XLI REUNION ANUAL
DE LA SOCIEDAD ARGENTINA
DE FARMACOLOGÍA EXPERIMENTAL

24 al 26 de Noviembre de 2009

ROSARIO, ARGENTINA

COMISION DIRECTIVA

Presidente
Carlos Lanusse
Vicepresidente
Carlos María Baratti
Secretaria
Gabriela Acosta
Tesorero
Sergio Sanchez Bruni
Vocales
Ana Genaro
Nora Brandan
Lilian Pelzer
Revisores de Cuentas
Carlos Reyes Toso
Damasia Becú
Revisores de Cuentas Suplentes
Marcela Rebuelto
Gabriel Cuadra

Representante ante

a)Foro de la Ciencias
b)Asociación Argentina para el Progreso de la Ciencia
Carlos María Baratti

Representantes Regionales

María Victoria Aguirre (Corrientes)
Otto Orsingher (Córdoba)
Alejandra María (San Luis)
Ana Evangelista (Rosario)
Ignacio Alvarez (Tandil)
Ricardo Cabrera (Mendoza)
Roberto Rule (La Plata)
Gabriel Orce (Tucumán)

Comité Organizador Local

Dr Ricardo Duffard
Dra Ana Maria Evangelista de Duffard
Dra Adriana Torres
Dr Nelson Stürtz
Bioq. Cintia Konjuh
Bioq Valeria Cholich
Lic Silvana Biolatto
Bioq. Arístides Pochettino

Domicilio

Junín 956, 5° piso. (1113 AAD). Buenos Aires - Argentina

Tel: (54-11)-4964-8266. FAX: (54-11)-4964-8266
Email: safe@canopus.com.ar
www.safe-digital.org

OII-13

EFFECTS OF GLP-2 ON INTESTINAL XENOBIOTIC METABOLISM AND ELIMINATION.

Villanueva SSM, Ruiz ML, Arias A, Rigalli JP, Luquita MG, Catania VA, Mottino AD. IFISE-CONICET, Fac. Cs. Bioq. y Farm., UNR, *Suipacha 570 (2000) Rosario, Argentina. E-mail: villanueva@ifise-conicet.gov.ar*

Glucagon like-peptide 2 (GLP-2) produces intestinal hypertrophy and increases the activity of sugar transporters in intestine. Plasmatic GLP-2 is increased in postpartum rats, which could be responsible for the augmented intestinal secretion of conjugated xenobiotics observed in these animals. Here, we evaluated the effect of GLP-2 (25 µg/100g/day, 5 days, s.c.) on the expression and activity of GST, phase II cytosolic enzyme, and the apical transporter of organic anions, Mrp2, in jejunum of female Wistar rats (n=4). Control rats (C, n=4) received the vehicle (PBS). **Results:** GLP-2 increased *in vitro* GST total activity towards 1-chloro-2,4-dinitrobenzene (CDNB) (+52%) and expression of GST class µ (+46%) detected by western blotting. Mrp2 activity, evaluated *in vivo* for administration i.v. of CDNB (30 µmol/kg bw) and detection of its derivates: dinitrophenyl glutathione and dinitrophenyl cysteinyl glycine in intestinal perfusate, was higher in GLP-2 group (+52%) than in C group. Mrp2 expression (western blotting) was also increased in GLP-2 group (+67 %) respect to C. **Conclusion:** These effects of GLP-2 can explain the changes observed in postpartum rats, which implicate a higher protection against the absorption of dietary xenobiotics since food intake is increased in this situation.

OII-14

EFFECT OF DEXAMETHASONE CHRONIC ADMINISTRATION ON THE HEPATIC SULPHOXIDATION OF ALBENDAZOLE IN SHEEP

Virkel, G.[(1)]; Maté, L.[(1)]; Lifschitz, A.[(1)]; Sallovitz, J.[(1,2)]; Ballent, M.[(1)]; Lanusse, C.[(1)]

[(1)] Laboratorio Farmacología, FCV-UNCPBA - CONICET (ARGENTINA). [(2)] CICPBA (ARGENTINA).

e-mail: **gvirkel@vet.unicen.edu.ar**

Albendazole (ABZ), a broad spectrum antiparasitic drug, is oxidized into albendazole sulphoxide (ABZSO) by both flavin-containing monooxygenase (FMO) and cytochrome P450 (CYP). Changes on the metabolic activities of both enzyme systems may affect the persistence of these anthelmintic molecules in target tissues. We hypothesized that chronic administration of the CYP3A inducer dexamethasone (DEX) increases the CYP-mediated metabolism of ABZ in sheep liver. The enantioselective sulphoxidation of ABZ was evaluated in hepatic microsomes obtained from untreated and DEX-treated sheep (7 days at 3 mg/kg/day). CYP3A-mediated erythromycin and triacetyl-oleandomycin N-demethylations were, respectively, 3.6- and 2.7-fold higher ($P<0.05$) in liver microsomes obtained from DEX-treated sheep. However, the hepatic CYP-mediated sulphoxidation of ABZ was not affected by DEX chronic administration. On the other hand, the FMO-dependent activity (methimazole S-oxidation) was 28 % lower in liver microsomes from DEX-treated sheep, which correlated with a lower FMO-mediated enantioselective sulphoxidation of ABZ. In conclusion, the CYP3A subfamily is not involved in ABZ hepatic sulphoxidation. Moreover, chronic administration of DEX in sheep may have detrimental effects on the FMO-mediated metabolism. This may affect the disposition of ABZ and its active metabolite in target tissues of parasite location.

OIII-15

ORAL CONTRACEPTIVES IN CHOLESTATIC FEMALE RATS: ROLE OF CYTOKINES.

Fernández-Martínez E, Pérez-Soto E, González-Hernández C, Pérez-González R, Ortiz-Ramírez MI. CIBIOR, Medicina-I.C.Sa., Universidad Autónoma del Estado de Hidalgo. Calle Dr. Eliseo Ramírez Ulloa no. 400, Col. Doctores, C.P. 42090, Pachuca Hidalgo, México. efernan@uaeh.edu.mx

Oral contraceptives (OC) may cause cholestasis or increase a pre-established liver damage. Effects on hepatic injury markers are contradictory and the role of cytokines in those processes is quite unknown. Eight groups of female rats were used. Four groups underwent sham operation (Sham) and were orally administered once a day during 14 days with vehicle, OC (100 µg/kg norgestrel, 10 µg/kg ethinylestradiol), OC double dose or the last one with OC single dose but during 28 days. The remaining groups were bile duct ligated (BDL) to induce cholestasis and were administered under the same schedule. Markers of cholestasis (AP, GGTP, bilirubins), necrosis (ALT) as well as cytokines TNF-α, IL-10 and TGF-β were determined in plasma. In liver, collagen, lipid peroxidation, glycogen and cytokines were quantified. Cholestasis induced changes in plasma and liver biochemical markers as well as on cytokine levels, but OC modified even the values in Sham groups and these were more pronounced in BDL rats. Administration of OC induces changes that may establish and perpetuate liver damage or worsen any prior one wherein cytokines participate strikingly; all those processes are influenced by dose, time and OC formulation. PROMEP/103.5/05/1919 and CONACyT 50733-Q, Mexico.

OIII-16

EXPRESSION OF KIDNEY AND LIVER BILITRANSLOCASE (BTL) IN RESPONSE TO ACUTE BILIARY OBSTRUCTION (ABO).

Brandoni A, Di Giusto G, Franca R*, Passamonti S*, Torres AM. *Farmacología. Fac. Cs. Bioq. y Farm. U.N.R. Suipacha 531. (2000) Rosario. CONICET. Email anabelbrandoni@gmail.com.*

**Universidad de Trieste, Italia.*

Renal organic anion transporters play an important role in the elimination of anionic drugs, including β-lactam antibiotics, diuretics and antiviral drugs. We have recently demonstrated that ABO is associated with modifications in the renal expression and function of organic anion transporters such as Oat1, Oat3 and Oatp1. In this study the expression and function of the electrogenic basolateral transporter, BTL, were examined in liver and kidney from rats with ABO (n=3). A parallel group of sham rats (S, n=3) was employed. BTL expression was evaluated in renal homogenates (H), renal basolateral membranes (B) and liver membranes (L) by immunoblotting. BTL function was studied by measuring the kinetics parameters (Vmax, µmol BSP/min/mg prot; Km, µM) of electrogenic bromosulfophthalein (BSP) uptake in B and L by a spectrophotometric technique. Immunoblotting revealed a significant increase in BTL expression in B from ABO rats without modifications in H and in L. **B**: *Vmax*, S= 1.61±0.04; ABO= 2.12±0.04*; *Km*, S= 21±2; ABO= 26±1. **L**: *Vmax*, S= 1.84±0.34; ABO= 1.82±0.04; *Km*, S= 5.4±0.4; ABO= 6.3±0.6. (*$p<0.05$). The higher renal expression and function of BTL in B from rats with ABO might also contribute to the dramatic increase in BSP renal excretion previously observed in these rats. This would be other compensation mechanism to overcome the hepatic dysfunction in the elimination of organic anions.