females were divided in four groups and housed under controlled environmental conditions in the laboratory facilities of UNITOX. Food and water were available ad libitum. Three groups received Nifedipine (0,4; 1,2 and 2,0 mg/Kg), once a day, for 20 days before mating and continuing during mating and pregnancy periods. Control group received Tween 80 as vehicle. On day 20 of pregnancy, females were sacrificed and submitted to histological analysis. The litters were examined for visceral and skeletal anomalies. It was observed no effects in the body weight gain, food and water consumption of the dams. It was observed no difference between control and Nifedipine groups in the visceral and skeletal analysis of the fetuses. In histological analysis of the dams, about 90% of animals presented multifocal chronic hepatitis and diffuse nefrosis with the higher dose of Nifedipine. This study has shown that chronic administration of Nifedipine before mating and during pregnancy does not influence the organogenic period, but increased the appearance of multifocal chronic hepatitis and diffuse nefrosis, which needs further investigation.
Thanks to Laboratório Biosintética by furnishing Nifedipine.

701.3

THE EFFECTS OF PARAQUAT ON PREIMPLANTATION EMBRYO DEVELOPMENT AND GLUTATHIONE CONCENTRATION

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Paraquat (PQ) is an herbicide, which causes the formation of reactive oxygen species (ROS). The preimplantation embryo is very sensitive to ROS and toxicants in vitro; however, we hypothesize that in vivo, maternal mechanisms protect the embryo from the adverse effects of ROS and toxicants. Embryos treated with PQ in vitro exhibited decreased development to later stages (% blastocyst: control 88, 1.0 mM PQ 0; $p<0.05$), but embryonic GSH concentration was not affected (C 0.20 pmol/embryo, 1.0 mM PQ 0.23). In vivo treatment of dams with 30 mg/kg PQ I.P. on day 0 of gestation did not affect development on day 1 (% two-cell: C 61, PQ 79) or on day 3 (% blastocyst: C 44, PQ 35). Embryonic GSH concentration was decreased on day 1 (C 0.44, PQ 0.38; $p<0.05$); but not on day 3 (C 0.16, PQ 0.15). In vivo treatment of dams on day 2 did not affect day 3 development (% blastocyst: C 24, PQ 19) or embryonic GSH concentration. GSH was decreased in the liver (C 6 mM, PQ 4 mM; $p<0.05$), but not in the ovary. In conclusion, PQ decreases preimplantation embryo development in vitro to later stages, but in vivo embryos are partially protected from the adverse effects of PQ.

701.4

Detection and characterization of DNA adducts formed from metabolites of fungicide ortho-phenylphenol

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ortho-Phenylphenol (OPP) is commercially manufactured and used in agriculture and industry as fungicides and disinfectants. It is well reported that OPP is metabolized involving the cytochrome P-450-mediated formation of phenylhydroquinone (PHQ) and further oxidation of PHQ to phenyl-1,4-benzoquinone (PBQ) by the cytochrome P-450 enzymes. Although evidence exists that OPP metabolites can bind DNA, the structure of these DNA adducts and their biological significance remain undefined. To address these issues, we designed the present investigation and DNA adducts formed from OPP-derived quinones with deoxyguanosine or Calf Thymus DNA were detected by LC-ESI-MS. The mechanism for the DNA adduction is proposed as nucleophilic attack by the exocyclic amine nitrogen, N2, of the deoxyguanosine on the electrophilic carbon from the quinones, followed by stabilization through enolization. PBQ-2N-dG adduct isomers were further characterized by NMR spectrometry. Cell culture studies confirmed that PBQ incubated in HepG2 cells form the same DNA adducts which accompanied cytotoxicity. These studies illuminate toxicological effects of OPP metabolites on genetic macromolecules in hepatic cells.

701.5

Determination of Dialkyldithiocarbamate Accelerator Residues in Latex Condoms

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Considerable attention has been paid to potential human health hazards arising from *N,N*-dialkyldithiocarbamate (DTC) type vulcanization accelerators in latex products. A commonly used accelerator zinc diethyldithiocarbamate (ZDEC) has been detected in leachates from medical devices including gloves and surgical drains. It and several other zinc DTCs have been found to be causative agents of allergic contact dermatitis. Quantitation of these compounds is complicated by their labile nature and thermal instability. A simple assay was used to screen fourteen brands of condoms for zinc DTCs. After acetonitrile extraction the extracts were treated with cobalt chloride to effect formation of cobalt DTC from zinc DTC. A green colored solution suggested the presence of a DTC while blue indicated a negative result. Six positive results were observed and two of these were confirmed to contain ZDEC by GC/MS. ZDEC concentrations were determined by measuring UV absorbances of transmetalated samples at 320 nm. When analyzing large numbers of samples this preliminary screening method should prove useful for identifying latex products with free DTCs.

701.6

Mitochondrial toxicity of anti-HIV nucleoside reverse transcriptase inhibitors (NRTIs): In vitro assessment of the mechanism and comparison with tenofovir.

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A number of clinical adverse effects induced by NRTIs are due to drug-associated mitochondrial (mt) toxicity. Frequently, depletion of mtDNA is the underlying molecular mechanism. We compared the clinically used NRTIs with a novel anti-HIV nucleotide analog tenofovir for their potential to induce mt toxicity in human hepatoblastoma, skeletal muscle, and renal proximal tubule cells. The potency of inhibition of mtDNA synthesis by the tested NRTIs was ddC > ddI > d4T > ZDV > 3TC = abacavir = tenofovir, with comparable relative effects in all cell types. These results are approximately concordant with the efficiency at which each respective NRTI-triphosphate is incorporated into DNA by mt DNA polymerase γ. ddC and ddI, but not tenofovir, reduced expression of cytochrome c oxidase, presumably as a direct consequence of mtDNA depletion. Lactate production increased marginally in cells treated with tenofovir. In contrast, ddC and ZDV increased lactate production by 30-50% and >100 %, respectively, with the effects of ZDV observed in the absence of substantial mtDNA depletion. Thus, NRTI-associated mt toxicity can be mediated by various mechanisms and tenofovir is not associated with any form of mt toxicity.

701.7

An Astaxanthin-Containing Algal Extract Attenuates Selenite-Induced Nuclear Cataract Formation in Rat Pups.

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Age-related cataract is a leading cause of visual disability and blindness. The role of nutritional antioxidant supplements, such as vitamin C & E and the carotenoids, in promoting visual health has received much attention. In this study we examined the anticataractogenic effects of an astaxanthin-containing complex (ASTX), a very potent xanthophyll antioxidant found in algae and some marine animals (e.g., salmonoids). Pups (N=27) from pregnant Sprague-Dawley rats received 1 of 4 daily oral treatments starting on postnatal day (PD) 10: vehicle (stripped corn oil); ASTX (10 mg/kg); ASTX (100 mg/kg); vitamin E (1000 mg/kg). The ASTX employed was a microalgae oleoresin extract containing 85% of the xanthophyll. On PD-12 sodium selenite (19 mg/kg; s.c.) was administered. Daily visual inspections for cataracts occurred until sacrifice (PD-19), when lenses were removed and inspected. The incidence of lenticular nuclear opacities in the vehicle and vitamin E groups was 92% and 90%, respectively. However, both ASTX treatments significantly attenuated opacity formation (40% incidence in both groups). These results support a potent antioxidant action in the lens of this algae-derived xanthophyll-complex.

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