MEDICAL

Long-term safety of bisphosphonates 2
Short- and long-term efficacy and safety of risperidone in adults with disruptive behavior disorders 2
Life and Times in Biochemical Toxicology 2
Cycad consumption and neurological disease 2
A Review of the Toxicology and Epidemiology of Wollastonite 3
Impact of ecotoxicants on blood nuclease activity 3
Contact allergy to gold in patients with gold-plated intracoronary stents 4
Determination of Biological Reference Values for Chlorpyrifos Metabolites in Human Urine Using a Toxicokinetic Approach 4
Genotoxic effects of commonly used pesticides of south India in human lymphocytes 5

Contents
Long-term safety of bisphosphonates
2005-09-01
Current knowledge of bone physiology suggests that bisphosphonates would increase bone strength by preventing trabecular plate perforation and improving bone mineralization in undermineralized bone. Many physicians do not even consider the possibility that bisphosphonates could have some adverse effects on the bone.
Authors: Ott, Susan M.
Full source: Journal of Clinical Endocrinology and Metabolism 2005, 90(3), 1897-1899 (Eng)

Short- and long-term efficacy and safety of risperidone in adults with disruptive behavior disorders
2005-09-01
The study observed function in society can be severely affected by disruptive behaviors in adults. This study examines the efficacy and safety of risperidone in the treatment of disruptive behavior disorders in intellectually disabled adults. Intellectually disabled patients with disruptive behavior disorder were randomly assigned to receive risperidone in a flexible dosage ranging from 1 to 4 mg/day or placebo for 4 weeks of double-blind treatment. Risperidone was well tolerated, and patients treated with risperidone demonstrated significantly greater improvement at endpoint on the ABC than those who received placebo and also improved on Behavior Problems Inventory and Clinical Global Impressions ratings. The results were achieved with a mean modal dosage of 1.8 mg/day. Risperidone is efficacious and well tolerated in managing disruptive behavior disorders in adults with intellectual disability.
Authors: Gagiano, Carlo; Read, Stephen; Thorpe, Lilian; Eerdekens, Marielle; Hove, Ilse
Full source: Psychopharmacology 2005, 179(3), 629-636 (Eng)

Life and Times in Biochemical Toxicology
2005-09-01
The biochemical facets of toxicology have always had a major role in providing insight into mechanisms. Some of the history of the development of this area is summarized, including metabolism, enzymolecular, and the chemistry of reactive intermediates. Knowledge in these fields has had a major impact in the areas of drug metabolism and safety assessment, which are both critical steps in the development of pharmaceuticals and the rational use of commodity chemicals. The science of toxicology has developed considerably with input from other disciplines and today is poised to emerge as a predictive science with even more dramatic impact. The challenges ahead are considerable but there is renewed excitement in the potential of the field. As in the past, further advances in the field of toxicology will require the input of knowledge from many disciplines.
Authors: Guengerich, F.
Full source: International Journal of Toxicology 2005, 24(1), 5-21 (Eng)

Cycad consumption and neurological disease
2005-09-01
Amyotrophic lateral sclerosis-parkinsonism dementia complex (ALS-PDC) has been termed the Rosetta Stone of neurological disease, due to its component amyotrophic lateral sclerosis, Parkinson’s disease, and Alzheimer’s disease symptomatology and neuropathology. The largest
Medical and most-studied geog. focus of ALS-PDC is that of the island of Guam in the South Pacific. The consumption of the seeds of a local, indigenous species of cycad, Cycas micronesica, is thought to play a causal role in the development of ALS-PDC. Cycad contains many toxins, and traditional processing methods have therefore been developed with the aim of removing them. Water-soluble, cycad-specific toxins such as cycasin, macrozamins, and beta-methylamino-L-alanine are removed by washing the cycad. This refutes early cycad theories of ALS-PDC that these toxins are causal in the development of ALS-PDC. Since cycad consumption still appeared to be linked to ALS-PDC, the laboratory has reexamined the cycad hypothesis. By feeding mice processed cycad flour, the authors have created a valid mouse model of ALS-PDC. This information, in conjunction with data on the effects of various genetic conditions, sex, and age, will allow to template-match the findings against the human experience of ALS-PDC. This will allow to distinguish between the disease’s causal, coincidental, and compensatory (successful or failed) components, and thus provide targeted therapeutics with which to move from palliative to preventative care for patients suffering from ALS-PDC as well as those diagnosed with amyotrophic lateral sclerosis, Parkinson’s disease, or Alzheimer’s disease.

Authors: Schulz, Jeff D.; Hawkes, Erin L.; Shaw, Christopher A.

Full source: Reviews in Food and Nutrition Toxicity 2005, 4, 233-270 (Eng)

A Review of the Toxicology and Epidemiology of Wollastonite
2005-09-01
Wollastonite is a naturally occurring calcium silicate (CaSiO3) that is produced in both powder and fibrous forms. It is a valuable industrial mineral used in plastics, ceramics, metallurgical applications, paint, and friction products. For some applications wollastonite serves as an asbestos replacement. To varying degrees, wollastonite grades contain respirable particles/fibers, some of which have lengths and diameters that might be biologically active if deposited and retained in the lung. In this review authors provide background information on wollastonite properties, markets, production and use, regulatory classification, and occupational exposure limits. The authors also summarize the available studies on the toxicology and epidemiology of wollastonite. The authors conclude that there is inadequate evidence for the carcinogenicity of wollastonite in animals and, based on strong evidence that wollastonite is not biopersistent, believe that a well-designed animal inhalation bioassay would have a negative result. The epidemiological evidence for wollastonite is limited, but does not suggest that workers are at significant risk of an increased incidence of pulmonary fibrosis, lung cancer, or mesothelioma. Morbidity studies have demonstrated a nonspecific increase in bronchitis and reduced lung function. It is prudent, however, to continue product stewardship efforts by wollastonite producers to control workplace exposures and to monitor scientific developments.

Authors: Maxim, L.; McConnell, E. E.

Full source: Inhalation Toxicology 2005, 17(9), 451-466 (Eng)

Impact of ecotoxicants on blood nuclease activity
2005-09-01
It was found out that DNA nuclease activity increased with certainty in children whose blood showed lead level equal or exceeding the reference level. A certain correlation of changes in DNase activity and the erythrocyte oligopeptide level was noticed. In adult carriers of manganese, cadmium and lead, the decrease of blood plasma RNA nuclease activity was shown.
The assessment of blood plasma nuclease activity in women carriers of manganese, correlation of changes in RNase activity and of the level of blood plasma oligopeptides was revealed.

Authors: Yelayeva, N. L.; Semyonov, Ye. V.; Ivanova, T. M.; Rutkovskiy, G. V.
Full source: Toksikologicheskii Vestnik 2005, (1), 27-32 (Russ)

**Contact allergy to gold in patients with gold-plated intracoronary stents**

2005-09-01

An increasingly common and effective method for the treatment of atherosclerotic disease in the coronary arteries is percutaneous transluminal coronary angioplasty (PTCA) and stenting. The stents are made of different metals. An increased rate of restenosis when using Au-plated stents was shown. Contact allergy to Au is common in many countries. Recently, a study has shown an increased rate of contact allergy to nickel among patients with restenosis and a nickel-containing stent. The aims of this study were to investigate whether there was an increased rate of contact allergy to Au among patients with Au-plated stents and if this increased the risk of restenosis. In the stent group, 10/22 (45.5%) had a contact allergy to Au, in the control group 18/88 (20.5%); the difference is statistically significant. There was no significant difference regarding frequency of restenosis. This study indicates that there is a risk of sensitizing the patient when implanting a Au-plated stent. Further studies are needed to confirm these results and to evaluate whether there is an increased risk of restenosis.

Authors: Svedman, C.; Tillman, C.; Gustavsson, C. G.; Moeller, H.; Frennby, B.; Bruze, M.
Full source: Contact Dermatitis 2005, 52(4), 192-196 (Eng)

**Determination of Biological Reference Values for Chlorpyrifos Metabolites in Human Urine Using a Toxicokinetic Approach**

2005-09-01

Urinary biomarkers of chlorpyrifos (CPF) exposure are often measured in field studies, although biological reference values (BRVs) are not yet available to assess health risks. This study aimed at proposing BRVs for CPF metabolites in workers’ urine based on a toxicokinetic approach. Model simulations under a variety of exposure scenarios showed that the safest BRVs are obtained from a dermal exposure scenario with the slowest absorption rate compatible with available literature data rather than from respiratory or oral exposure scenarios. Also, model simulations showed that, for a given total absorbed dose, absorption over 8 h results in smaller 3,5,6-TCP and AP urinary excretion rates than those obtained from the same dose absorbed over shorter durations. From these considerations, BRVs were derived by simulating an 8-h dermal CPF exposure such that the total absorbed daily dose corresponds to the absorbed NOEL. The reference values are proposed in the form of total amounts of 3,5,6-TCP and AP metabolites excreted in urine over chosen time periods.

Authors: Bouchard, Michele; Carrier, Gaetan; Brunet, Robert; Bonvalot, Yvette; Gosselin, Nathalie
Full source: Journal of Occupational and Environmental Hygiene 2005, 2(3), 155-168 (Eng)
Genotoxic effects of commonly used pesticides of south India in human lymphocytes

2005-09-01

India, the second largest manufacturer of pesticides in Asia, accounts for one-third of the pesticide poisoning in developing countries. About 3 lakh Indian farmers lose their lives due to pesticide poisoning annually. During 1999-2000, India used around 46,195 mt of technical grade pesticides to cover 182.5 million ha of cultivated area. In the present investigation, an attempt has been made to study the genotoxic effect of commonly used pesticides of South India, like 2,4-D, lindane, Sevin, and phosphamidon, in human lymphocytes by comet assay and chromosomal analysis. The results highlight that 2,4-D is capable of inducing higher DNA damage as well as chromosomal aberrations in human lymphocytes.

Authors: Nair, R. Sreekumaran; Paulmurugan, R.; Wilsanand, V.

Full source: Pollution Research 2005, 24(1), 7-12 (Eng)