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2005-08-24

Recently, 5-[123I]iodo-3-(2(S)-azetidinylmethoxy)pyridine ([123I]5IA) was developed as a ligand for imaging the nicotinic acetylcholine receptor (nAChR) in human brain using single photon emission computed tomography (SPECT). In the present study, the toxicity and radiation absorbed dose of [123I]5IA were investigated. Behavior and physiological parameters were examined in mice and rats after administration of 5IA. There were no changes in these parameters in animals administered 1 mug/kg of 5IA or less, indicating that the no observed effect level (NOEL) of 5IA was 1 mug/kg. [123I]5IA was then administered to healthy human subjects and serial whole-body images were acquired over 24 hours. Initially, high levels of radioactivity were observed in the liver and urinary bladder and moderate levels in the lungs, kidneys, and brain. Whole brain activity at 1 hour was 4.6±0.4% of the injected dose and this value gradually decreased with time. The majority (75%) of the radioactivity was excreted in urine within 24 hours, and less than 1% remained in all organs tested. The biological half-life of [123I]5IA averaged 7.2±4.0 h. SPECT images clearly revealed a cerebral distribution of radioactivity that was consistent with the known distribution of central nAChRs in humans.

Authors: Ueda, Masashi; Iida, Yasuhiko; Mukai, Takahiro; Mamede, Marcelo; Ishizu, Koichi; Ogawa, Mikako; Magata, Yasuhiro; Konishi, Junji; Saji, Hideo

Full source: Annals of Nuclear Medicine 2004, 18(4), 337-344 (Eng)

Study on chronic toxicity to rats of implantation of super-high molecular weight polylactate

2005-08-24

To make sure whether super-high molecular weight polylactate is toxic to the body after it has been implanted into the body for a long period, authors implanted super-high molecular weight polylactate into the rats and took the specimens of blood at 3, 6, 9, 12 months after the operation. At 3, 6, 9, 12 months after the operation, the levels of albumin, globulin, total bilirubin, direct bilirubin, direct bilirubin, triglyceride, glucose, K+, Na+, Cl-, Ca2+, alkaline phosphatase, glutamic-pyruvic transaminase in the blood plasma were all in the normal range; there were no significant differences between the experimental group and the control group. The level of lactate dehydrogenase increased slightly, but there was no statistically significant difference between the experimental group and the control group. There were no non-reversible immune rejection around the implants in the histological observation. Super-high molecular weight polylactate is not toxic to the body after it has been implanted into the animals for a long period.

Authors: Liu, Lei; Li, Shengwei; Tian, Weidong; Zheng, Qian; Wei, Shicheng; Xiong, Chengdong; Peng, Zhe

Full source: Sichuan Daxue Xuebao, Yixueban 2004, 35(6), 764-766 (Ch)

Cobalt

2005-08-24

Cobalt is one of the most important trace elements in the world of animals and humans. In the form of vitamin B12 (cobalamin), this metal plays a number of crucial roles in many biological functions. Cobalamin is necessary for DNA synthesis, formation of red blood cells, maintenance of the nervous
**Medical**

Vitamin B12 deficiency induces different pathological states such as anemia and neuropsychiatric disorders. Cobalt deficiency symptoms in ruminant animals include a loss of appetite, emaciation, weakness, anemia, and decreased production. There is evidence to support the role of this metal in immune processes. Some cobalt containing compounds are proved to possess anti neoplastic activity. Cobalt I has a relatively low toxicity but occupational exposure to this element may result in adverse health effects in different organs or tissues.

Authors: Alexandrova, R.; Tudose, R.; Arnaudova, E.; Costisor, G.; Patron, L.
Full source: Experimental Pathology and Parasitology 2004, 7(2), 3-14 (Eng)

**A 13- week toxicity study of bismuth in rats by intratracheal intermittent administration**

2005-08-24

Although bismuth is widely used as a lead substitute in the industrial field, the toxicity of bismuth by inhalation is little known. Authors performed a 13-week intratracheal intermittent bismuth dose toxicity study. The results showed foreign body inflammation in the lungs, which was caused by intratracheal administration of bismuth, and physical changes related to pulmonary lesions; however, there were no serious changes in other organs. Authors concluded that dose-dependent, but not specific adverse effects, were attributable to bismuth inhalation in the rat.

Authors: Sano, Yuri; Satoh, Hiroshi; Chiba, Momoko; Shinozaka, Atsuko; Okamoto, Masahide; Serizawa, Koji; Nakajima, Hiroshi; Omae, Kazuyuki
Full source: Journal of Occupational Health 2005, 47(3), 242-248 (Eng)

**Concentrations of N-methyl-2-pyrrolidone (NMP) and its metabolites in plasma and urine following oral administration of NMP to rats**

2005-08-24

The primary aims were to study the metabolism in rats and to determine the biological levels after one oral developmentally toxic dose of N-methyl-2-pyrrolidone (NMP), a widely used industrial chemical. In both plasma and urine NMP, 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP), N-methylsuccinimide and 2-hydroxy-N-methylsuccinimide (2-HMSI) and 2-pyrrolidone (2-P) were identified. In urine 48% of the administered dose was recovered as 5-HNMP and 2-5% as 2-HMSI. The total recovery in urine was 53-59%. The peak concentrations for NMP in plasma were 1.2 and 6.9 mmol/l, 0.42 and 0.76 mmol/l for 5-HNMP, 0.07 and 0.31 mmol/l for MSI and for 2-HMSI the concentrations were 0.02 and 0.05 mmol/l for groups 1 and 2, respectively. In summary, the same metabolites were found in rats as in humans and the biological levels were reported for NMP and its metabolites after oral exposure to a developmentally toxic dose and one non-toxic dose of NMP.

Authors: Carnerup, Martin A.; Saillenfait, Anne Marie; Joensson, Bo A. G.
Full source: Food and Chemical Toxicology 2005, 43(9), 1441-1447 (Eng)

**Safety and efficacy of enzyme replacement therapy in combination with hematopoietic stem cell transplantation in Hurler syndrome**

2005-08-24

Hurler syndrome is a debilitating genetic disease with a typical life span...
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of 5 to 8 years. Early hematopoietic stem cell transplantation (HSCT) mitigates disease symptoms and improves survival. However, morbidity and mortality associated with HSCT can limit its success. Authors describe the initial experience with combined use of enzyme replacement therapy (ERT, laronidase) and HSCT in Hurler syndrome. In children with Hurler syndrome, ERT with HSCT is feasible and well tolerated. Development of antibodies against exogenous enzyme does not appear to correlate with infusion reactions or response to ERT. A prospective study is needed to determine the effect of concomitant ERT on transplant outcomes.

Authors: Grewal, Satkiran S.; Wynn, Robert; Abdenur, Jose E.; Burton, Barbara K.; Gharib, Maged; Haase, Claudia; Hayashi, Robert J.; Shenoy, Shalini; Silence, David; Tiller, George E.; Dudek, Martha E.; Van Royen-Kerkhof, Annet; Wraith, James E.; Woodard, Paul; Young, Guy A.; Wulffraat, Nico; Whitley, Chester B.; Peters, Charles

Full source: Genetics in Medicine 2005, 7(2), 143-146 (Eng)

Interspecies metabolism of heterocyclic aromatic amines and the uncertainties in extrapolation of animal toxicity data for human risk assessment

2005-08-24

Heterocyclic aromatic amines (HAAs) are potent bacterial mutagens that are formed in cooked meats, tobacco smoke condensate, and diesel exhaust. Many HAAs are carcinogenic in experimental animal models. Because of their wide-spread occurrence in the diet and environment, HAAs may contribute to some common types of human cancers. The extrapolation of animal toxicity data on HAAs to assess human health risk has many uncertainties, which can lead to tenuous risk assessment estimates. Perhaps the most critical and variable parameters in interspecies extrapolation are the effects of dose, species differences in catalytic activities of xenobiotic metabolism enzymes (XMEs), human XME polymorphisms that lead to interindividual differences in carcinogen metabolism, and dietary constituents that may either augment or diminish the carcinogenic potency of these genotoxins. The impact of these parameters on the metabolism and toxicological properties of HAAs and uncertainties in extrapolation of animal toxicity data for human risk assessment are presented in this article.

Authors: Turesky, Robert J.

Full source: Molecular Nutrition & Food Research 2005, 49(2), 101-117 (Eng)

Clinical correlates of environmental endocrine disruptors

2005-08-24

Endocrine disrupting chemicals (EDCs), such as environmental estrogens, are hypothesized to be associated with a global decrease in sperm counts, other male reproductive tract problems and increasing rates of female breast cancer. Results of human population studies do not support the association between certain organochlorine EDCs and female breast cancer. Moreover, there is minimal evidence linking EDCs or exposure to other environmental chemicals with male reproductive tract problems. With the exception of the increasing incidence of testicular cancer, it is also questionable whether male reproductive tract problems are increasing, decreasing or unchanged. However, several studies report large differences in sperm count and quality and other endocrine-related problems within countries and regions, but the environmental, dietary and/or lifestyle factors responsible remain unknown.

Authors: Safe, Stephen

Full source: Trends in Endocrinology and Metabolism 2005, 16(4), 139-144 (Eng)
Determination of polychlorinated biphenyls in cerumen by GC-MS

2005-08-24

This study establishes a method of GC-MS for determination of polychlorinated biphenyls (PCBs) in human cerumen. The detection limit, average recovery rate and precision of this method were 0.15 μg/g fat, 92.1% and 3.0%-4.6% respectively. The contents of PCBs in 90 cerumen samples collected in polluted and control areas were detected. The levels (0.00-18.42 μg/g fat) of PCBs in cerumen collected in polluted area were significantly higher than that in the control area. This methods is practical, simple and reliable. The cerumen, as a biological specimen, is suitable for environmental epidemiological investigation in PCBs polluted area.

Authors: Jiang, Shi-xi; Yu, Su-xia; Chai, Jian-rong; Zheng, Ming-you; Wu, Nan-xiang; Zhang, Xing

Full source: Huanjing Yu Jiankang Zazhi 2005, 22(1), 50-52 (Ch)

Vascular dysfunction in patients with chronic arsenosis can be reversed by reduction of arsenic exposure

2005-08-24

Chronic arsenic exposure causes vascular diseases associated with systematic dysfunction of endogenous nitric oxide. Replacement of heavily arsenic-contaminated drinking water with low-arsenic water is a potential intervention strategy for arsenosis, although the reversibility of arsenic intoxication has not established. In the present study, the authors examined urinary excretion of cyclic guanosine 3',5'-monophosphate (cGMP), a second messenger of the vasoactive effects of nitric oxide, and signs and symptoms for peripheral vascular function in 54 arsenosis patients before and after they were supplied with low-arsenic drinking water in an endemic area of chronic arsenic poisoning in Inner Mongolia, China. The arsenosis patients showed a marked decrease in urinary excretion of cGMP, and a 13-month period of consuming low-arsenic drinking water reversed this trend and improved peripheral vascular response to cold stress. The authors’ intervention study indicates that peripheral vascular disease in arsenosis patients can be reversed by exposure cessation and has important implications for the public health approach to arsenic exposure.

Authors: Pi, Jingbo; Yamauchi, Hiroshi; Sun, Guifan; Yoshida, Takahiko; Aikawa, Hiroyuki; Fujimoto, Wataru; Iso, Hiroyasu; Cui, Renzhe; Waalkes, Michael P.; Kumagai, Yoshito

Full source: Environmental Health Perspectives 2005, 113(3), 339-341 (Eng)

Factors influencing the difference between maternal and cord blood lead

2005-08-24

This study determines the factors that affect why some infants receive higher exposures relative to the mother’s body burden than do others. A total of 159 mother-infant pairs from a cohort of women receiving prenatal care at Magee-Womens Hospital in Pittsburgh, PA from 1992 to 1995 provided blood samples at delivery for lead determination. The difference between cord and maternal blood lead concentration (PbB) and a dichotomous variable indicator of higher cord than maternal PbB were examined as indicators of relative transfer. Higher blood pressure was associated with relatively greater cord compared with maternal PbB, as was maternal alcohol use. Sickle cell trait and higher Hb were associated with a lower cord relative to maternal
blood lead PbB. No association was seen with smoking, physical exertion, or calcium consumption. While reduction in maternal exposure will reduce fetal exposure, it may also be possible to mitigate infant lead exposure by reducing transfer from the pregnant woman. Interventions aimed at reducing blood pressure and alcohol consumption during pregnancy may be useful in this regard.

Authors: Harville, E. W.; Hertz-Picciotto, I.; Schramm, M.; Watt-Morse, M.; Chantala, K.; Osterloh, J.; Parsons, P. J.; Rogan, W.

Full source: Occupational and Environmental Medicine 2005, 62(4), 263-269 (Eng)

Evaluation of chronic cough in chemical chronic bronchitis patients
2005-08-24
Coughing is one of the chronic respiratory symptoms of patients exposed to sulfur mustard (SM) used against Iranian combatants and civilians by Iraq during the Iran-Iraq war, between 1983 and 1989. This study was carried out on SM-exposed patients who were referred to the clinic because of an exacerbation of chronic cough. Fifty male SM-injured patients in the age range 21-79 years, all having chronic bronchitis and suffering from chronic cough (>3 weeks), were evaluated. Apart from having chronic bronchitis as a const. disease in all the patients, the other main causative factors behind chronic cough were bronchospasm, post-nasal drip syndrome (PNDS), and gastroesophageal reflux disease (GERD), which accounted for 66%, 46%, and 44% of the chronic cough of the patients, respectively. A single cause for chronic cough was found in 4 patients (8%), 2 causes in 17 patients (34%), 3 causes in 23 patients (46%), and 4 causes in 6 patients (12%). Since a high majority of the patients had more than a single cause for chronic cough, multiplicity of causes of chronic cough in a patient is indicative for evaluation of possible exposure to chemical fumes, especially SM. Because of the high prevalence of chronic bronchitis (100%) and bronchospasm (66%) among the study group it is concluded that they should be considered at first, before assessment of other causes.
Authors: Ghanei, Mostafa; Hosseini, Ali Reza; Arabbaferani, Zohre; Shahkarami, Efat

Full source: Environmental Toxicology and Pharmacology 2005, 20(1), 6-10 (Eng)

DNA Damage in T and B Lymphocytes, Bone Marrow, Spleens, and Livers of Rats Exposed to Benzene
2005-08-24
Single-cell gel electrophoresis assays were performed in order to evaluate DNA damage occurring in the T and B lymphocytes, spleens, bone marrow, and livers of rats exposed to benzene at a concentration of 100, 200, or 400 ppm for 2 or 4 weeks. In conclusion, the present study demonstrates that benzene exposure results in significant DNA damage in the T and B lymphocytes, bone marrow, spleens, and livers of rats. DNA damage in the blood cells and organs was also discovered to vary directly with benzene exposure, in both a dose-dependent and time-dependent manner. In addition, a similar trend regarding DNA damage was found in the blood cells and organs, and evidenced a good association with the level of t,t-MA in the urine.

Authors: Lee, Eunil; Im, Hosub; Oh, Eunha; Jung, Woon-Won; Kang, Hyung-Sik; Sul, Donggeun

Full source: Inhalation Toxicology 2005, 17(7-8), 401-408 (Eng)
Prevalence of pesticide exposure in young males (\(\leq 50\) years) with adenocarcinoma of the prostate

2005-08-24

Evidence implicating pesticides as causative agents of prostate cancer is controversial and, specifically, data in young adults is lacking. Hence, the authors performed a preliminary study evaluating the relation between pesticide exposure and prostate cancer in young males. Between 1991 and 2001, 61 young males with adenocarcinoma of the prostate were identified, of whom 56 patients with a mean age of 47 years had complete records of treatment and could be contacted for completion of the questionnaire. The most common stage at presentation was Stage III and the mean Gleason's score was 7.5. Interestingly, almost a third of patients had stage IV disease at presentation. 37/56 (66.1%) Patients had significant exposure in the study. In addition, interestingly, the mean survival in the subgroup of patients with pesticide exposure was 11.3 months, while the mean survival in the patients without pesticide exposure was 20.1 months, with p-value <0.01. Although the study is relatively small, it does reveal preliminary evidence linking pesticide exposure to the early development of, possibly aggressive, prostate adenocarcinoma. Future, larger, epidemiological studies are needed to confirm the findings of the study.

Authors: Potti, Anil; Panwalkar, Amit W.; Langness, Eric


Two year maintenance of efficacy and safety of infliximab in the treatment of ankylosing spondylitis

2005-08-24

This study obtains results of the second year extension of an original 3 months randomized, placebo controlled trial assessing the use of infliximab, a monoclonal antibody to tumor necrosis factor alpha, for the treatment of patients with ankylosing spondylitis (AS). Patients with AS treated for 2 years with infliximab 5 mg/kg exhibited a good and durable clinical response.

Authors: Braun, J.; Brandt, J.; Listing, J.; Zink, A.; Alten, R.; Burmester, G.; Gromnica-Ihle, E.; Kellner, H.; Schneider, M.; Soerensen, H.; Zeidler, H.; Sieper, J.

Full source: Annals of the Rheumatic Diseases 2005, 64(2), 229-234 (Eng)