.37 \pm 4.47 \mu\text{g/mL}$ and to PK15 was $16.63 \pm 5.47 \mu\text{g/mL}$. The cytotoxicity of pyrocidine A to HepG2 cells was more potent than other known mycotoxins, e.g. deoxynivalenol ED₅₀ = $8.36 \mu\text{g/mL}$, fumonisin B₁ ED₅₀ > $100 \mu\text{g/mL}$, zearalenone ED₅₀ > $100 \mu\text{g/mL}$ and moniliformin ED₅₀ = $3.5 \mu\text{g/mL}$. A sequential morphological study using time-lapse motion photography suggested that the cell death in PK15 cells induced by pyrocidine A was consistent with apoptosis. This is the first report of toxicity in a mammalian system. *In vivo* study are essential for risk assessment.

1448 IMMUNOTOXICITY OF NIVALENOL LACKING XENOBIOTIC METABOLISM AFTER ORAL ADMINISTRATION FOR 90-DAY IN RATS.

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Nivalenol (NIV), one of the trichothecene mycotoxins produced by *Fusarium* species, is an important contaminant of wheat and barley showing worldwide distribution. In the present study, we examined exposure effect of NIV through diets at doses of 0, 6.25, 25, and 100 ppm for 90 days on immune function and activities of detoxifying enzymes in the liver of male F344 rats. Examination of serum immunoglobulin levels revealed a slight increase of IgM at 100 ppm, while IgM at lower doses and IgG or IgA at any doses did not fluctuate. Flow cytometric analysis of splenic cells revealed increases of B-cell population from 25 ppm and decrease of T-cell population at 100 ppm associated with an elevation in the ratio of helper/cytotoxic T lymphocytes at 100 ppm. On the other hand, increases of