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BI-05

COMPARED BILIAR DISPOSITION OF SUPROFEN ENANTIOMERS IN DOMESTIC CARNIVORES.

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Suprofen (SPF) is a non-steroidal anti-inflammatory drug (NSAID) who belongs to the 2-arylpropionic acids subclass. As result of its chiral characteristics, this compounds have shown a marked enantioselective behaviour [i.e, chiral inversion (CH.I) of (R) to (S) enantiomer, with a high degree of interspecies variation. They are mainly eliminated by glucuronidation. Previous data shown that SPF is poorly inverted or not in all the species that it had been tested. Our data about rac- SPF disposition in the cat are accordingly with that (Castro *et al*, 2001). Biliar and urine disposition of racemic SPF was investigated to evaluate the contribution of the glucuronidation pathway to the detoxification of racemic SPF. The total amount of glucuronides excreted in the bile represented 1% of the total dose administered. No SPF glucuronides were found in urine. Racemic SPF showed an enantioselective disposition in none of the biological matrix investigated. This results, compared with those obtained in a similar experiment in dogs (Soraci *et al* ,1995) suggest that the biological fate of SPF in the cat is not influenced by enantioselective physiological processes and that other pathways different from glucuronidation and CH.I. may be responsible for the clearence of SPF.*(Modalidad - POSTER).*

BI-06

2,4-DICHLOROPHENOXYACETIC ACID EFFECT ON RAT GRANULOSA CELLS IN CULTURE

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2,4-Dichlorophenoxyacetic acid (2,4-D) and its derivatives are herbicides widely used to control the growth of broadleaf. Exposure of rats to this herbicides would have adverse effects on reproduction. The aim of the present study was to investigate if the ovarian Granulosa cell (GC) viability was afected by 2,4-D *in vitro.* Ovaries of immature 24 to 25-day-old Wistar rats were excised 3 days after the animals were implanted sc with diethylstilbestrol. GC were harvested from de ovaries by follicular puncture using a fine needle. The cells were resuspended in McCoy's 5A medium and cultured in 24 well plastic plates (100,000 viable cells/well in 0.4 ml of culture medium) in McCoy's 5A medium supplemented with penicillin (100 U/ml), streptomycin (100 µg/ml) and L-glutamine 2 mmo/l), in a humidified atmosphere of 95% air and 5% CO_2 at 37ºC. Cells were incubated in the presence or absence of 0.2 mM, 0.5 mM, 1 mM or 2 mM 2,4-D concentrations. The 3-(4,5-dimetylthiazol-2-yl)- 2,5-diphenyl tetrazolium bromide (MTT) assay was used as a quantitative colorimetric measurement of cell death. Mean cell viability was decreased significantly by 2,4-D in a dose depending way. This observation was according to *in vivo* studies where we demonstrated a decrease in the number of ovarian follicles by the herbicide.

BI-07

EFFECT OF EXPERIMENTAL INTOXICATION WITH METALLIC MERCURY ON BONE TISSUE

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At present, metallic mercury (mm) is one of the mayor environmental contaminants. There are no reports in the literature about its effects on bone tissue. The objective was to study the effect of mercury intoxication on bone volume (BV). We evaluated bones presenting endochondral ossification (femur) and endomembranous bone (maxillae) in mice. Adult male BALB/c mice, (25 and 30 g body weight) were divided into groups and treated as follows: Group A (n=8): absolute control, and Group B (n=8): treated with a single intraperitoneal 0.1ml dose of mm. All the animals were euthanized 48 hours after the onset of the experiment. Group C (n=8) and Group D (n=8) received the same treatment as Groups A and B respectively, but were euthanized at 14 days. All femurs and mandibles were resected to perform histologic and histomorphometric studies. The specimens were fixed in buffered formalin. The sections were stained with hematoxylin - eosin. Digital photographs were obtained and analyzed using Image Pro Plus software. Our results allow stating that the alterations in bone volume observed following administration of the dose of mm used in this study (0.1 ml) are not only associated with the experimental time points but also with the type of bone tissue.

BI-08

COMPARATIVE ACTIVITIES OF XENOBIOTIC METABOLIZING ENZYMES IN SHEEP LIVER AND SMALL INTESTINE MUCOSAS.

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Intestinal mucosa has the ability to metabolize a great number of xenobiotics by both phase 1 and phase 2 reactions. The objective of this work was to evaluate xenobiotic metabolizing enzyme activities in cytosolic and microsomal fractions obtained from sheep liver and small intestine mucosas (duodenum, jejunum and ileum). Oxidative (cytochrome P450-dependent), reductive (carbonyl reductase) and enzymatic conjugative activities were measured by using known marker substrates. Metabolic activities measured in liver subcellular fractions were used as reference values. Intestinal N-demethylase P450-dependent activities ranged between 11.0-46.1 % (P450 3A) and 3.0-7.1 % (P450 2C) than those measured in the liver. These metabolic activities did not decrease nor increase along the small intestine. Conversely, microsomal O-deethylase P450-dependent activities (CYP 1A) were not detected in sheep small intestine mucosas. Intestinal carbonyl reductase activities were 14.3-23.4 % (microsomes) and 18.7-33.1 % (cytosol) than those measured in the liver. Intestinal microsomes were able to conjugate 1-naphthol, (an UGT-mediated reaction) and 1-cloro,2,4-dinitrobenzene (a GST probe). Metabolic reactions, taking place in the intestinal mucosa, may contribute to the pre-systemic metabolism of orally administered drugs. These results contribute to further current knowledge on the extra-hepatic biotransformation pathways in ruminants.