



**XLI REUNION ANUAL
DE LA SOCIEDAD ARGENTINA
DE FARMACOLOGÍA EXPERIMENTAL**

[PROGRAMA](#)

[RESUMENES](#)

[AUTORES](#)

24 al 26 de Noviembre de 2009

ROSARIO, ARGENTINA

COMISION DIRECTIVA

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

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PROGRAMA CIENTÍFICO	
23 al 25 de Noviembre de 2009	
Curso de Post-grado: “Animales de laboratorio: su aplicación en la Fisiología, Farmacología y Toxicología” Con evaluación y créditos para programas formales de post-grado. Información adicional sobre programa, contenidos e inscripción disponibles en www.safe-digital.org Lugar: Aula 2 y/o 3.	
Lunes 23 de Noviembre de 2009 Conferencia Satélite a SAFE 2009 Lugar: Colegio de Farmacéuticos de Rosario. Buenos Aires 1262, Rosario	
21.00 h	Dr. Carlos María Baratti (Profesor Titular de Farmacología, Facultad de Farmacia y Bioquímica, UBA) "Aspectos Neurobiológicos de las Adicciones"
Martes 24 de Noviembre de 2009 <u>Lugar:</u> Sede central de la Facultad de Ciencias Bioquímicas y Farmacéuticas. Suipacha 531 Rosario	
15:00-17:30 h	INSCRIPCIÓN Lugar: Salón de Reuniones de Graduados Aulas 1 y 2
17.30 h	INAUGURACIÓN OFICIAL Anfiteatro de la Fac de Cs Bioquímica y Farmacéuticas. Suipacha 580 Rosario Himno Nacional Actuación: “ESCUELA ORQUESTA DEL BARRIO LUDUEÑA” Palabras del Presidente de SAFE y del Presidente del Comité Organizador Local Dres. Carlos Lanusse y Ricardo Duffard
18:00-19.00 h	<u>C1</u> CONFERENCIA PLENARIA I Dr. William Slikker (Director, National Center for Toxicological Research/ FDA, Jefferson Arkansas USA) “Nanotechnology :Pharmacological applications and approaches to safety assessment” Coordinador: Dr Ricardo Duffard Lugar: Anfiteatro de la Facultad de Ciencias Bioquímicas y Farmacéuticas. Suipacha 580
19:00-20:30 h	COMUNICACIONES ORALES I Coordinadores: Dra. Damasia Becú; Dra. Alicia Consolini Lugar: Sala de Graduados
19.00	<u>OI-01</u> DETERMINATION OF HYPOTHALAMIC LEVELS OF MONOAMINERGIC NEUROTRANSMITTERS IN ADULT RATS EXPOSED PRE AND POSTNATALLY TO 2,4-DICHLOROPHOXYACETIC ACID (2,4-D) Cholich V.; Rassetto M.; Pochettino A.; Duffard R.; Evangelista de Duffard A.M. LATOEX. Facultad de Cs. Bioquímicas y Farmacéuticas. UNR. <i>Suipacha 531. 2000 Rosario. Argentina. E-mail: vcholich@fbioyf.unr.edu.ar</i>
19.15	<u>OI-02</u> EFFECT OF ELECTRICAL AND CHEMICAL STIMULATION OF THE SUBTHALAMIC NUCLEUS ON THE RELEASE OF STRIATAL DOPAMINE Pazo JH ¹ , Höcht C ² , Barceló AC ³ , Fillipini B ¹ , Lomastro MJ ¹ . ¹ Laboratorio de Neurofisiología, Departamento de Fisiología y Biofísica, Facultad de Medicina; ² Facultad de Farmacia y Bioquímica and ³ Facultad de Odontología, Universidad de Buenos Aires. Buenos Aires, Argentina. E.mail: jpazo@fmed.uba.ar

19.30	OI-03	ROLE OF THE GABA_B RECEPTORS IN THE EFFECTS INDUCED BY NICOTINE ON ANXIETY-LIKE BEHAVIOUR IN MICE Varani A ¹ , Calvo M ¹ , Moutinho L ¹ , Induni A ^{1,2} and Balerio G ^{1,2} ¹ ININFA (CONICET) y ² Cát. de Farmacología (FFyB, UBA) Junín 956, 5ºPiso. Buenos Aires. E-mail: gbalerio@ffyb.uba.ar
19.45	OI-04	DORSAL STRIATUM MEDIATION OF COCAINE-SEEKING AFTER VARIED PERIODS OF COCAINE SELF-ADMINISTRATION AND WITHDRAWAL IN RATS. Pacchioni AM, Gabriele A, and See RE. Dept Neurosciences, Medical University of South Carolina, 173 Ashley Avenue, Charleston, SC29425, USA. Email: alepacchi@hotmail.com
20.00	OI-05	LONG-TERM ANTICONVULSANT TREATMENT WITHOUT MEMORY IMPAIRMENT Krawczyk MC, Blake MG, Boccia MM, Carcaboso AM, Chiappetta DA, Höcht C, Sosnik A, Baratti CM Cátedra de Farmacología, FFyB, UBA Junín 956, Buenos Aires, Argentina cbaratti@ffyb.uba.ar
20.15	OI-06	ARE GLUCOCORTICOIDS RECRUITING ENDOCANNABINOIDS TO MODULATE AVERSIVE MEMORY CONSOLIDATION IN THE HIPPOCAMPUS? Oliveira Alvares L. de, Engelke D.S., Diehl F., Genro B.P., Molina V.A., Quillfeldt J.A Universidade Federal do Rio Grande do Sul, LPBNC, Porto Alegre Brasil. Rua Carlos Silveira Martins Pacheco, 55/1104 A. Bairro Cristo Redentor. CEP: 91350300. Porto Alegre-RS, Brasil
20:30 h		COCKTAIL DE BIENVENIDA Lugar: Aula 1
Miércoles 25 de Noviembre de 2009		
Lugar: Sede central de la Facultad de Ciencias Bioquímicas y Farmacéuticas. Suipacha 531		
8:00-8:30 h		Inscripción y colocación de todos los pósters presentados (se exhibirán durante todo el Congreso) Lugar: Aulas 1 y 2
8:30-10.30 h		COMUNICACIONES ORALES II Coordinadores: Dres Alejandro Serra y Hugo Solana Lugar: Aula 1 y 2
8.30 h	OII-07	A MODEL OF METFORMIN ABSORPTION Serra H. A., Rizzo L. F. 1ª Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. Paraguay 2155 piso 15 1121 Buenos Aires, Argentina. Dirección Médica, Química Montpellier S.A. Virrey Liniers 673 1220 Buenos Aires, Argentina. E-Mail: haserrafarmaco@gmail.com
8.45 h	OII-08	COMPARATIVE PLASMA PHARMACOKINETICS, TISSUE DISTRIBUTION AND EFFICACY OF TWO FORMULATIONS CIPROFLOXACIN-BASED IN MOUSE-MODEL Breda A ^{1,a} , Gonzalez C ² , Confalonieri A ² , Sanchez Bruni S ² , Manzo R ¹ , Olivera M ^{1,b} . ¹ Facultad de Ciencias Químicas, UNC, Córdoba, ² Facultad de Veterinaria, UNCPBA, Tandil, Argentina. ^a andrebreda@fcq.unc.edu.ar ; ^b meoliver@fcq.unc.edu.ar
9.00 h	OII-09	EFAVIRENZ-LOADED PEO-PPO POLYMERIC MICELLES ENHANCE THE ORAL BIOAVAILABILITY IN THE ANTI-HIV PHARMACOTHERAPY. Chiappetta D, Höcht C, Taira C, Sosnik A. FFyB, UBA. Junín 956 (1113) CABA. e-mail: alesosnik@gmail.com.
9.15 h	OII-10	KINETICS AND DYNAMICS OF LAMOTRIGINE IN 3-MERCAPTOPROPIONIC ACID INDUCED-SEIZURES Höcht C, ¹ Lazarowski A, ¹ Opezzo JA, ¹ Taira C, ¹ Girardi E. ² INFIBIOC, IBCN. chocht@ffyb.uba.ar .
9.30 h	OII-11	IN VITRO ASSESSMENT OF SEX INFLUENCE ON THE INTESTINAL P-GLYCOPROTEIN ACTIVITY IN RATS Ballent, M. ^{1,2} , Lifschitz, A. ^{1,2} , Virkel, G. ^{1,2} , Sallovitz, J. ¹ , Maté, L. ^{1,2} , Lanusse, C. ^{1,2} 1. Lab. Farmacología, FCV, UNCPBA. 2. CONICET. Email : mballent@vet.unicen.edu.ar
9.45 h	OII-12	AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME produced MODIFICATION OF P-gp EXPRESSION IN THE INTESTINE AND IN BLOOD BRAIN BARRIER. ^{1,3} Filia, M.F., ^{1,2} Novak, A., ¹ Godoy, Y., ¹ Rubio M.C., ^{1,2} Ghanem C.I., ¹ Celuch, S.M. ¹ ININFA (CONICET-UBA); Cát. ² Fisiopatología y ³ Farmacotecnia II (FFyB, UBA). Junín 956, 5º P. Buenos Aires. cghanem@ffyb.uba.ar

10.0 h	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, <i>Suipacha 570 (2000) Rosario, Argentina.</i> E-mail: villanueva@ifise-conicet.gov.ar
10.15h	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
10:30 h		Café
11.00 a 12.30 h		DISCUSIÓN Y DEFENSA ORAL DE POSTERS I Lugar: Sala de Graduados
BLOQUE I		
Coordinadores: Dr Roberto Rule y Dr. Mariano Boccia		
B1-01		EFFICACY OF AN IMMUNOMODULATOR COMPOUND OBTAINED FROM <i>Enterococcus faecalis</i> CECT7121 CELL WALL ¹ Confalonieri A, ¹ Sparo M, ^{1,2} Urbizu L, ^{1,2} Rivulgo M, ^{1,2} Sánchez Bruni S ¹ - Laboratorio de Farmacología, Facultad de Ciencias Veterinarias -UNCPBA, (B7000APA) Tandil – Argentina. ² -CONICET-. e-mail: ssanchez@vet.unicen.edu.ar
B1-02		CHARACTERISATION OF ENTEROCOCCUS RESISTANT TO VANCOMYCIN IN MEAT AND MILK DERIVED ARTISANAL FOOD. Delpech G ¹ , Schell C ² , Pourcel G ¹ , Sánchez Bruni S ^{1,3} , Tabera A. ¹ , de Luca M ² ; Basualdo J ² ; Sparo M. ^{1,2} 1-Universidad Nacional del Centro de la Provincia de Buenos Aires. Escuela Superior de Ciencias de la Salud. 2-Universidad Nacional de La Plata. Facultad de Ciencias Médicas. 3- CONICET e-mail: monicasparo@speedy.com.ar
B1-03		MULTIDOSE PHARMACOKINETIC STUDY OF AZITHROMYCIN IN PNEUMONIC FOALS ^{1,3} Rivulgo V.M, ¹ Fumuso E., ¹ Sparo M., ^{2,3} Landoni F., ^{1,3} Sanchez Bruni. S. 1.Facultad de Ciencias Veterinarias,UNCPBA. Tandil (B7000APA)-2. Facultad de Ciencias Veterinarias, UNLP.-3.CONICET.e-mail: ssanchez@vet.unicen.edu.ar
B1-04		EVALUATION OF THE FLUBENDAZOLE-NITAZOXANIDE COMBINATION AGAINST CYSTIC ECHINOCOCCOSIS IN MICE Ceballos L ¹ , Elissondo C ² , Denegri G ² , Sanchez Bruni S ¹ , Lanusse C ¹ , Alvarez L ¹ ¹ Lab. Farmacología, FCV, UNCPBA; ² CONICET; ³ Lab. Zoonosis Parasitarias, FCEyN, UNMdP. E-mail: ceballos@vet.unicen.edu.ar
B1-05		IN VITRO CEPHALEXIN ACTIVITY ON <i>Escherichia coli</i> STRAINS IN BHI, CANINE SERUM AND URINE USING A DYNAMIC MODEL Picco, E.; Cerra, M.; Michel, P.; Stiefel, S.; Formentini, E. Cátedra de Farmacología, Facultad de Ciencias Veterinarias UNL Kreder 2805 (3080) Esperanza e-mail eforment@fcv.unl.edu.ar
B1-06		IN VITRO ACTIVITY OF TULATHROMYCIN ON <i>Staphylococcus aureus</i>; EFFECT OF pH, INOCULUM SIZE AND BOVINE SERUM Picco, E.; Baroni, E.; Delgado, A.; Fernández, H.; Formentini, E. Cátedra de Farmacología, Facultad de Ciencias Veterinarias UNL Kreder 2805 (3080) Esperanza e-mail eforment@fcv.unl.edu.ar
B1-07		IN VITRO EFFECT OF THE REDUCED FLUBENDAZOLE METABOLITE AGAINST <i>ECHINOCOCCUS GRANULOSUS</i> PROTOSCOLECES Elissondo, M.C. ^{1,2} , Ceballos, L. ^{3,2} , Alvarez, L. ^{3,2} , Sánchez Bruni, S. ^{3,2} , Lanusse, C. ^{3,2} , Denegri, G. ^{1,2} ¹ Lab. Zoonosis Parasitarias, FCEyN, UNMdP; Argentina. ; ² CONICET; ³ Lab. Farmacología, FCV, UNCPBA. E-mail: mceliss@mdp.edu.r
B1-08		IN VITRO ANTIMICROBIAL SUSCEPTIBILITY TEST OF <i>Paenibacillus larvae</i> ISOLATED FROM DISEASE HONEYBEES IN BUENOS AIRES PROVINCE. Huber, B.; Quintero, M.; Marchetti, M.L.; Errecalde, J.; Mestorino, N. Cátedra de Farmacología. Facultad de Cs. Veterinarias. Universidad Nacional de La Plata. CC 296, 1900 La Plata. e-mail: barhuber@gmail.com

B1-09	ANTIMICROBIAL RESISTANCE IN COMMERCIAL FARMS OF BUENOS AIRES FROM FAECAL SAMPLES USING <i>Escherichia coli</i> AS AN INDICATOR Marchetti, M.L., Lucas M., Lambertini, A., Quintero, M., Errecalde J., Mestorino, N. Cátedra de Farmacología. Facultad de Ciencias Veterinarias. UNLP, 60 y 118, CC 296, 1900. La Plata, Bs.As, Argentina. mlauramarchetti@yahoo.com.ar
B1-10	EFFECT OF pH ON THE ANTIBACTERIAL ACTIVITY OF DANOFLOXACIN AGAINST <i>Staphylococcus aureus</i> Moncada Cárdenas, L.A.; Daniele M; Quintero M.; Errecalde, J.O.; Mestorino, N. Cátedra de Farmacología, Facultad de Ciencias Veterinarias, UNLP, 60 y 118 CC 296, 1900 La Plata. e-mail noram@fcv.unlp.edu.ar; jerrecal@fcv.unlp.edu.ar
B1-11	ALTERATIONS IN THE BACTERIAL MEMBRANE INTEGRITY INDUCED BY EU-CI-OFLO ENHANCE THE BACTERICIDAL ACTION OF OFLOXACIN. Romero V ¹ ., Sanchez N ¹ ., Pons, P ³ ., Bocco, J.L ² ., Manzo R ¹ ., Alovero F ¹ . Dptos. de ¹ Farmacia y ² Bioquímica Clínica, FCQ y ³ Centro de Microscopía Electrónica, FCM; UNC. Cdad Universitaria 5016. Córdoba. Argentina. E-mail: fallover@fcq.unc.edu.ar
B1-12	HEMATOLOGICAL AND BIOCHEMICAL PROFILE OF TRIFLURALIN-TREATED GOATS Villagra S ¹ , Manilla G ² , Lacchini R ² , Zaidenberg A ^{1,3} , Martins E ¹ , Rule R ^{3,4} ¹ IDIP CICPBA “Dr. Fernando Viteri”; ² Zootecnia, FCA; ³ Farmacología, FCM UNLP; ⁴ CIC PBA. Calle 60 y 120, 1900, La Plata. sergionivillagra@yahoo.com.ar
B1-13	LEVEL OF TUMOR NECROSIS FACTOR ALFA (TNF)- α IN SEPSIS. Ricarte Bratti, JP, Montrull, HL and Brizuela NY. Dpto. de Farmacología. FCM. Universidad Nacional de Córdoba. Santa Rosa 1085. Córdoba, Argentina jpricarte@yahoo.com.ar
BLOQUE II	
Coordinadores: Dra Susana Gorzalczany, Dr Gabriel Orce	
B2-14	ANTIPLIFERATIVE ACTION OF LIMONENE ON A LYMPHOMA CELL LINE: RELATION BETWEEN NITRIC OXIDE AND REACTIVE SPECIES OF OXYGEN Micucci P; Davicino R; Ferraro G and Anesini C. Instituto de Química y Metabolismo del Fármaco (IQUIMEFA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Junín 956, 2° piso 1113. Buenos Aires, Argentina. E-mail: canesini@yahoo.com.ar
B2-15	“IN VITRO” COMPARATIVE EFFECT OF AN AQUEOUS EXTRACT OF <i>LARREA DIVARICATA</i> CAV. AND NDGA ON H₂O₂ METABOLISM OF NORMAL RATS SUBMANDIBULAR GLANDS. Turner S, Zettler G, Davicino R and Anesini C. Instituto de Química y Metabolismo del Fármaco (IQUIMEFA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Junín 956, 2° piso 1113. Buenos Aires, Argentina. E-mail: canesini@yahoo.com.ar
B2-16	STUDY OF DIURETIC EFFECT OF <i>Artemisia douglasiana</i> Besser IN RATS Gil L, Garcia Aseff S, Wendel G, Pelzer L. Farmacología. Fac Qca, Bioqca y Fcia, UNSL. Chacabuco y Pedernera, San Luis 5700. E-mail: aseff@unsl.edu.ar
B2-17	POTENTIAL ROLE OF OPIOID RECEPTORS ON THE EFFECTS OF HESPERIDIN AND ITS AGLYCON HESPERETIN. Loscalzo LM, Wasowski C, Marder M Instituto de Química y Físicoquímica Biológicas, Facultad de Farmacia y Bioquímica, Junín 956 (C1113AAD), Buenos Aires, Argentina. e-mail: mmarder@qb.ffyb.uba.ar
B2-18	SPRAY DRYING OF <i>RHAMNUS PURSHIANA</i> EXTRACT FOR DIRECT COMPRESSION AND EVALUATION OF LAXATIVE EFFECT ^{1,2} Gallo L., ² Bucciarelli A., ³ Bianchi M., ² Skliar M., ¹ Allemandi D. ¹ Dpto.de Farmacia. Univ. Nac. de Córdoba., (5000) Córdoba. ² Dpto.de B., B. y Farmacia., San Juan 670. ³ Dpto.de Ing. Qca., La Carrindanga Km.7. ²⁻³ Univ. Nac. del Sur (8000) Ba. Bca, Bs. As. CONICET. E-mail: loreana.gallo@uns.edu.ar

B2-19	<p>EFFECT ON GASTRIC ACID SECRETION OF METHANOLIC EXTRACT OF <i>LARREA DIVARICATA</i> CAV IN RAT Pedernera AM¹, Guardia T¹, Guardia Calderón CE², Pelzer LE¹ ¹Farmacología, ²Bromatología. Fac Qca, Bqca y Fcia Univ Nac San Luis. 5.700 San Luis. e- mail: tguardia@unsl.edu.ar</p>
B2-20	<p>ANTIOXIDANT ACTIVITY AND TOTAL PHENOLIC CONTENT OF 21 ARGENTINEAN MEDICINAL PLANT EXTRACTS. Tournier, H., Fioravanti, D., Dadé, M. and Schinella, G. Cátedra de Farmacología Básica. Facultad de Cs. Médicas, UNLP- CIC Pcia de Bs As, La Plata, Argentina. E-mail: schinell@uv.es</p>
B2-21	<p>BIOGUIDED PURIFICATION AND PHARMACOLOGICAL CHARACTERIZATION OF NEUROACTIVE COMPOUNDS PRESENT IN <i>ALOYSIA VIRGATA</i>. Wasowski C., Marder M. IQUIFIB (UBA-CONICET), Facultad de Farmacia y Bioquímica, Junín 956 (C1113AAD), Buenos Aires, Argentina. mmarder@qb.ffyb.uba.ar</p>
B2-22	<p>GASTROINTESTINAL EFFECTS OF <i>Solidago chilensis</i> AND DEVELOPMENT OF A DRY PLANT EXTRACT WITH ADEQUATE PHYSICO-MECHANICAL PROPERTIES Bucciarelli A, Gallo L, Milczakowsky MC, Skliar MI. Dpto. de Biología, Bioquímica y Farmacia, San Juan 670, UNS, (8000) Bahía Blanca. E-mail: mskliar@uns.edu.ar</p>
B2-23	<p>N VITRO ANTIMICROBIAL ACTIVITY OF PROPOLIS EXTRACTS AGAINST MICROORGANISMS ISOLATED FROM THE EXTERNAL AUDITORY CANAL OF CANINE ¹Lozina, L.; ¹Peichoto, M.E., ²Granero, G., ¹Acosta O. ¹Facultad de Ciencias Veterinarias - UNNE. Sgto. Cabral 2139 (3400) Corrientes, Argentina e-mail: llozina@vet.unne.edu.ar ² Facultad de Ciencias Químicas. UNC, Córdoba, Argentina</p>
B2-24	<p>EFFECTS OF THE PHYTOESTROGEN GENISTEINE ON THE ISCHEMIA-REPERFUSION IN ISOLATED GUINEA-PIG HEARTS. Colareda, G., Ragone, M.I., Consolini, A.E. Cátedra de Farmacología, Dpto Cs. Biológicas, Fac. Cs Exactas, UNLP, La Plata, Argentina. dinamia@biol.unlp.edu.ar</p>
B2-25	<p>THE ANTISPASMODIC EFFECTS OF <i>ALOYSIA POLYSTACHYA</i> AND <i>A. GRATISSIMA</i> TINCTURES ARE NOT DUE TO K⁺ CHANNELS ACTIVATION NOR CA²⁺ CHANNELS INHIBITION ON ISOLATED RAT INTESTINE. Berardi, A. and Consolini, A.E Cátedra de Farmacología, Área Farmacia, Dpto Cs. Biológicas, Fac. Cs Exactas, UNLP. La Plata, Arg. dinamia@biol.unlp.edu.ar</p>
B2-26	<p>ANTIINFLAMMATORY ACTIVITY OF A PARTIALLY PURIFIED EXTRACT FROM <i>Bromelia hieronymi</i> FRUITS Errasti ME¹, Bruno MA¹, Rotelli AE², Caffini NO¹, Pelzer LE². ¹LIProVe, Dpto Cs Biológicas, FCE, U.N. de La Plata, 115 y 47, (1900) La Plata, Argentina. ²Lab. de Farmacología, FQByF, U.N. de San Luis, Chacabuco y Pedernera, (5700) San Luis, Argentina. E-mail: arotelli@unsl.edu.ar.</p>
B2-27	<p>EFFECTS OF <i>Medicago sativa</i> ETHANOL EXTRACT ON MICE AND RAT INTESTINAL TRACT Wendel G^a, Toso R^b, Boeirs M^b, Mitjans N^a, Pelzer L^a. ^aFarmacología, FQBF, UNSL; ^bCentro de Investigación y Desarrollo de Fármacos, FCV, UNLPam. Chacabuco y Pedernera. San Luis. 5700. E-mail: gwendel@unsl.edu.ar</p>
B2-28	<p><i>URTICA CIRCULARIS</i>: ANTINOCICEPTIVE AND ANTI-INFLAMMATORY EFFECTS ON EXPERIMENTAL MODELS Marrassini C.¹, Miño J.², Acevedo C.², Ferraro G.¹ and Gorzalczany S.², ¹Cátedra de Farmacognosia, ²Cátedra de Farmacología IQUIMEFA (UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Junín 956 (1113), Buenos Aires, Argentina. sgorza@ffyb.uba.ar</p>
12:30-13:30 h	<p>ASAMBLEA ANUAL SAFE Lugar: Sala de Graduados</p>
13:30-14:00 h	<p>Almuerzo libre</p>

14:00-15:00 h	<p>C2</p> <p style="text-align: center;">CONFERENCIA PLENARIA II</p> <p>Dr. Segura-Aguilar (Profesor Titular de Farmacología Molecular y Clínica de la Facultad de Medicina, Universidad de Chile)</p> <p style="text-align: center;">“Efectos neurotóxicos del aminocromo y sus posibles implicancias en la enfermedad de Parkinson”</p> <p>Coordinador: Dr Juan Carlos Piola</p> <p>Lugar: Sala de Graduados</p>
15:00-17:00 h	<p>S1-1</p> <p style="text-align: center;">SIMPOSIO I</p> <p>"Rigor y ética en Investigación Clínica" Coordinadores: Dres. Marcela Rebuerto y Carlos Reyes Toso</p> <p>-Dr. Oscar Bottasso (Instituto de Inmunología de la Facultad de Medicina, UNR) “Fuentes de error en investigación clínica. Estrategias de manejo”</p> <p>-Dra. Miryam Pires (Secretaria de Ciencia y Tecnología de la Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR) “Ensayos clínicos: aspectos éticos”</p> <p>-Dr. Nelson Stürtz (Director Técnico Farmacéutico de la Planta Piloto de Medicamentos de la Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR) “Medicamentos huérfanos: Experiencia piloto”</p>
17:00-17:30 h	Café
17.30 a 18.30 h	<p>C3</p> <p style="text-align: center;">CONFERENCIA PLENARIA III</p> <p>Prof Dr Luis María Zieher (Ex Profesor Titular de Farmacología, Facultad de Medicina-UBA, Director de la Maestría en Psiconeurofarmacología de la Universidad Favaloro. Investigador Principal, CONICET. Presidente del Comité Independiente de Etica para Ensayos en Farmacología Clínica)</p> <p style="text-align: center;">"Desarrollo de nuevos antidepresivos: Problemas en la investigación básica y clínica".</p> <p>Coordinador: Dra Gabriela Acosta Lugar: Sala de Graduados</p>
18:30-20:30 h	<p style="text-align: center;">DISCUSIÓN Y DEFENSA ORAL DE POSTERS II</p> <p>Lugar: Aula 1 y/o 2</p>
<p>BLOQUE III</p> <p>Coordinadores: Graciela Balerio, Carlos Reyes Toso</p>	
B3-29	<p>EFFECT OF VANADIUM ON ANXIETY-LIKE BEHAVIOR IN WISTAR RATS Cuesta S., Cholic V.¹ and García G. Area Morfología. ¹LATOEX. Facultad de Ciencias Bioquímicas y Farmacéuticas. UNR. Suipacha 570. Rosario. Santa Fe. Argentina. ggarcia@fbioyf.unr.edu.ar</p>
B3-30	<p>ROS GENERATION AND ANTIOXIDANT STATUS IN RATS' BRAIN AREAS AFTER EXPOSURE TO SODIUM METAVANADATE Cuesta S., Frances D¹., Pochettino A.², Quiroga A¹, Martínez A., García G. Area Morfología. ¹IFISE. ²LATOEX. Facultad de Ciencias Bioquímicas y Farmacéuticas. UNR. Suipacha 570. Rosario. Santa Fe. Argentina</p>
B3-31	<p>WNT FACTORS AND NEURONAL POLARITY: INVOLVEMENT OF PI3K PATHWAY. Bernis, M.E. Eugenia; Quiroga, S. and *Rosso, S.B. CIQUIBIC- CONICET. Dpto. Química Biológica. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba. *Dirección actual: Laboratorio de Toxicología Experimental. Facultad de Ciencias Bioquímicas y Farmacéuticas. Universidad Nacional de Rosario. Argentina.</p>

B3-32	IMPACT OF LOUD NOISE ON ASSOCIATIVE MEMORY. RAT HIPPOCAMPAL NEURONAL ALTERATION AND OXIDATIVE STATUS IMBALANCE. Uran ¹ S.L., Aón ² L., Caceres ¹ L.G., Capani ² F., Guelman ¹ L.R. ¹ Facultad de Medicina (UBA), CEFyBO-CONICET. ² Instituto de Investigaciones Cardiológicas “Prof. Dr. Alberto C. Taquini” ININCA-UBA-CONICET. <i>Paraguay 2155, Bs As, Argentina. E-mail: whooma@hotmail.com</i>
B3-33	PARTICIPATION OF THE OXIDATIVE STRESS IN THE IMMUNE ALTERATION IN BALB/C AND C57 DIABETIC MICE. Rubinstein R, Albarracín R, Genaro AM y Wald MR CEFyBO- UBA-CONICET. Paraguay 2155. Bs As. Argentina. roxirubin@yahoo.com.ar
B3-34	ANTICONVULSANT SULFAMIDES WITH AFFINITY FOR THE GABA_A RECEPTOR AND ANXIOLYTIC ACTIVITY IN MICE. Wasowski C. ^a , Gavernet L. ^b , Barrios I.A. ^b , Bruno-Blanch L.E. ^b , Marder M. ^a ^a IQUIFIB (UBA-CONICET), Facultad de Farmacia y Bioquímica, Junín 956 (C1113AAD), Buenos Aires, Argentina. ^b Química Medicinal, Departamento de Ciencias Biológicas, UNLP, calle 47 y 115 (B1900BJW), La Plata, Argentina. mmarder@qb.ffyb.uba.ar
B3-35	MONOSODIUM GLUTAMATE (MSG): NEONATAL HYPOTHALAMIC IN MALE RATS Cardamone L, Mahieu S, Millen N, Contini M de C. LIFE. FBCB. UNL. Santa Fe. Argentina. Ciudad Universitaria. Paraje El Pozo. CC 242. mcontini@fbc.unl.edu.ar
B3-36	ACUTE AND CHRONIC POSTNATAL STRESS ALTERS GLUTAMATE TRANSPORTER AND BEHAVIORAL STRESS RESPONSE. Odeón MM, Salatino, AE Orta, ML Acosta. GB ININFA- (CONICET-UBA). Junín 956. 5 th floor, C1113AAD, Buenos Aires. E-mail: merodeon@hotmail.com
B3-37	HIGH AFFINITY [³H]-OUABAIN BINDING TO CEREBRAL CORTEX MEMBRANES. CHARACTERIZATION OF INHIBITORY EFFECT OF PEPTIDE NEUROTENSIN Rosin C., López Ordieres, M.G., Rodríguez de Loes Arnaiz, G. Inst Biol Cel y Neuroc “Prof. E. De Robertis”, Fac Med, and Cátedra de Farmacol, Fac Farm y Bioq, UBA. <i>Paraguay 2155, 1121-Buenos Aires, Argentina.</i> E-mail: grodrig@ffyb.uba.ar
B3-38	PREVIOUS STRESS ATTENUATES THE SUCCEPTIBILITY TO MIDAZOLAM’S DISRUPTIVE EFFECT ON FEAR MEMORY RECONSOLIDATION: INLUENCE OF D-CYCLOSERINE. Bustos SG ⁽¹⁾ , Giachero M ⁽¹⁾ , Maldonado H, ⁽²⁾ and Molina V ⁽¹⁾ . ⁽¹⁾ IFEC CONICET. UNC. Cdad Universitaria. 5000 Cba. ⁽²⁾ Lab. de Neurobiología de la Memoria..IFIBYNE-CONICET. Facultad de Ciencias Exactas y Naturales. UBA. e-mail: sgbustosvillegas@hotmail.com
BLOQUE IV	
Coordinadores: Fabiana Landoni; Stella Celuch	
B4-39	PHARMACOKINETIC STUDY OF TOPOTECAN IN A SWINE MODEL AFTER INTRA-ARTERIAL (OPHTALMIC) ADMINISTRATION. POTENTIAL IMPLICATION IN RETINOBLASTOMA TREATMENT. Schaiquevich P*, Lipsich J., Sierre S., Buitargo E., Asprea M., Fandiño A., Bramuglia GB. and Chantada G. CONICET. Hosp.Pediatría JP Garrahan. Combate de los Pozos 1991, Buenos Aires, Argentina. paula.schaiquevich@gmail.com*
B4-40	CEPHALEXIN TISSUE CONCENTRATIONS AFTER INTRAVENOUS, INTRAMUSCULAR AND SUBCUTANEOUS ADMINISTRATION TO DOMESTIC CATS. Albarellos, G.; Montoya, L.; Quaine, P.; Velo, M.; Lupi, M.; Landoni, M. FCV UBA Chorroarín 280, Cap. Fed. (1427); FCV UNLP Calle 60 y 118, prov. Bs As. (296). E-mail: albarell@fvvet.uba.ar (V002, UBACyT 2008-2010)
B4-41	RENAL EXPRESSION AND URINARY EXCRETION OF OAT5 IN RATS WITH ACUTE BILIARY OBSTRUCTION (ABO). Brandoni A., Torres A.M. Farmacología. Fac. Cs. Bioq. y Farm. U.N.R. Suipacha 531. (2000) Rosario. CONICET.
B4-42	NADC1 RENAL EXPRESSION AND URINARY EXCRETION IN RATS EXPOSED TO MERCURIC CHLORIDE (HGCL₂). Di Giusto G., Torres A. M. Area Farmacología, Fac. Cs. Bioq. y Farm., UNR. CONICET. Suipacha 531, (2000) Rosario. E-mail: giseladg@hotmail.com

B4-43	INDUCTION BY ETHANOL OF NIFURTIMOX AND BENZNIDAZOLE BIOTRANSFORMATION CATALYZED BY RAT HEPATIC MICROSOMES. Bartel LC, Montalto de Mecca M, Castro JA Centro de Investigaciones Toxicológicas (CEITOX) CITEFA-CONICET. J B de La Salle 4397. Villa Martelli, Prov Bs As. jcastro@citefa.gov.ar
B4-44	THERAPEUTIC NIFURTIMOX AND BENZNIDAZOLE MONITORING IN BLOOD Bulffer, R.F., Fanelli, S.L., Castro, J. A. Centro de Investigaciones Toxicológicas (CEITOX) CITEFA-CONICET. J B de La Salle 4397. Villa Martelli, Prov. Bs. As. jcastro@citefa.gov.ar
B4-45	NANOSTRUCTURES BASED ON ALKYL VITAMIN C DERIVATIVES (ASC_n) AND EX VIVO SKIN PERMEATION. Saino V ^a , Chetoni ^b P, Monti D ^b , Burgalassi S ^b , Tampucci S ^b , Palma S ^a and Allemandi D ^a . ^a Departamento de Farmacia, Fac. de Ciencias Químicas, Haya de la Torre and Medina Allende, UNC, Córdoba, Argentina. ^b Dipartimento di Scienze Farmaceutiche, Via Bonanno 33, University of Pisa, Pisa, Italy. e-mail: vsaino@gmail.com
B4-46	PHARMACOKINETICS OF CEPHALEXIN IN NON LACTATING AND LACTATING GOATS Ambros, L.; Tarragona, L.; Monfrinotti, A.; Prados, A.P.; Hallu, R.; Rebuelto, M. (UBACYT V 026) Farmacología FCV, UBA. Chorroarín 280 (1427), Buenos Aires. e-mail: ambros@fvet.uba.ar
B4-47	PLASMA DISPOSITION KINETICS OF ALBENDAZOLE AND ITS METABOLITES IN LAYING HENS Bistoletti M, Moreno L, Ferreira R, Alvarez L, Lanusse C Laboratorio de Farmacología, Facultad de Ciencias Veterinarias, UNCPBA, Tandil; CONICET, Argentina.
B4-48	PHARMACOKINETICS OF CEFQUINOME IN LLAMAS (<i>Lama glama</i>) AFTER AN INTRAVENOUS ADMINISTRATION Himelfarb M ¹ , Lorenzutti M ¹ , Zarazaga P ¹ , Aguilar S ² , Litterio NJ ¹ , Boggio JC ¹ . ¹ Cát de Farmacología y Toxicología. ² Cát Clínica de Grandes Animales. Universidad Católica de Córdoba. Ob. Trejo 323. 5000. Córdoba, Argentina. martinhim@hotmail.com
B4-49	PHARMACOKIETIC INTERACTION BETWEEN MARBOFLOXACIN AND FLUNIXIN MEGLUMINE OR DEXAMETHASONE, AFTER INTRAVENOUS ADMINISTRATION IN GOATS. Lorenzutti M ¹ , Himelfarb M ¹ , Zarazaga P ¹ , Auad J ² , Boggio JC ¹ , Litterio NJ ¹ . ¹ Universidad Católica de Córdoba. Cát. de Farmacología y Toxicología. ² Cat. Enf Infecciosas. Obispo Trejo 323. 5000. Córdoba. Argentina. matiaslorenzutti@hotmail.com .
B4-50	ABSENCE OF PHARMACOKINETIC INTERACTION BETWEEN MELOXICAM AND PHENOBARBITAL IN HEALTHY DOGS. Montoya, L.; Kreil, V.; Monfrinotti, A.; Tarragona, L.; Ambros, L.; Rebuelto, M. Farmacología. Facultad de Ciencias Veterinarias, BA. Chorroarín 280. (1427) Buenos Aires, Argentina. lmontoya@fvet.uba.ar .
BLOQUE V	
Coordinadores: Dras, Damasia Becú, Susana Zachino	
B5-51	INCREASE NITRIC OXIDE SYNTHASE ACTIVITY IN PAROTID GLAND, FROM RATS WITH EXPERIMENTAL PERIODONTITIS. Miozza V, Borda E, Sterin Borda L, Busch L. Cátedra de Farmacología. Facultad de Odontología. U BA.
B5-52	^{99m}Tc-SESTAMIBI UPTAKE FOR THE DIAGNOSIS AND FOLLOW-UP OF SKIN TUMORS INDUCED IN MICE. Collia N ¹ , Salgueiro MJ ¹ , Tesán F ¹ , Palmieri M ² , Durán H ³ , Medina V ¹ , Leonardi N ^{1,4} , Goldman C ¹ , Boccio J ¹ y Zubillaga M ¹ . ¹ FFyB, UBA; ² FCEN, UBA; ³ CONICET, USAM, CNEA; ⁴ Laboratorios BACON SAIC, Argentina. Junín 956 Piso Bajo – (1113) CABA. jsalgueiro@ffyb.uba.ar
B5-53	APOPTOTIC ACTIVITY OF ISOESPINTANOL AND RELATED COMPOUNDS IN HUMAN POLYMORPHONUCLEAR CELLS Dade, M ¹ ; Rojano, B ² ; Tournier, H ¹ ; Schinella, G ¹ . ¹ Cátedra de Farmacología Básica. Facultad de Cs Médicas-UNLP. CIC-Pcia. Buenos Aires, La Plata, Argentina. ² Lab. de Ciencias de los Alimentos. Universidad Nacional de Colombia (sede Medellín), Colombia. E-mail: martindade26@hotmail.com.ar

B5-54	EFFECT OF PRENATAL ACE INHIBITION ON MEDIATORS OF APOPTOTIC SIGNALLING DURING POSTNATAL LUNG DEVELOPMENT Capelari DN, Fuentes LB, Ciuffo GM. Area de Farmacología. IMIBIO SL – CONICET. UNSL. 5700. San Luis. E-mail: lfuen@unsl.edu.ar
B5-55	STRUCTURAL VARIATION OF QUERCETIN IMPROVES INHIBITORY ACTIVITY ON LPS-STIMULATED INDUCIBLE NITRIC OXIDE SYNTHASE (iNOS) EXPRESSION IN J774 CELLS Ortega, M.G ¹ , Saragusti, A. ² Chiabrando, G. ² y Cabrera, J. ¹ ¹ Dpto. de Farmacia. Fac. de Cs. Qcas. UNC-IMBIV-CONICET ² Dpto de Bioquímica Clínica .Fac. de Cs. Qcas. UNC. CIBICI-CONICET. Medina Allende y Haya de la Torre. Ciudad Universitaria, Córdoba 5000 gortega@fcq.unc.edu.ar
B5-56	EFFECT OF PRENATAL STRESS ON LYMPHOCYTE PROLIFERATIVE RESPONSE. PARTICIPATION OF CATECHOLAMINES AND CORTICOSTERONA. Pascuán C, Wald M, Palumbo ML and Genaro AM. CEFYO-Dto Farmacología, CONICET-UBA. Facultad de Medicina. Paraguay 2155. ceciliapascuan@gmail.com
B5-57	ASSOCIATION OF STRESS, SLEEP, HABITS WITH FIBROMYALGIA Castagnino J, Rodríguez López E, Garce S, , Fleitas Rumak P, Maritano J, Steimberg J, Lipszyc P, Genaro AM, Scublinsky D. Cátedra I Farmacología, Facultad Medicina. U.B.A. Paraguay 2155, piso 15, Buenos Aires, Argentina. jcastagnino@hotmail.com
B5-58	UP REGULATION OF NIACINE RECEPTOR IN MOUSE MACROPHAGES BY IN VIVO LPS INOCULATION. POTENTIAL ROLE IN LPS-INDUCED ENDOTOXIC SHOCK. Zorrilla Zubilete M, Cremaschi G, Genaro A, Wald M, Lipszyc P. School of Med, Bs As, Argentina. mariazorrillaz@gmail.com
B5-59	VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN RAT HEART DEVELOPMENT García LE, Capelari DN, Ciuffo GM, Fuentes LB. Área de Farmacología. Área de Biología Molecular. UNSL. San Luis, Argentina. E-mail: lfuen@unsl.edu.ar
BLOQUE VI	
Coordinadores: Dra Alicia Consolini, Dr Guillermo Virkel	
B6-60	EFFECT OF α-LIPOIC ACID ADMINISTRATION ON ACETYLCHOLINE-INDUCED AORTIC RING RELAXATION IN FRUCTOSE FED RATS. Linares LM, Wallinger ML, Reyes Toso, ML, Vázquez, M Rosón, M, Planells F, <u>Reyes Toso CF</u> . Departamento de Fisiología. Facultad de Medicina. UBA. Paraguay 2155 Piso 7. Bs As. Argentina. creyesto@fmed.uba.ar
B6-61	VITAMIN E ADMINISTRATION PARTIALLY RESTORES METABOLIC VARIABLES IN FRUCTOSE FED RATS. <u>Wallinger ML</u> , Linares LM, Witriw, AM, Reyes Toso ML, Ricci CR, Reyes Toso CF. Departamento de Fisiología. Facultad de Medicina. UBA. Paraguay 2155 Piso 7. Bs As. Argentina. creyesto@fmed.uba.ar
B6-62	USE OF ANTIHYPERTENSIVE DRUGS AND PHARMACOLOGICAL INTERACTIONS IN DIABETIC PATIENTS IN A PUBLIC HOSPITAL FROM ROSARIO Marzi M, Odetto C, Bertero J, Nuñez M, Quaglia N. Area Farmacol. Facultad de Cs Bioq y Farm. UNR. Suipacha 531. 2000 Rosario- mail: nquaglia@fbioyf.unr.edu.ar
B6-63	USE OF HYPOGLYCEMIC DRUGS IN A PUBLIC HOSPITAL FROM ROSARIO, SANTA FE. Marzi M, Bertero J, Odetto C, Cuis N, Nuñez M, Quaglia N. Area Farmacol. Facultad de Cs Bioq y Farm. UNR. Suipacha 531. 2000 Rosario- mail: nquaglia@fbioyf.unr.edu.ar
B6-64	FUNCTIONAL RELEVANCE OF ENDOTHELIAL ANGIOTENSIN-CONVERTING ENZYME (ACE) IN BIOLOGICAL INACTIVATION OF BRADYKININ (BK) IN HUMAN UMBILICAL VEIN (HUV). Nowak W., Ireizo J., Daich M., Migliore D., Rothlin R. 3° Cátedra de Farmacología. Facultad de Medicina (UBA). Paraguay 2155. Piso 9. CP 1121. farmaco3@fmed.uba.ar

B6-65	EFFECT OF DAILY EXPOSURE TO AROMATIC HYDROCARBONS ON FOLLICULAR GROWTH IN RATS Barreiro KA, Di Yorío MP, Artillo Guida RD, Faletti AG CEFYBO-CONICET, Facultad de Medicina-Universidad de Buenos Aires. Paraguay 2155, CABA. agfaletti@yahoo.com.ar
B6-66	ANTIHYPERTENSIVE DRUG THERAPY IN ADULT PATIENTS Verdugo R, Wendel G, Trujillo L, Fuentes L. Farmacología.UNSL.5700.San Luis. E-mail: lfuen@unsl.edu.ar
B6-67	EFFECT OF XANTHATIN ON GASTRIC MUCOSAL LESIONS INDUCED BY COMPOUND 48/80 IN RATS Maria AO ^a , Wendel GH ^a , Favier LS ^b , Alvarez ME ^b , Piezzi RS ^c , Tonn CE ^b , Pelzer L ^a , Penissi AB ^c . ^a IHEM-CONICET, Universidad Nacional de Cuyo. Áreas de ^a Farmacología y ^b Química Orgánica. Universidad Nacional de San Luis. Chacabuco y Pedernera. 5700. San Luis. Argentina. E-mail: alemaria@unsl.edu.ar
B6-68	2,4-DICHLOROPHENOXYACETIC ACID (2,4-D) EFFECTS ON THE PUP RAT BRAINS. MEASURE OF HYDROXYL RADICAL. Biolatto, S.; Pochettino, A.; Duffard, R. and Evangelista, A. LATOEX – Facultad de Ciencias. Bioquímicas y Farmacéuticas UNR – Suipacha 531 - 2000 - Rosario. sbiolatto@gmail.com
B6-69	SEMI-QUANTIFICATION OF ANDROGEN RECEPTOR MRNA AND DETERMINATION OF HORMONE LEVELS IN MALE RATS BY A PRE-AND POSTNATAL EXPOSURE TO 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D). Pochettino, A.; Hapon, MB. (*); Jahn, G.(*); Duffard, R.; Evangelista, A. LATOEX – Facultad de Ciencias. Bioquímicas y Farmacéuticas UNR – Suipacha 531 - 2000 - Rosario. - (*JIMBECU – CRICYT (CONICET) – MENDOZA aristidespochettino@gmail.com
B6-70	EFFECTS OF SWANSONINA ISOLATED FROM IPOMOEA CARNEA ON GUINEA PIGS Cholich L, García E, Teibler G, Lértora J, Acosta O. Cátedra de Farmacología, Facultad de Ciencias Veterinarias, Universidad Nacional del Nordeste, Sargento Cabral 2139, Corrientes 3400. lucianacholic@hotmail.com
Jueves 26 de Noviembre de 2009 Lugar: Sede central de la Facultad de Ciencias Bioquímicas y Farmacéuticas. Suipacha 531	
8:30-10:00 h	COMUNICACIONES ORALES III Coordinadores: Dres. Ricardo Furlan y Carlos Taira Lugar: Sala de Graduados
8.30	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
8.45	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. E-mail: anabelbrandoni@gmail.com.*Universidad de Trieste, Italia.
9.00	OIII-17 COPAXONE REVERTED CHRONIC STRESS-INDUCED ALTERATIONS IN BEHAVIOUR AND TH1/TH2 BALANCE IN BALB/C MICE. Palumbo ML, Zorrilla-Zubilete M, Cremaschi GA and Genaro AM. CEFyBO-CONICET-UBA, 1° Cátedra de Farmacología, Fac. Medicina, U.B.A. Paraguay 2155, Piso 15, Bs As, Argentina. E-mail: molecula_21@yahoo.com.ar
9.15	OIII-18 SHIFT IN THE BAX/BCL-XL BALANCED MAY ACTIVATE CASPASE 3 AND MODULATE APOPTOSIS/NECROSIS ASSOCIATED WITH PROGRESSIVE RENAL DELETION THROUGH INOS, HSP60 AND HIF-1α IN MURINE NEPHROTIC SYNDROME. Stoyanoff T, Todaro J, Aguirre M, Juaristi J, Álvarez M, Ruiz Díaz D, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. UNNE. Moreno 1240 (3400) Corrientes. E-mail:nbrandan@med.unne.edu.ar

9.30	OIII-19	<p>GASTROPROTECTION AND ANTIMICROBIAL ACTIVITY OF <i>Lithraea molleoides</i> AGAINST <i>Helicobacter pylori</i> Garro MF^b, Dalfvo MC^a, Vega AE^a, Cortiñas TI^a, Silva HJ^a, Saad JR^c, María AO^b, Pelzer L^b. Áreas de ^aMicrobiología, ^bFarmacología y Toxicología y ^cQuímica Orgánica. Universidad Nacional de San Luis. San Luis. E-mail: alemaria@unsl.edu.ar</p>
9.45	OIII-20	<p>CHEMICAL ASSESSMENT OF THE NEW ANTIMICROBIAL PEPTIDE AP-CECT7121 ^{1,2} Urbizu, L.; ¹ Sparo, M.; ^{1,2} Virkel, G.; ^{1,2} Soraci, A.; ¹ Confalonieri, A., ^{1,2} Rivulgo M., ^{1,2} Sánchez Bruni, S ¹ Laboratorios de Farmacología y Toxicología, Facultad de Ciencias Veterinarias -UNCPBA, (B7000APA) Tandil – Argentina. ² CONICET-. e-mail: ssanchez@vet.unicen.edu.ar</p>
10:00-10:30 h		Café
10:30-12:30 h	S2-2	<p style="text-align: center;">SIMPOSIO II</p> <p>“Avances en Investigación Neurofarmacológica” Coordinadores: Dras. Adriana Torres y María Zorrilla Zubilete</p> <p>-Dra. Gabriela Acosta. (Instituto de Investigaciones Farmacológicas, ININFA, CONICET-UBA) “Efecto del estrés postnatal sobre los transportadores aminoacídrgicos”</p> <p>-Dr Víctor Molina (Prof Farmacología, Universidad Nacional de Córdoba) “Manipulación farmacológica de la reconsolidación de la memoria de miedo”</p> <p>Dra. Fernanda Blasina (Instituto de Investigaciones Biológicas Clemente Estable Montevideo, Uruguay) “Neurofarmacología de flavonoides. Perspectiva Clínica”</p> <p>Lugar: Sala de Graduados</p>
12:30-14:00 h		Almuerzo libre
14:00-15:00 h		<p style="text-align: center;">PRESENTACIÓN TÉCNICA</p> <p>Coordinador: Dr. Sergio Sánchez Bruni Dr Waldo Salazar LabChart y LabTutor, nuevas herramientas para la investigación y enseñanza de las ciencias Auspicia AD Instruments</p> <p>Lugar: Aula 3</p>
15:00-15:30 h		Café
15:30-17:30 h	S3-1	<p style="text-align: center;">SIMPOSIO III</p> <p style="text-align: center;">Calidad e higiene alimentaria: enfoque biomédico de la seguridad del consumidor</p> <p>Coordinadores: Dres. Maria Victoria Aguirre y Sergio Sánchez Bruni</p> <p>- Dra Claudia Balagué. (Facultad de Cs Bioquímicas y Farmacéuticas, UNR) “ Efectos de antibióticos y conservantes sobre cepas de <i>Escherichia coli</i> productora de Síndrome Urémico Hemolítico aisladas de alimentos”</p> <p>-Dra Mónica Sparo. (Universidad Nacional del Centro Pcia Bs As) “Control biológico de infecciones bacterianas transmitidas por alimentos”</p> <p>-Dra Alicia Faletti (CEFYBO, CONICET). “Bioacumulación de hidrocarburos aromáticos policíclicos (PAHs) en la cadena alimentaria. Efectos silenciosos”</p> <p>-Dr Jorge Errecalde. (Universidad Nacional de La Plata) ¿Es posible el uso prudente de antimicrobianos en producción animal? Impacto de los residuos químicos y el desarrollo de resistencia en Salud Humana”</p> <p>Lugar: Sala de Graduados</p>
17:00-17:30 h		Café

17:00-19:00 h	<p align="center">DISCUSIÓN Y DEFENSA ORAL DE POSTERS III</p> <p align="center">Lugar: Aula 1 y/o 2</p>
<p>BLOQUE III</p> <p>Coordinadores: Dra Graciela Balerio, Dr Carlos Reyes Toso</p>	
B3-71	<p>THE REACTIVATION OF A CONSOLIDATED FEAR MEMORY INCORPORATES NEW ADVERSIVE INFORMATION FROM A STRESSFUL SITUATION. Giachero M, Bustos SG and Molina V. IFEC-CONICET. UNC. Cdad Universitaria. 5000 Córdoba. e-mail:iachero_9@hotmail.com</p>
B3-72	<p>GLUTAMATERGIC ROL IN THE LIGHT NEUROFILAMENT DECREASE IN CA3 HIPPOCAMPAL NEURONS OF ANIMALS EXPOSED TO INESCAPABLE STRESS Cladouchos M.L., Fernández Macedo G.V., Sifonios L y Wikinski S. Instituto de Investigaciones Farmacológicas (CONICET-UBA) Junín 956 piso 5° C.A.B.A., Argentina E-mail: mlclado@ffyb.uba.ar</p>
B3-73	<p>FLUOXETINE EFFECTS ON THE ALTERED SIGNAL TRANSDUCTION OF CRF1 IN AN ANIMAL MODEL OF DEPRESSION. Fernández Macedo G.V., Sifonios L., Cladouchos M.L., Wikinski S. ININFA. Junín 956 piso 5°. Buenos Aires, Argentina. e-mail: georginafm@ffyb.uba.ar</p>
B3-74	<p>EXPLORING MODAFINIL NEUROPROTECTIVE EFFECTS ON METHAMPHETAMINE ACUTE TOXIC DOSE Bisagno V., Raineri, M., Peskin V., Urbano, F.J., Wikinski S.I. ININFA-UBA-CONICET, Junín 956, Sto. C1113, Buenos Aires, IFIBYNE-UBA-CONICET Ciudad Universitaria, C1428 Buenos Aires E-mail: ybisagno@ffvb.uba.ar</p>
B3-75	<p>EFFECTS OF EARLY ADVERSE LIFE EVENTS ON GABAERGIC NEURONS. Salatino AE, Odeón MM, Orta ML, Acosta. GB ININFA- (CONICET-UBA). Junín 956. 5th floor, C1113AAD, Buenos Aires. E-mail: adrian86@gmail.com</p>
B3-76	<p>SEX DIFFERENCES IN THE MODULATION BY BACLOFEN OF ANXIETY-LIKE BEHAVIOUR ASSOCIATED TO NICOTINE WITHDRAWAL SYNDROME Calvo M¹, Varani A¹, Induni A^{1,2} and Balerio G^{1,2} ¹ININFA (CONICET) y ²Cát. de Farmacología (FFYB, UBA) Junín 956, 5°Piso. Buenos Aires. E-mail: gbalerio@ffyb.uba.ar</p>
B3-77	<p>SEXUALLY DIMORPHIC ANXIETY-LIKE BEHAVIOR DURING MORPHINE WITHDRAWAL SYNDROME ^{1,2}Induni, A S, ¹Varani, A, ¹Machado, L, ¹Calvo, M, and ^{1,2}Balerio G. ¹ININFA (CONICET), ²Cát. de Farmacología, FFyB (UBA). Junín 956 5° piso (1113), Buenos Aires. E-mail: gbalerio@ffyb.uba.ar</p>
B3-78	<p>FLUOXETINE EFFECTS ON HIPPOCAMPAL SYNAPTIC CONNECTIVITY AND PSA-NCAM DEPENDENT REMODELLING IN AN EXPERIMENTAL MODEL OF DEPRESSION. Podestá MF, Lorenzo Lopez JR, Codagnone M, López M, Brusco A, Wikinski S, Reinés, A. Instituto de Investigaciones Farmacológicas (CONICET-UBA). Email: podestamf@ffyb.uba.ar</p>
B3-79	<p>BACLOFEN REESTABLISHES C-FOS EXPRESSION DURING NICOTINE WITHDRAWAL SYNDROME IN MICE Moutinho L¹, Induni A^{1,2}, Varani A¹ and Balerio G^{1,2} ¹ININFA (CONICET) y ²Cát. de Farmacología, FFYB (UBA) Junín 956, 5°Piso. Buenos Aires. E-mail: gbalerio@ffyb.uba.ar</p>

BLOQUE IV	
Coordinadores: Dra. Fabiana Landoni; Dra. Stella Celuch	
<u>B4-80</u>	PHARMACOKINETICS OF ORAL AMOXICILLIN AFTER METOCLOPRAMIDE ADMINISTRATION IN DOGS Rebuelto, M.; Montoya, L.; Kreil, V.; Monfrinotti, A.; Prados, A. P.; Tarragona, L.; Quaine, P.; Hallu, R. (UBACYT V 026) Farmacología, Facultad de Ciencias Veterinarias, Universidad de Buenos Aires. Chorroarín 280 (1427), Buenos Aires.e-mail: rebuelto@fvet.uba.ar
<u>B4-81</u>	PLASMA PHARMACOKINETICS AND MILK PENETRATION OF AMOXICILLIN IN LACTATING GOATS. Ambros, L.; Kreil, V.; Tarragona, L.; Veksler Hess, J.2.; Monfrinotti, A.; Brynkier, J.3 1Farmacología, 2Producción de ovinos, 3Clínica de Rumiantes Fac.Cs.Veterinarias, UBA. Chorroarín 280 (1427), Buenos Aires. e-mail: ambros@fvet.uba.ar
<u>B4-82</u>	THIOSTERIFICATION OF R-(-) FENOPROFEN ENANTIOMER IN HEALTHY CATS. AN IN VITRO STUDY. Castro, E., Soraci, A., Tapia, O., Solana, H., Fogel, F., Franci, R. Departamentos de Fisiopatología, Clínica, y Cs Biológicas, FCV, UNCPBA, Tandil, Argentina, Campus Universitario, Pje Arroyo Seco s/n. E-mail: edcast@vet.unicen.edu.ar
<u>B4-83</u>	ENHANCE OF TRASCORNEAL PERMEATION USING NOVEL EUDRAGIT-FLURBIPROFEN COMPLEXES Quinteros D., Tártara I., Palma S and Allemandi D. Depto de Farmacia, Fac. de Cs Químicas, Ciudad Universitaria, 5016.Córdoba.Arg. danielaq@fcq.unc.edu.ar
<u>B4-84</u>	IMPACT OF IVERMECTIN AND TRICLABENDAZOLE RESIDUES ON MILK PROCESSING. Iezzi, S.; Imperiale, F.; Farias, C.; Lifschitz, A.; Sallovitz, J.; Lanusse, C. Laboratorio de Farmacología, FCV-UNCPBA, Tandil, Argentina. Email: fernanda@vet.unicen.edu.ar
<u>B4-85</u>	DEVELOPMENT OF AN HPLC ASSAY TO DETERMINE CLOSANTEL IN GOAT MILK. Imperiale, F.; Farias, C.; Iezzi, S.; Sallovitz, J.; Lanusse, C. Lab. Farmacología, FCV-UNCPBA. Tandil, Argentina. E-mail: fernanda@vet.unicen.edu.ar
<u>B4-86</u>	INTERACTION BETWEEN THE EFFLUX TRANSPORTER BCRP (ABCG2) AND THE ANTI-HIV DRUG EFAVIRENZ IN RATS. Peroni RN ^{1,2} , Di Gennaro SS ¹ , Hocht C ² , Chiappetta DA ³ , Sosnik A ³ , Rubio MC ^{1,2} , Bramuglia GF ² . ¹ ININFA (CONICET-UBA); ² Farmacología (FFyB-UBA); ³ Farmacotecnia (FFyB-UBA) rperoni@ffyb.uba.ar
<u>B4-87</u>	PERMEABILITY STUDY OF CIPROFLOXACIN AND CIPROFLOXACIN ALUMINUM COMPLEX THROUGH THE RAT SMALL INTESTINE IN SIDE-BY-SIDE DIFFUSION CHAMBERS Guzman M ¹ , Ballent M ² , Lifschitz A ² , Lanusse C. ² , Breda S ¹ , Manzo R ¹ , Olivera M ¹ ¹ Depto de Farmacia, Facultad de Ciencias Químicas, UNC, Córdoba, Argentina. meoliver@fcq.unc.edu.ar
<u>B4-88</u>	ENHANCED ACTIVITY OF GLUTATHION-S-TRANSFERASE IN THE FLUKE FASCIOLA HEPATICA RESISTANT AT TRICLABENDAZOLE Scarcella S ¹ , Alzola P ² , Alzola R., Solana H ³ . ¹ Becaria ANPCyT, ² Becaria CIC BA, ³ Prof. Principal CIC BA Lab. Biol. Cel. y Mol. Dpto. Cs. Biológicas – FCV-UNCPBA (7000) Tandil-ARGENTINA
<u>B4-89</u>	HEPATIC CYTOCHROME P450 AND FLAVIN-CONTAINING MONOOXYGENASE METABOLIC ACTIVITIES IN MALE AND FEMALE SHEEP Maté, L. ⁽¹⁾ ; Virkel, G. ⁽¹⁾ ; Lifschitz, A. ⁽¹⁾ ; Ballent, M. ⁽¹⁾ ; Sallovitz, J. ^(1,2) ; Lanusse, C. ⁽¹⁾ ⁽¹⁾ Laboratorio Farmacología, FCV-UNCPBA - CONICET (ARGENTINA). ⁽²⁾ CICPBA (ARGENTINA). e-mail: gvirkel@vet.unicen.edu.ar
<u>B4-90</u>	PK MODEL CONTRIBUTION TO VANCOMYCIN DOSAGE ADJUSTMENT IN RENAL PATIENTS Miceli M. B., Serra H. A. Ira Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. Paraguay 2155 piso 15 1121 Buenos Aires, Argentina. E-Mail: haserrafarmaco@gmail.com

B4-91	<p>ACETAZOLAMIDE CORNEAL PERMEATION FROM INTERPOLYELECTROLITE-DRUG COMPLEXES. Palena, M., Tártara, I., Quinteros, D., Palma, S., Allemandi, D., Manzo, R. Jimenez-Kairuz, A1. Dpto. de Farmacia, Fac. de Cs. Químicas, UNC. Ciudad Universitaria, X5000HUA Córdoba. 1E-mail: alvaro@fcq.unc.edu.ar</p>
<p>BLOQUE V</p> <p>Coordinadores: Dra. Damasia Becú, Dra. Susana Zachino</p>	
B5-92	<p>IMPAIRED BLOOD BRAIN BARRIER PERMEABILITY IN SEVERE CHOLESTASIS IN A RAT ANIMAL MODEL. Coll CT; Fernández MA; Coll SG; Coll TA; Filinger EJ; Lemberg A. Cátedras de Fisiopatología y Farmacia Clínica, FFyB, UBA, Junín 956, 1113. efilin@ffyb.uba.ar</p>
B5-93	<p>ENDOTHELIUM-DEPENDENT RESPONSE TO ANGIOTENSIN II AND NORADRENALINE IN RABBITS FEED ON A HIGH FAT DIET Scacchi F, Sierra L., Guerrero R, Peral M. and Jerez S. INSIBIO (UNT-CONICET). fabrizioscacchi@yahoo.com.ar</p>
B5-94	<p>HIGH FAT DIETS MODIFY PLASMA LIPID LEVELS AND INTERACTION BETWEEN NORADRENALINE- AND ANGIOTENSIN II-RESPONSES IN RABBITS. Sierra L, Scacchi F, Medina M, Saad S, Peral M and Jerez S. INSIBIO (UNT-CONICET). sierraliliana@arnet.com.ar</p>
B5-95	<p>PRELIMINARY STUDIES ABOUT MONOSODIUM GLUTAMATE (MSG) INTAKE AND RENAL FUNCTIONS Juriol L., Contini M. del C., Millen N., Mahieu S. LIFE. FBCB. UNL. Santa Fe. Argentina. Ciudad Universitaria. CC 242. smahieu@fcb.unl.edu.ar</p>
B5-96	<p>SEROTONIN TRANSPORTER PROMOTER POLYMORPHISM IN ARGENTINEAN POPULATION. ¹Errasti A, ¹Armesto A, ¹Daray F, ²Facone D, ²Giron S, ^{1,2}Maffia P. ¹III Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. ²Laboratorio de Estudios Genéticos Aplicados (EGA), Universidad Nacional de Quilmes (UNQ). farmaco3@fmed.uba.ar</p>
B5-97	<p>POTENTIATION OF 5-HYDROXYTRYPTAMINE (5-HT) RESPONSES BY A 5-HT UPTAKE INHIBITOR, CITALOPRAM, IN HUMAN UMBILICAL ARTERY Errasti A, Armesto A, Del Rey G, Rothlin R. III Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. farmaco3@fmed.uba.ar</p>
B5-98	<p>INCREASED LEVEL OF CYTOKINES AND MATRIX METALLOPROTEINASES IN OSTEOARTHRITIC Ricarte Bratti, JP, Montrull, HL, Demurtas, S, Meirovich, CI and Brizuela NY. Dpto. de Farmacología. FCM. Universidad Nacional de Córdoba. Santa Rosa 1085. Córdoba, Argentina. nildabrizuela@hotmail.com</p>
B5-99	<p>A MODEL OF EXPERIMENTALLY INDUCED OCULAR HYPERTENSION IN RABBITS THROUGH CAUTERIZATION OF EPISCLERAL VEIN Tártara LI., Llabot JM., Allemandi DA., and Palma SD. Laboratorio de Farmacotecnia. Departamento de Farmacia, Facultad de Ciencias Químicas, Haya de la Torre and Medina Allende, UNC, Córdoba, Argentina. CONICET</p>
B5-100	<p>USE OF PERTECNETATE (^{99m}TcO₄⁻) FOR THE IMAGING DIAGNOSIS OF ACUTE OSTEOARTICULAR INFLAMMATION IN MICE Collia N¹, Noto Llana M², Salgueiro MJ¹, Goldman C¹, Leonardi N^{1,3}, Boccio J¹, Cerquetti MC², Zubillaga M¹. ¹FFyB, UBA; ²FMED, UBA; ³Laboratorios BACON SAIC, Argentina. Junín 956 Piso Bajo – (1113) CABA. mzubif@ffyb.uba.ar</p>

BLOQUE VI	
Coordinadores: Dra Alicia Consolini, Dr Guillermo Virkel	
B6-101	ALLOPREGNANOLONE ACUTE EFFECT ON THE RAT OVARY FUNCTIONALITY. Laconi M., Cerioni S., Vega A., Yunes R. and Cabrera R.. LINCE-IMBECU-CONICET), F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza. Mendoza. Argentina. milaconi@lab.cricyt.edu.ar
B6-102	ALLOPREGNANOLONE HAS MNEMONIC-ENHANCING EFFECTS IN FEMALE RATS. Escudero C, Cerioni S, García S, Yunes R and Cabrera R. LINCE-IMBECU-CONICET, F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza.
B6-103	EFFECT OF ALLOPREGNANOLONE ON GLUTAMATE RELEASE IN PUBERTY. Giuliani F, García S, Casas S, Escudero C, Nanfaro F, Bazzocchini V and Cabrera R. LINCE-IMBECU-CONICET, F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza.
B6-104	HIGH DOSES OF ALENDRONATE IMPROVES THE PLASTIC COMPONENT OF RESISTANCE OF THE RAT FEMORAL FRACTURE, WITHOUT AFFECTING THE MINERALIZATION AND ELASTIC BEHAVIOR. ¹ Isla L., ¹ De Simone E., ¹ Alvarez E., ² Roldán E., ³ Cointry G., ³ Capozza R., ³ Ferretti JL., ¹ Chiappe Barbará A. ¹ Dept of Physiology, Fac of Veterinary, Univ of Buenos Aires; ² Gador SA, Buenos Aires; ³ Centre for P-Ca Studies (CEMFOC), Natl Univ of Rosario, Argentina.
B6-105	POTENTIAL PHARMACOLOGICAL USE OF BOTHROPIC PLA2 IN HEMOSTASIS García Denegri M.E ¹ ; Bustillo S. ¹ ; Tejada R. ^{1,2} ; Ponce-Soto L.A. ³ ; Acosta O ¹ ; Leiva L. ¹ . ¹ Universidad Nacional del Nordeste. Av. Libertad 5400, (3400) Corrientes, Argentina. E-mail: emiliadenegri@hotmail.com ; ² Hospital J.R. Vidal, Corrientes, Argentina 3UNICAMP, Brazil.
B6-106	DOWN-STREAM ACTION OF EPO-R IN BONE MARROW ERYTHROID COMPARTMENT UNDER PACLITAXEL EFFECT Aguirre M, Todaro J, Juaristi J, Alvarez M, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. Moreno 1240 (3400). Corrientes. UNNE.e-mail: nbrandan@med.unne.edu.ar
B6-107	BONE MARROW AND SPLEEN CELL DEATH FOLLOWING HEMORRHAGIC SHOCK: CRITICAL IMPLICATIONS FOR BAX AND BCL-XL. Todaro J, Aguirre M, Stoyanoff T, Juaristi J, Alvarez M, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. Moreno 1240 (3400) Corrientes. UNNE. e-mail: nbrandan@med.unne.edu.ar
B6-108	SUBLETHAL DOSES OF DHL INDUCE MALFORMATIONS IN RHINELLA ARENARUM (ANURA: BUFONIDAE) EMBRYOS Moreno, LE, Juárez, AO, Pelzer LE Farmacología, Fac. Qca. Bqca. y Fcia. Univ. Nac. San Luis. San Luis 5700. Argentina lmoreno@unsl.edu.ar
B6-109	CHLORIDE PASSAGE ACROSS THE ISOLATED SKIN OF THE TOAD BUFO ARENARUM Orce G., Castillo G., Chanampa Y. and Razouk G. Inst. of Physiology, Faculty of Medicine, UNT - Dept. Physiology, INSIBIO (UNT-CONICET) Junín 1229, 4000 Tucumán - orcegap@yahoo.com
B6-110	PHARMACOLOGICAL PROFILE OF SELF-MEDICATION IN ELDERLY Ponce Lucía N. ; Brizuela Nilda Y. Cátedra de Farmacología, Facultad de Ciencias Médicas. Universidad Nacional de Córdoba. Santa Rosa 1085-Córdoba-Argentina-CP5000. E-mail: poncenuri@hotmail.com
B6-111	LYMPHOCYTE FUNCTION IN TRANSGENIC MICE OVER EXPRESSING THE TRH GENE. A Klecha ^{1,2} , ML Barreiro Arco ² , S García ³ , C Pirola ³ , A Genaro ^{1,2} , G Cremaschi ^{1,2} . ¹ CEFYO-CONICET, ² Fac Farmacia y Bioquímica, UBA e IDIM-CONICET. alijut@ffyb.uba.ar
B6-112	2,4-Dichlorophenoxyacetic acid (2,4-D) effects on mRNA expression of myelin proteins. <i>Konjuh, C.; Evangelista de Duffard, A.M. and Duffard R.O. LATOEX – Facultad de Ciencias Bioquímicas y Farmacéuticas. UNR. Suipacha 531. 2000 - Rosario. e-mail: ckonjuh@fbioyf.unr.edu.ar</i>

19:00-20:00 h	Reunión Comité de Selección de Premios SAFE
22:00 h	CENA DE CAMARADERÍA. CEREMONIA PREMIACIÓN SAFE 2009.

Comité para evaluación de posters/comunicaciones orales y selección mejores trabajos para PREMIO SAFE 2009

Coordinación General	Dres. Carlos Baratti y Carlos Lanusse
Evaluación Presentaciones orales	Dres. Carlos Baratti, Gabriela Acosta; Ana Genaro; Ofelia Acosta.

Evaluación Posters		
Comite	Posters	Integrantes
1	B1-01 al B1-13	Dres. Roberto Rule y Mariano Boccia
2	B2-14 al B2-28	Dres. Susana Gorzalczany, Gabriel Orce
3	B3-29 al B3-38 y B3-71 al B3-79	Dres. Graciela Balerio, Carlos Reyes Toso
4	B4-39 al B4-50 y B4-80 al B4-91)	Dres. Fabiana Landoni; Stella Celuch
5	B5-51 al B5-59 y B5-92 al B5-99	Dres. Damasia Becú, Susana Zachino
6	B6-60 al B6-70 B6-100 al B6-109	Dres. Alicia Consolini, Guillermo Virkel

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CONFERENCIAS

C1

NANOTECHNOLOGY: PHARMACOLOGICAL APPLICATIONS AND APPROACHES TO SAFETY ASSESSMENT.

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Nanotechnology is the manipulation of matter at a scale between 1-100 nm. The application of this new field has been claimed to improve products in many fields that will affect world energy needs including photovoltaic cells, material strength and durability, combustion efficiency, and energy storage. An additional area of focus is the application of nanotechnology to medicine. This includes the development of smaller particle sizes for more efficient or more rapid dissolution of drugs. This has also led to the development of new drugs that are entirely nanoparticles, or are drugs attached to a nanoparticle platform. The US Food & Drug Administration released a task-force report in 2008 identifying the need for guidelines to address potential issues with the submission of nanotechnology-based products for approval. Most experts agree that the toxicology and safety assessment for nanotechnology-based products will most likely be equivalent to the current safety assessment paradigm, with the exception that more information will be required regarding the particle behavior during the manufacture process, and biological distribution and elimination phase. As an example, we have examined the dermal penetration of 37 nm PEG-coated quantum dots in the skin of mice. Our studies, along with other published studies, have demonstrated that sound scientific approaches to examine disposition of nanoscale materials dermal penetration are adequate; however, our studies do indicate that skin integrity may be an important consideration regarding the risk assessment to nanomaterials.

C2

EFFECTOS NEUROTÓXICOS DEL AMINOCROMO Y SUS POSIBLES IMPLICANCIAS EN LA ENFERMEDAD DE PARKINSON

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Han pasado 40 años de la introducción de L-dopa en tratamiento de la enfermedad de Parkinson y aún sigue siendo la terapia fundamental. La razón que no hayan nuevos fármacos es que no se sabe el mecanismo que conduce a la muerte las neuronas dopaminérgicas. Para desarrollar nuevos fármacos se requiere descubrir la identidad de la neurotoxina que gatilla la neurodegeneración. Nuestra hipótesis es que la neurotoxina tiene que ser de origen endógeno ya que neurotoxinas exógenas como el MPTP inducen síntomas de parkinsonismo severo en solo tres días. Mientras que en el Parkinson hidropático la neurodegeneración y el mismo proceso de desarrollo de la enfermedad toman años. Por esta razón nosotros postulamos que la neurotoxina debe ser de origen exógeno. Otro dato importante a tener en cuenta es que las neuronas que desaparecen en la enfermedad de Parkinson contienen neuromelanina. Este pigmento es el producto de la oxidación de la dopamina a aminocromo que se polimeriza generando la neuromelanina. Aminocromo tiene dos vías metabólicas neurotóxicas: (i) formación de aductos con proteínas como alfa sinucleína; y (ii) reducción con un electrón a leucoaminocromo *o*-semiquinona radical catalizado por flavo enzimas que usan NADH or NADPH. Este radical es extremadamente reactivo con oxígeno generando un ciclo redox que reduce oxígeno a súper óxido y consume el NADH necesario para generar energía en la cadena de transporte y/o NADPH que se necesita para reacciones de biosíntesis y para la reducción de glutatión. Por lo tanto nuestra hipótesis de trabajo es que el aminocromo puede ser metabolizado en dos vías metabólicas. Aminocromo también participan en tres reacciones neuroprotectoras tales como (i) formación de neuromelanina en neuronas dopaminérgicas; (ii) reducción con dos electrones catalizada por DT-diaforasa que previene que aminocromo participe en las dos reacciones neurotóxicas en neuronas dopaminérgicas, y (iii) conjugación de aminocromo y su precursor con GSH catalizado por GST M2-2 en los astrocitos. Nuestra hipótesis es que DT-diaforasa y GST M2-2 pueden ser usadas para una terapia regenerativa y terapia génica para impedir el avance de la enfermedad. Fondecyt 1061083

C3

DESARROLLO DE NUEVOS ANTIDEPRESIVOS: PROBLEMAS EN LA INVESTIGACIÓN BÁSICA Y CLÍNICA

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Presidente del Comité Independiente de Ética para Ensayos en Farmacología Clínica.

El desarrollo de nuevos antidepresivos que pudieran mejorar el perfil de los actualmente en uso tropieza con una serie de dificultades. En primer término la falta de modelos experimentales (animales) específicos, ya que los existentes se muestran activos tanto en depresión como en ansiedad, por lo que no resultan específicos. La investigación clínica también es difícil en depresión ya que muchos países y organismos regulatorios no permiten el uso de placebos y estos tienen una alta efectividad, por lo que los fármacos activos (y los aprobados con larga experiencia terapéutica) sólo incrementan un 20-25% la efectividad de los placebos.

Se resumen los centros emocionales del cerebro vinculados con la depresión y sus modificaciones en imagenología funcional, así como las principales líneas de desarrollo de fármacos, por fuera de los mecanismos monoaminérgicos de los actualmente empleados.

S1-1

MEDICAMENTOS HUÉRFANOS: EXPERIENCIA PILOTO.

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Los medicamentos huérfanos son aquellos que teniendo valor científico y terapéutico no han sido desarrollados o no son elaborados en la actualidad. De acuerdo a la OMS, se considera que un medicamento es huérfano si se destina a establecer un diagnóstico, prevenir o tratar una enfermedad que afecte al menos a cinco personas por cada diez mil en la comunidad. Sin embargo, suele existir escaso interés por parte de las empresas farmacéuticas para producir estos medicamentos, debido a: el fármaco no es patentable o su patente está vencida, los procedimientos tecnológicos son muy difíciles y de alto costo, existe un número reducido de personas que necesitan el tratamiento, hay razones de índole comercial.

La definición de medicamentos huérfanos incluye el concepto de agentes terapéuticos para el tratamiento de enfermedades raras o poco frecuentes (baja incidencia aunque alto impacto socio-económico).

Podemos encontrar diferentes situaciones que permiten clasificar una enfermedad como rara, por ejemplo: enfermedades para las cuales existe un medicamento conocido, que no se elabora debido a su baja rentabilidad; enfermedad para la cual la droga existe, pero no se elabora en la forma de administración/dosificación requerida; enfermedad en la cual el medicamento debe ser importado.

S1-2**FUENTES DE ERROR EN INVESTIGACIÓN CLÍNICA. ESTRATEGIAS DE MANEJO**

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Resulta claro que al momento de inferir sobre los resultados de una investigación debemos prestar especial atención a los factores de error que podrían haber operado, desde el mismo diseño, la implementación del estudio, o bien en el análisis de los resultados. Esta suerte de desaciertos se los agrupa en dos grandes categorías error: aleatorio y error sistemático. El error aleatorio está relacionado con la presencia de algún factor desconocido que pueda distorsionar en cualquier dirección la muestra y los datos sobre lo que estamos trabajando y así disminuir la precisión de lo que se estima. Este tipo de error puede reducirse por un aumento del tamaño muestral y a la vez procurar que la muestra guarde la mayor similitud posible con la población blanco. El error sistemático, por el contrario, tiene que ver con la existencia de un sesgo que altera los resultados en una dirección. El sesgo atenta contra la validez de lo que se estima y no puede atemperarse con un aumento en el número de participantes. El mismo puede generarse en distintos momentos del estudio, tales como preparación del protocolo, ejecución, recolección y análisis de datos, interpretación de los resultados, y finalmente publicación. El sesgo de selección es una eventualidad que se da cuando no existe uniformidad en cuanto a los criterios para la incorporación de los participantes. Algunos diseños son más proclives a este tipo de error, por ejemplo el estudio de casos y controles. En cuanto al sesgo de realización, se puede producir cuando no se presta un especial cuidado en cuanto al modo en que se aplica la intervención (ensayo clínico) o se pondera la exposición al predictor (estudio analítico (observacional)). Prosiguiendo con los pasos del estudio, posteriormente se nos puede presentar el sesgo por recolección de datos, también denominado sesgo de información u observación. Esto se halla vinculado a deficiencias en cuanto a la obtención de información respecto a la presencia del predictor o los cambios en el fenómeno de interés. Las fallas pueden provenir de mediciones defectuosas (binomio equipo/operador), fuentes de datos inexacta, errores provenientes de los participantes del estudio y problemas durante el procesamiento de los datos. Otro inconveniente está referido al análisis de los datos y en esta instancia los sesgos pueden deberse a una falta de control para los factores de confusión (FC), pruebas inapropiadas, y análisis *post hoc* de los resultados. El sesgo por FC no debe ser confundido con los eventos relacionados a la cadena causal de la enfermedad. Los FC más bien se nos presentan ante la existencia de exposiciones a múltiples predictores, muestra donde los participantes están agrupados por estratos, grupos heterogéneos de pacientes con diferentes proporciones respecto a la severidad o duración de la enfermedad, entre otros. Con algunas similitudes los ensayos clínicos terapéuticos también plantean una serie de sesgos particulares en las etapas de asignación del tratamiento, concreción del mismo, en el seguimiento tras completarse la terapia y en la evaluación de los puntos finales. Este abanico de errores potenciales puede llevarnos consecuentemente a un sesgo de interpretación con las consabidas fallas inferenciales. Finalmente existe otro sesgo que si bien no depende del investigador tiene consecuencias nefastas a la hora de efectuar generalizaciones sobre un problema en particular. Se trata del sesgo de publicación, vale decir la predilección a publicar determinados hallazgos, lo que repercute directamente sobre las conclusiones de un meta-análisis y revisiones sistemáticas. Ante tanta posibilidad de error, no seamos presa, sin embargo, de aquella sentencia Dantesca “*lasciate ogni speranza*”. Aún cuando el monje budista advierte “a todo hombre se le da la llave que abre la puerta del cielo, pero la misma llave abre la puerta del infierno”, no por eso la arrojaremos.

S1-3**CLINICAL TRIALS: ASPECTS ETHICAL**

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Clinical trials are now more the safest way to bring a drug and/or therapy to the market. However, this does not mean that it is safe for the subjects of research institutions, populations that are made, etc.

Clinical trials have several phases starting with a pre-clinical phase and continuing through the phases I, II, III, and phase IV (called phase of the market or pharmacovigilance).

Phases I, II and III involve the experimentation on animals and healthy human beings and patients.

It's important to give an ethical insight to the project because the inclusion of animals and humans in it.

As a clinical trial becomes a tool to generate knowledge, it must comply with international and national regulations to ensure ethical aspects in each of its stages.

The Research Ethics Committee is the ... “*collegiate body that carries out the ethical review of research protocols..*” (OPS definition). It's of those Committee's responsibility a strict review taking into account rules, conventions, declarations, etc. raised by international as the World Health Organization, the World Medical Association, the Organization of the United Nations Educational, scientific and cultural (UNESCO), among other entities.

The correct design of a research and the enforcement of its compliance are key elements to ensure the generation of knowledge without any abuse and in total agreement with human rights of the persons involved in such research.

S2-1

EFFECTS OF POSTNATAL STRESS ON THE ACTIVITY OF AMINOACIDERGIC TRANSPORTERS ON THE BRAIN

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During postnatal development, the central nervous system (CNS) is highly sensitive to the effects of drugs, stressors and environment. Early life events have profound consequences in growth and development. It is well known that animals exposed to stressful stimuli during their early life develop different neurological disorders when they become adults.

The aim of this study was to evaluate the consequences of repeated early maternal separation and exposure to cold stress on adult brain on GABAergic function and determine whether the combination between desensitization to maternal separation and cold was an age-specific. Rats' pups were separated from their mother plus cold exposure (4°C) for 1 h at postnatal day (PD) 5, 7, 13 and 21 during 20 days. These animals were allowed a 30 days recovery period until adulthood. The rats were killed by decapitation and collecting trunk blood. Frontal cortex (FC) and hippocampus (Hic) were dissected. We studied GABA uptake, corticosterone levels and GAT-1 expression by western blot. Repeated stress decreased GABA uptake only on FC at PD5, while at PD7 diminished significantly either FC or Hic after stress. Chronic stress decreased the levels of corticosterone at the different ages studied. While GAT-1 expression increased on FC. We would support the idea that early life environmental manipulations have an influence on hypothalamic-pituitary-adrenal (HPA) axis and alter the expression of plasticity related neuronal protein. Furthermore early stress in the life affects the FC of adult rat brain. The findings are in agreement with hypothesis of compensatory changes develop in response to repeated stress and we suggest that these time-dependent alterations might reflect adaptive processes and FC as a key in the development. These results suggest that a repeated early maternal separation in different periods after birth modified GABA uptake, levels of corticosterone and the expression of GAT-1, which could be relevant to function of transporter in the adult rat brain.

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S2-2

PHARMACOLOGICAL MANIPULATION OF FEAR MEMORY RECONSOLIDATION

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It is known that under certain boundary conditions, the retrieval of a stable consolidated memory results into a labile one followed by a stabilization period termed reconsolidation. During the instability phase, memory trace can be disrupted by a number of pharmacological agents. In the current research, adult male rats were conditioned in a contextual fear paradigm; the consolidated fear memory was reactivated by the re-exposure to the associated context for different periods of time that were followed by midazolam (MDZ) administration. In the first set of experiments, we study the effectiveness of different MDZ doses in preventing reconsolidation of different memory ages. Memory reconsolidation was disrupted when the reactivation lasted 3-5 min. Over a 10 min reactivation session, all rats gradually reduce their fear response, which indicates the emergence of an extinction period. Following this period, MDZ blocked the consolidation of extinction. In a brief reactivation session, MDZ (1-1.5 mg/Kg) attenuated the reconsolidation of recent memories. Remote memories were only disrupted with higher MDZ doses (3 mg/Kg) regardless of the reactivation trial's duration. An additional goal of the present study was to evaluate the vulnerability of recent and remote memories in animals that have experienced a stressful situation. The results show that MDZ did not affect memory reconsolidation in older-than-one-day memories of stressed animals, not even after the administration of higher MDZ doses and a longer reactivation session. We investigated whether activating NMDA sites prior to reactivation by D-cycloserine (DCS), a partial NMDA agonist, promotes the destabilization of resistant memories such as those of stressed rats. Our findings indicate that DCS prior to reactivation promotes retrieval-induced lability in a resistant memory trace since MDZ-induced memory impairment in stressed animals became evident with pre-reactivation DCS but not after pre-reactivation vehicle. In sum, MDZ could be potentially used as a pharmacological intervention to interfere with traumatic memories. The combined treatment with DCS favours the effectiveness of MDZ's disruptive effect on fear memory reconsolidation.

S2-3

“FLAVONOIDS NEUROPHARMACOLOGY. CLINICAL PERSPECTIVE”

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Pathologies involving focal or massive neuronal cell death, either in adults or newborns, are a frequent cause of handicap or death in Uruguay and all over the world.

However there are not effective therapies that could help nowadays affected people.

After research conducted in the Department of Neurochemistry of the Instituto de Investigaciones Biológicas Clemente Estable it was determined that Quercetin, a compound from the popular used medicinal plant called “Marcela” (*Achyroclines satureioides*), protects cell cultures *in vitro* and brain tissue *in vivo* from oxidative stress or ischaemia in rats, respectively, specially when is delivered in liposomes.

In this context and in association with the Department of Neonatology from the University Hospital from Montevideo, Quercetin was evaluated in a newborn piglet hypoxia model which simulates perinatal asphyxia in humans. Liposome preparation of Quercetin showed effectively in neuroprotection from brain damage after hypoxia, however there were secondary effects on pulmonary haemodynamia.

In order to obtain a preparation guaranteeing absence of adverse effects and showing *in vivo* neuroprotection, the group is developing a nanosomal preparation of Quercetin with haemodynamic security and therapeutic neuroprotective efficacy in the control of brain damage, creating the main guidelines for the future intravenous application in human pathology.

For the first time in Uruguay the proposal tends to complete the necessary preclinical stages for leading a national project on Quercetin clinical efficacy. The research uses also the new field of nanotechnology applied to biomedicine, designing a drug delivery system for natural occurring compounds with neuroprotective activity in frequent brain diseases.

S3-1

EFFECT OF ANTIBIOTICS AND PRESERVATIVES ON HEMOLYTIC UREMIC SYNDROME-PRODUCING *Escherichia coli* STRAINS ISOLATED FROM FOOD

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In Argentina, where hemolytic uremic syndrome is endemic, the estimated annual incidence rate in children is 10.2 per 100,000, the highest in the World. The etiological agent of this syndrome is *Escherichia coli* O157:H7 and another 150 Shiga toxin-producing serotypes, sharing similar pathogenic potential. The incidence of these strains in cattle (their reservoir) varies from 0.1 and 16%, depending on the area analyzed. Bacteria colonize and grow in the cattle colon, and then they disseminate to raw food, water and ready-to-eat food by cross-contamination. The objective of this study was to examine hemolytic uremic syndrome-producing *E. coli* strains in samples obtained from supermarkets and shops selling ready-to-eat food in Rosario area. In addition, we studied the genotypic characteristics of the strains, their clonal relationship and the effect of antibiotics and food preservatives on the dissemination of phages encoding Shiga toxin, the strong cytotoxin which determines the syndrome.

During 18 months, 500 food samples were collected by the inspectors from the Rosario Food Institute and examined for pathogenic *E. coli* strains. Forty-nine strains were isolated from soft cheese, cottage cheese, salads with cream or mayonnaise and sandwiches. The isolates were assayed with four multiplex Polymerase Chain Reactions (PCRs) to detect the presence of 10 virulence genes. The 14.3% of the isolates expressed virulence factors, among these strains two were O157. In strain ATCC43895 (O157:H7) the toxin-encoding genes are located on lysogenic lamboid DNA phages, which are not only passive vectors for the dissemination of Shiga toxin, but are genetic entities where the phage cycle influence toxin production. Four isolates had phages, revealed as small lysis plaques on agar plates cultured with the strain DH5 α . Shiga toxin was detected by hybridization with the *stx2* probe, indicating that the toxin is encoded in the inducible phages. Two quinolones, norfloxacin widely used in human therapy and enrofloxacin for veterinary use, induced the phages lytic cycle. On the contrary, an inhibitory effect was observed with the preservatives treatment. The inhibition was from 84 to 99%, expressed as phages lysis plaque forming units. The most important inhibitory effect was revealed in the assay with potassium sorbate.

These results indicate that food preservatives diminish the dissemination of Shiga toxin-encoding phages. On the opposite, the results with quinolones indicate that these antibiotics contribute to the dissemination of phages in humans and animals receiving antibiotic therapy. Moreover, as Shiga toxin genes are co-transcribed with the late phage genes and the amount of toxin may therefore be enhanced prior to cell lysis, we conclude that quinolones enhance virulence whereas food preservatives diminish pathogenicity of hemolytic uremic syndrome-producing *E. coli* strains.

S3-2

BIOLOGICAL CONTROL OF BACTERIAL DISEASES TRANSMITTED BY FOOD**Dra. Sparo M.**Laboratorio de Farmacología, Facultad de Ciencias Veterinarias, Universidad Nacional del Centro de la Provincia de Bs.As. (7000). Argentina e-mail: monicasparo@speedy.com.ar

Diseases Transmitted by food (DTF) come up as infectious outbreak or poisons which affect several people in different period - time after ingestion of contaminated food. Recent epidemiological data obtained from 10 years ago in Argentina and worldwide, show a significant increase of DTF sourced by bacteria. The risk Groups for DTF are mainly children, elder, pregnant woman and immune- suppressed patients. Pathogens like entero-haemorrhagic *Escherichia coli* in food may become renal impairment in children and elderly people. Moreover *Salmonella* spp. may also developing arthritis and invasive diseases as well as *Listeria monocytogenes* with meningitis and miscarriages. Fresh food has been indentified as the more relevant factor in food preservation, although this concept is not compatible with chemical preservatives. At the present there is a trend of natural and organic ingestion food without chemical conservants. Biopreservation is related with the life extension of food and increase of microbiological safety using a natural microbiota and its antibacterial products. Lactic bacteria are overall recognised like GRAS (Generally Recognized As Safe), having it a pivotal roll on the preservation and fermentation of food, improving the hygienic quality by mean of the competitive microbiota including pathogens. Biopreservative effect in food may be attained by inoculation of protector cultures or by adding its antimicrobial products, namely bacteriocines or antimicrobial peptides. This paper will show the biopreservative effect of the *Enterococcus faecalis* CECT7121 strain in stuffed sausages, cheeses, ground meat and raw vegetable, making it a new attractive alternative of natural biopreservation. New information about the occurrence of DTF in whole America, indicates that the latter is a priority concern for the Public Health with direct consequences in activities as tourism and food commercialization.

S3-3

BIOACCUMULATION OF POLYCYCLIC AROMATIC HYDROCARBONS (PAHs) IN THE FOOD CHAIN. SILENT EFFECTS

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Polycyclic aromatic hydrocarbons (PAHs) are a heterogeneous group of chemicals showing a variety of adverse effects on both human and animal health. Members of this superfamily include polyhalogenated industrial pollutants such as dibenzo-*p*-dioxins, polychlorinated biphenyls and dibenzofurans, and nonhalogenated ones, such as benzo(*a*)pyrene, benzanthracenes and 3-methylcholanthrene. These compounds are products of diverse chemical reactions such as the production of organochlorines and chlorine, paper bleaching procedures, waste incineration, metal production and fossil fuel and wood combustion. High lipophilicity, chemical stability and very slow biodegradation are characteristic features of these persistent compounds. The primary route of both human and animal exposure to these compounds can be as a result of drinking contaminated water, breathing contaminated air, or ingesting contaminated food. The well-characterized biomagnification process can be represented as a pyramid of increasing pollutant concentrations that runs in opposition to the biomass pyramid which represents the different trophic levels. The high concentrations reached in the tissue of species at the top of the trophic chain may exceed toxicity thresholds, triggering biochemical disturbances and physiological changes in the contaminated individuals. It is also well known that many of these chemicals, even at low doses, trigger different toxic responses on reproductive health by activating the arylhydrocarbon (Ah) receptor. Since the presence of Ah receptors has been described in ovarian tissue, the ovary is an excellent target for these chemicals. Infertility disorders have increased from 8 to 20% over the past two decades in industrialized countries. The developmental stage in a reproductive lifespan determines the magnitude of the effects of a reproductive toxicant. Alterations in reproductive development are normally observed at concentrations far below those inducing toxicity in adult humans. Some of these effects, that we could call "silent effects", can be difficult to assess, because they are not likely to be observable until adulthood. In the mature female, fertility depends on the maintenance of a constant stream of growing follicles. Daily exposure to some PAHs at low doses can alter the follicular growth without causing systemic toxicity. In addition, the stage of development at which the follicle is impaired determines the impact that this particular toxicant will have on female reproduction. For example, toxicity to primordial follicles may not produce immediate signs of infertility but may ultimately shorten the reproductive lifespan. By contrast, toxicity to antral or preovulatory follicles may result in an immediate but reversible loss of reproductive function. Finally, impaired ovulation and direct destruction of the maturing oocytes can occur, leading to sub-fertility conditions. Thus, it is of particular concern to review the threshold dose and identify the effects and action mechanism of these persistent pollutants on the ovarian function.

S3-4

PRUDENT ANTIMICROBIAL USE IN FOOD ANIMALS, IS IT POSSIBLE? IMPACT OF CHEMICAL RESIDUES AND ANTIMICROBIAL RESISTANCE IN HUMAN HEALTH

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Drug residues in animal products represents major risks in public health. The increase in the sensitivity of the detection methods permit the determinations of very low levels of xenobiotics in tissues samples of animals. As a consequence, the term “residue zero” was no more used and maximum residue limits were fixed for a great number of drugs used in food producing animals. The consequences of ingesting residues of drugs in food above the permitted levels may be direct toxicity, allergy and antibacterial resistance. In the case of antimicrobials, however, toxicities are not frequent. Aminoglycosides accumulates in renal cortex and may be risky if food containing levels above the permitted ones, are consumed in high amounts and for long periods.

Chloramphenicol is the most dangerous, it can produce dose independent aplastic anemia, which motivated its ban in several countries since approximately 1990. Allergies are generally the consequence of presence of beta lactam antimicrobials, especially penicillin. The low concentrations generally found, however, are not able to sensitize patients but only to trigger rather mild allergic reactions. There have been, however, scarce reports of more severe allergic reactions. Antimicrobial resistance is by far the major problem that can be produced by the presence of residues of antimicrobials in food of animal origin. There is some controversy on the concentration of antimicrobial necessary to effectively select resistant bacteria. Probably below some “no bacteriological level”, antimicrobials residues are safe, but discussion continues. Presence of low antimicrobials concentrations (but with some antibacterial activity) in the gastrointestinal tract during long periods of time is the best situation to promote the emergence and dissemination of resistant bacteria, and this is the case when administration of antimicrobials is performed with growth promotion objectives. Antimicrobial resistance can be intrinsic or acquired, and in the last case, can be mutational or by transference of genetic material. There are reservoirs (GI tract, farms effluents, towns effluents, hospital effluents), where great amounts of different bacteria genera convive, in which there is intense exchange of genetic information, among these information, determinants of resistance can be included and disseminated. Resistance determinants from animal origin can reach the human population in three ways: a. Directly when a zoonotic bacteria acquires resistance in an animal and is transferred to humans, b. When a resistant bacteria from an animal transfers resistance determinants to a human pathogen, and c. When an animal pathogen transfers resistance determinants to saprofitic bacteria in a reservoir, and saprofitic bacteria transfers resistance to other bacteria, including human pathogens. All these processes can function in the inverse direction, i.e. from human to animal. The use of antimicrobials in animals can be therapeutic, prophylactic, metaphylactic and as growth promotion. The last is the most controversial. A very active international policy promoting expert training in prudent use of antimicrobials, monitoring of antimicrobial resistance emergence and dissemination, concomitant with risk analysis of the transference of resistant determinants from animals to humans, is necessary, especially in developing countries, before any restriction on the use of antimicrobials is implemented.

COMUNICACIONES ORALES

OI-01

DETERMINATION OF HYPOTHALAMIC LEVELS OF MONOAMINERGIC NEUROTRANSMITTERS IN ADULT RATS EXPOSED PRE AND POSTNATALLY TO 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D)
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LATOEX previous works demonstrated neurobehavioral changes related to serotonergic and dopaminergic systems alterations in 2,4-D exposed rats. The aim of this work was to measure hypothalamic levels of monoamines and their metabolites. Wistar rats were made pregnant and exposed to 2,4-D (50 or 70 mg/kg/day, through diet) from day 16th of gestation to weaning. After weaning, pups were divided in two subgroups: T₁ fed with untreated diet and T₂ treated until sacrifice. Both groups were sacrificed at postnatal day 90 and hypothalami were removed. Tissues were homogenated and from supernatants, levels of noradrenaline (NA), dopamine (DA), 3,4-dihydroxyphenilacetic acid (DOPAC), serotonin (5-HT) and 5-hydroxyndoleacetic acid (5-HIAA) were measured by HPLC. In treated male rats, 2,4-D exposure diminished monoamine hypothalamic levels and increased the ones of their metabolites. In treated female rats, DA and DOPAC levels were diminished but 5-HT level was increased. In conclusion, 2,4-D alters monoamines hypothalamic levels. This fact could modify sexual behavior and reproductive function in rats.

OI-02

EFFECT OF ELECTRICAL AND CHEMICAL STIMULATION OF THE SUBTHALAMIC NUCLEUS ON THE RELEASE OF STRIATAL DOPAMINE

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High frequency stimulation (HFS) of the subthalamic nucleus (STN) alleviates the cardinal symptoms of Parkinson's disease, but the mechanisms underlying these clinical results remain to be clarified. Our objective was to search the mechanisms involved in the release of dopamine (DA) by HFS of the STN. The experiments were performed in rats anesthetized with urethane (1.2 g/kg, i.p). DA was collected by means of microcannulae introduced in the striatum, while the STN was electrically stimulated with a concentric electrode. The STN was also stimulated by means of a microinjection of bicuculline or muscimol. The HFS of the STN produced a significant increase of DA in the striatum (One way ANOVA, P<0.001). The kainic lesion of the globus pallidus (GP) or the substantia nigra reticulata (SNr) did not modify the effect of HFS of the STN on the release of DA. The microinjection of bicuculline (25 ng / 200 nl) increased significantly striata DA I similarly to HFS (One way ANOVA, P<0.001) and the microinjection of muscimol (0.2 µg / 200 nl) decreased significantly the spontaneous release DA (One way ANOVA P<0.001). The above results support the assumption that the activation of the neurons of the STN and probably their efferents acting directly on the dopaminergic neurons of the substantia nigra pars compacta are responsible of the release of DA into the striatum

OI-03

ROLE OF THE GABA_B RECEPTORS IN THE EFFECTS INDUCED BY NICOTINE ON ANXIETY-LIKE BEHAVIOUR IN MICE

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The aim of the present study was to evaluate the possible involvement of the GABAergic system in the anxiolytic- and anxiogenic-like responses induced by nicotine (NIC) in mice, using both pharmacological and genetic approaches. Animals were only exposed once to NIC. The acute administration of low (0.05 mg/kg, sc) or high (0.8 mg/kg, sc) doses of NIC produced opposite effects in the elevated plus maze, anxiolytic-anxiogenic-like responses, respectively. The effects of the pretreatment with the GABA_B receptor antagonist, 2-OH Saclofen (SAC) (0.25, 0.5 and 1 mg/kg; ip) and the GABA_B receptor agonist, baclofen (BAC) (0.5, 1 and 2 mg/kg; ip), were evaluated on the anxiolytic- and anxiogenic-like responses induced by NIC. SAC completely abolished these NIC-induced effects (p<0.001; p<0.01, respectively) at the higher dose, suggesting an involvement of GABA_B receptor in these behavioural responses. On the other hand, BAC failed to modify the effects induced by NIC on anxiety-like behavior. In addition, in GABA_{B(1)} knockout mice the anxiolytic-like responses of NIC were blocked (p<0.001), suggesting a role of GABA_{B(1)} receptor in these behavioural responses, but not in the anxiogenic-like effects of NIC. These results demonstrate that the endogenous GABAergic system is involved in the regulation of NIC anxiety-like behaviour in mice and provide new findings to support a potential pharmacological therapeutic use of GABAergic drugs in the treatment of tobacco addiction. *Supported by UBACYT B016*

OI-04

DORSAL STRIATUM MEDIATION OF COCAINE-SEEKING AFTER VARIED PERIODS OF COCAINE SELF-ADMINISTRATION AND WITHDRAWAL IN RATS.

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Accumulating evidence has suggested that increased drug-seeking in cocaine addiction may occur as progressive drug-induced recruitment of more dorsal areas of the striatum exert greater control over drug-seeking via habitual stimulus-response mediated behaviors. The current study evaluated the contribution of the dorsal striatum (dlCPu) to cocaine-seeking following varied histories of cocaine self-administration and different periods of abstinence. We predicted that cocaine-seeking after longer cocaine histories would come under greater control of the dlCPu. Following implantation of a jugular catheter and bilateral intracranial guide cannulae, male Sprague-Dawley rats were trained to press a lever to receive cocaine infusions and were then divided into two groups: 1-hr and 6-hr access for 15 days. We then examined relapse of cocaine-seeking after 1, 14, and 60 days of abstinence. Before each relapse test, subjects received bilateral infusion of vehicle, or a combination of baclofen/muscimol into the dlCPu. All animals showed robust responding during each of the relapse tests after vehicle infusion, regardless of prior cocaine self-administration history. Inactivation of the dlCPu significantly attenuated responding on the relapse test days, with proportionally greater decrements seen in animals with the longest duration of cocaine self-administration. These data support the possibility that the dlCPu controls drug-seeking to a larger degree at the time of relapse in individuals with a history of greater cocaine use.

<p>OI-05 LONG-TERM ANTICONVULSANT TREATMENT WITHOUT MEMORY IMPAIRMENT Krawczyk MC., Blake MG, Boccia MM, Carcaboso AM, Chiappetta DA, Höcht C, Sosnik A, Baratti CM Cátedra de Farmacología, FFyB, UBA Junín 956, Buenos Aires, Argentina cbaratti@ffyb.uba.ar</p> <p>After more than a decade, the long-term clinical treatment with the anticonvulsant-antinociceptive drug gabapentin (GBP) is still related to adverse cognitive side effects. The administration of a single dose of GBP immediately after training improves retention performance of mice in an inhibitory avoidance task (IA). On the contrary, when GBP is given twice a day during 7 days, retention performance is impaired. In the present work we used a monolithic implant made of GBP-loaded poly(epsilon-caprolactone) matrices, which allowed the controlled release of the drug. When implants were inserted in a subcutaneous pocket in the side of the mice, immediately after training in the IA task, enhanced memory consolidation. Implants successfully protected against pentylenetetrazole-induced seizures by increasing not only latencies but also by decreasing the duration of convulsions. These results could lead to a clinically relevant conclusion: maintenance of stable GBP plasma levels protects against seizures without causing memory impairment. Hence, the adverse cognitive effects observed in the clinical practice could be avoided by stabilizing plasma levels of the drug.</p>	<p>OI-06 ARE GLUCOCORTICOIDS RECRUITING ENDOCANNABINOID TO MODULATE AVERSIVE MEMORY CONSOLIDATION IN THE HIPPOCAMPUS? Lucas de Oliveira Alvares, Engelke D.S., Diehl F., Genro B.P., Molina V.A., Quillfeldt J.A. De Oliveira Alvares L. Universidade Federal do Rio Grande do Sul, LPBNC, Porto Alegre Brasil.</p> <p>The modulation of memory process is one of the several functions of the endocannabinoid system (ECS) in the brain, with CB1 receptors highly expressed in areas such as the dorsal hippocampus (HPC). Experimental evidence suggested an important role of the ECS in aversively-motivated memories. Similarly, Glucocorticoids (GC) released in response to stress exposure also modulates memory formation, and both stress and dexamethasone activate the ECS. Here we investigate the interaction between the ECS and GCs in the HPC in the modulation of fear memory consolidation. Two protocols with different shock intensities were used in order to control the level of aversiveness. Local infusion of AM251 into the HPC immediately after training was amnesic in the strong, but not the weak protocol. Moreover, AM251 was amnesic in animals stressed 0, but not 30 min prior to the weak protocol, reverting the stress-induced facilitating effect. Finally, intrahippocampal AM251 infusion reduced memory in animals that received dexamethasone immediately, but not 30 min before training. These results are consistent with the view that ECS is activated on demand, in a rapid and short-lived fashion. In conclusion, ECS interact with the GC in the dorsal hippocampus, a decisive memory-processing structure, suggesting a local GC-dependent ECS recruitment modulating the consolidation of an aversive memory.</p>
<p>OII-07 A MODEL OF METFORMIN ABSORPTION Serra H. A., Rizzo L. F. 1^{ra} Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. Paraguay 2155 piso 15 1121 Buenos Aires, Argentina. Dirección Médica, Química Montpellier S.A. Virrey Liniers 673 1220 Buenos Aires, Argentina. E-Mail: haserrafarmaco@gmail.com</p> <p>Metformin (Met) is a drug choice in Type-2 Diabetes and other related metabolic disorders treatments. Despite its wide use, Met absorption is poorly understood. Available data suggest that it is incomplete and saturable.</p> <p>Aims: To analyze Met absorption in terms of a simplified kinetic model that could explain the low bioavailability and digestive intolerance of the drug.</p> <p>Methods: We have recreated a three compartmental model of Met mass movement (intestinal lumen, enterocytes and blood) with three kinetics constants running in MS Excel® for Windows®.</p> <p>Results: For a given dose of 500 mg, the model estimated masses (mg) were: absorbed (C3) = 192.63; stored in enterocytes (C2) = 121.04 and luminal (C1) = 186.3. The model constants (h⁻¹) were k13 ~ kabs = 1.1; k12 = 2.98 and k32 = 1.3. The acquired model data fitted well with the observed data for the first hour.</p> <p>Conclusions: The obtained data have allowed a better estimated of Met absorption. Enterocyte drug accumulation precludes the respiratory chain activity, reducing the ATP levels and the glucose intestinal uptake. As a consequence, gastrointestinal side effects could be produced proportionally to Met accumulation. The discrepancy between simulated and observed data after the hour could be explained by the existence of a simultaneous distribution process in Met pharmacokinetics.</p>	<p>OII-08 COMPARATIVE PLASMA PHARMACOKINETICS, TISSUE DISTRIBUTION AND EFFICACY OF TWO FORMULATIONS CIPROFLOXACIN-BASED IN MOUSE-MODEL Breda A^{1,a}, Gonzalez C², Confalonieri A², Sanchez Bruni S², Manzo R¹, Olivera M^{1,b}.</p> <p>¹Facultad de Ciencias Químicas, UNC, Córdoba, ²Facultad de Veterinaria, UNCPBA, Tandil, Argentina. ^aandreabreda@fcq.unc.edu.ar, ^bmeoliver@fcq.unc.edu.ar</p> <p>The aim of this study was to assess the plasma pharmacokinetics, tissue distribution and efficacy of a formulation ciprofloxacin (CIP)-Aluminum complex based (CIP-Al) in comparison with a conventional CIP formulation. For this study 96 Balb-C mice were divided in two groups and treated as follows: Group I received orally a single dose of CIP 5 mg/kg. Animals of Group II were identically treated but with CIP-AL formulation. Samples of blood, lung, intestine and kidney, were taken over 12 h post-treatment, and frozen until analysis by HPLC. The experimental efficacy study was based in an experimental <i>Salmonella</i> infection model in mice. Mice were divided into 3 groups: Control (distilled water treatment), CIP and CIP-Al. After 5 days of treatment survival was recorded. The plasma pharmacokinetics study outcomes revealed similar AUC values for CIP and CIP-Al. However, CIP concentration levels were statistically (P< 0.05) higher in lung, intestine and kidney after CIP-Al administration than those obtained for CIP conventional formulation group after 1h post treatment. The higher tissue concentrations of CIP-Al may have contributed to the observed efficacy trend where survived 33% of mice treated compared with the conventional CIP formulation assayed (0%). This fact would be related to the improved aqueous compatibility of CIP after aluminum complexation. We found that CIP-Al is at least as effective as CIP and exhibited advantageous pharmacokinetic and dispositional properties. It may become a valuable asset based on its formulation versatility due to higher solubility.</p>

<p>OII-09 EFAVIRENZ-LOADED PEO-PPO POLYMERIC MICELLES ENHANCE THE ORAL BIOAVAILABILITY IN THE ANTI-HIV PHARMACOTHERAPY. Chiappetta D, Höcht C, Taira C, Sosnik A. FFyB, UBA. Junín 956 (1113) CABA. e-mail: alesosnik@gmail.com. Aiming to improve dose adjustment features and bioavailability of efavirenz (EFV), we explored the suitability of encapsulation of EFV into polymeric micelles of commercial poly(ethylene oxide)-poly(propylene oxide) block copolymers. Oral bioavailability of EFV (40 mg/kg and 80 mg/kg) in a 10% F127 drug-loaded micelles solution was compared with an extemporaneous suspension obtained by manipulation of commercial capsules and an oily solution in male Wistar rats (220-250 g). Levels of EFV in plasma samples were analyzed by HPLC-UV. Encapsulation of EFV led to a significant increase of the maximal plasma concentration (C_{max}) (40 mg/kg: 2.9±0.7 µg/ml; 80 mg/kg: 7.1±1.5 µg/ml, p<0.05) when compared with suspension (40 mg/kg: 1.5±0.6 µg/ml; 80 mg/kg: 3.4±1.7 µg/ml) and oily solution (40 mg/kg: 1.8±0.7 µg/ml; 80 mg/kg: 2.7±0.6 µg/ml). F127 EFV-loaded micelles solution showed an enhanced AUC compared with both suspension and oily solution. In addition, a lower intersubject variability was found in PK parameter estimation after F127 EFV-loaded micelles solution administration. In conclusion, pharmacokinetic results support encapsulation of EFV in polymeric micelles as a strategy toward the development of an optimized EFV liquid formulation for the treatment of pediatric HIV/AIDS.</p>	<p>OII-10 KINETICS AND DYNAMICS OF LAMOTRIGINE IN 3-MERCAPTOPROPIONIC ACID INDUCED-SEIZURES Höcht C,¹ Lazarowski A,¹ Opezzo JA,¹ Taira C,¹ Girardi E.² INFIBIOC, IBCN. chocht@ffyb.uba.ar. We studied pharmacokinetics and pharmacodynamics of lamotrigine (LTG) in an experimental model of epilepsy, induced by repetitive 3-mercaptopropionic acid (MP) administration. Wistar rats were divided in 4 groups: Groups A received a single dose i.p. of MP (40-45mg/kg) daily injected during 10 days. During the same period, group B, was daily treated with LTG (20mg/kg), previous to MP administration, group C received nimodipine (2mg/kg) 1 hour previous to MP and as control (groupD) rats were injected with saline solution (V). Hippocampal and plasma pharmacokinetics of LTG were evaluated in the different groups after single iv administration of 10 mg/kg by using central microdialysis and traditional blood sampling. Pharmacodynamics studies showed that LTG and Nimo did not protect from MP induces seizures. In rats pretreated with V, hippocampal LTG levels were similar in MP rats (maximal concentration (C_{max}):1.36±0.42 µg/ml) compared to C animals (C_{max}: 1.80±0.19 µg/ml µg/ml). NIMO pretreatment did not modify central kinetics of LTG in C and MP animals (C rats: C_{max}: 1.68±0.50 µg/ml; MP rats: C_{max}: 1.58±0.41 µg/ml). Our results indicate that LTG does not protect from MP seizures. Hippocampal LTG levels were similar in MP rats than in controls and in the presence of the Pgp inhibitor NIMO, suggesting that LTG is not a good substrate of P-gp.</p>
<p>OII-11 IN VITRO ASSESSMENT OF SEX INFLUENCE ON THE INTESTINAL P-GLYCOPROTEIN ACTIVITY IN RATS Ballent, M.^{1,2}; Lifschitz, A.^{1,2}; Virkel, G.^{1,2}, Sallovitz, J.¹, Maté, L.^{1,2}, Lanusse, C.^{1,2} 1. Lab. Farmacología, FCV, UNCPBA. 2. CONICET. Email:mballent@vet.unicen.edu.ar Sex-based differences in P-glycoprotein (P-gp) activity have been suggested. The aim of the present work was to characterize <i>in vitro</i> the sex influence on the intestinal P-gp-mediated transport of drugs using both the everted gut sac and the Ussing chamber technique in the rat. In Experiment 1, intestinal sacs (ileum) of male and female Wistar rats were incubated with ivermectin (IVM) (0.5 µM) either alone or with PSC833 (10 µM) as a P-gp modulator. For Experiment 2, the flat sheets of intestinal mucosa of both sex were mounted into Ussing chambers. Rhodamine 123 (Rho 123) (5 µM) was added to mucosal (M) and serosal (S) sides, either alone or with PSC833 (10 µM). Samples were analyzed by HPLC (IVM) and spectrofluorometer (Rho 123). The intestinal accumulation of IVM and the effective permeability (P_{eff}) of Rho 123 were calculated. A higher accumulation (IVM)/absorption (Rho 123) was observed in female compared to male intestine. At 60 min, the IVM accumulation in the intestinal sacs was 2-fold higher in female than male. The secretion of Rho 123 was 87% higher in male than female. The response to P-gp modulation with PSC833 was higher in male than female suggesting a greater P-gp activity and/or expression in male animals. In conclusion, substantial sex-related differences were observed with both methods. Further works are needed to clarify the mechanisms involved in this phenomenon, which may have a considerable clinical relevance.</p>	<p>OII-12 AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME produced MODIFICATION OF P-gp EXPRESSION in the intestine and IN Blood Brain Barrier. ^{1,3}Filia, M.F., ^{1,2}Novak, A., ¹Godoy, Y., ¹Rubio M.C., ^{1,2}Ghanem C.I., ¹Celuch, S.M. ¹ININFA (CONICET-UBA); Cát. ²Fisiopatología y ³Farmacotecnia II (FFyB, UBA). Junín 956, 5° P. Buenos Aires. cghanem@ffyb.uba.ar Several studies demonstrated alterations in P-gp expression or activity in type 1 diabetes. The metabolic syndrome (MS) is a combination of risk factors leading to type 2 diabetes and cardiovascular disease. The aim of this study was to investigate P-gp expression and activity in an experimental model of MS. Male Sprague-Dawley rats received standard solid diet and either tap water (C) or drinking water containing 15% fructose (FRU) during two months. The animals were fasted for 12 h before the experiments. The P-gp expression was estimated by western-blot in intestine brush border and in blood-brain barrier capillaries (BBB). The activity of P-gp was measured in everted intestinal sacs using rhodamine 123 (Rho, 15 µM) as substrate. The expression of intestinal P-gp decreased in FRU vs C (FRU=44±15 %; C=100±13%; p<0.05; n=3). The expression of P-gp in BBB was also decreased in FRU rats (FRU=49±17 %; C=100±19%; p<0.05). The intestinal activity of P-gp was decreased to 50 % of the control group value (p<0.05; n=5). The Rho excretion was lineal up to 40 min and the slope was 0.0284±0.0040 in FRU group compared to 0.0552±0.0089 in C, expressed as nmol Rho/min/g tissue (p<0.05; n=5). P-gp activity was confirmed in the presence of verapamil (100 µM), a known P-gp inhibitor, which abolished the differences between groups. It is concluded that MS decreased intestinal P-gp expression and activity in rats. This effect did not appear to be tissue-specific. These changes could modify the pharmacokinetics of drugs that are substrates of the P-gp. <i>Supported by PIP 112-200801-00330 CONICET, B609- UBA and PICT 2007-1039, ANPCyT.</i></p>

<p>OII-13 EFFECTS OF GLP-2 ON INTESTINAL XENOBIOTIC METABOLISM AND ELIMINATION.</p> <p>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</p> <p>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 <i>in vitro</i> 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 <i>in vivo</i> for administration i.v. of CDBN (30 µmol/kg bw) and detection of its derivatives: 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.</p>	<p>OII-14 EFFECT OF DEXAMETHASONE CHRONIC ADMINISTRATION ON THE HEPATIC SULPHOXIDATION OF ALBENDAZOLE IN SHEEP</p> <p>Virkel, G.⁽¹⁾; Maté, L.⁽¹⁾; Lifschitz, A.⁽¹⁾; Sallovitz, J.^(1,2); Ballent, M.⁽¹⁾; Lanusse, C.⁽¹⁾</p> <p>⁽¹⁾ Laboratorio Farmacología, FCV-UNCPBA - CONICET (ARGENTINA). ⁽²⁾ CICPBA (ARGENTINA). e-mail: gvirkel@vet.unicen.edu.ar</p> <p>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.</p>
<p>OIII-15 ORAL CONTRACEPTIVES IN CHOLESTATIC FEMALE RATS: ROLE OF CYTOKINES.</p> <p>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</p> <p>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.</p>	<p>OIII-16 EXPRESSION OF KIDNEY AND LIVER BILITRANSLOCASE (BTL) IN RESPONSE TO ACUTE BILIARY OBSTRUCTION (ABO).</p> <p>Brandoni A, Di Giusto G, Franca R*, Passamonti S*, Torres AM. <i>Farmacología. Fac. Cs. Bioq. y Farm. U.N.R. Suipacha 531. (2000) Rosario. CONICET. Email anabelbrandoni@gmail.com.</i> *Universidad de Trieste, Italia.</p> <p>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 bromosulphophthalein (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.</p>

<p>OIII-17 COPAXONE REVERTED CHRONIC STRESS-INDUCED ALTERATIONS IN BEHAVIOUR AND TH1/TH2 BALANCE IN BALB/C MICE. Palumbo ML, Zorrilla-Zubilete M, Cremaschi GA and Genaro AM. CEfYBO-CONICET-UBA, 1° Cátedra de Farmacología, Fac. Medicina, U.B.A. Paraguay 2155, Piso 15, Bs As, Argentina. E-mail: molecula_21@yahoo.com.ar</p> <p>Stress has been related to cognitive deficit. The hippocampus, a limbic area involved in learning and memory, is particularly sensitive to the effects of chronic stress. Cytokines have been shown to affect some behaviour, including memory. Moreover, IL-2, IFN-γ and IL-6 has been implicated in psychiatric disorders. Glatiramer acetate (Copaxone®) is a synthetic amino acid polymer that can weakly cross-react with CNS-resident autoantigens and can safely simulate the protective and reparative effects of autoreactive T cells. The aim of the present work was to study copaxone effects in the behaviour and in the TH1/TH2 balance induced by chronic stress in BALB/c mice. We found that BALB/c mice exposed to chronic stress had a poor learning performance respect to control mice in both, alternation behaviour in Y-maze task and habituation in open field. The lymphoid production of cytokines analysed by ELISA showed a decrease of IFN-γ and not changes in IL-2 (TH1-cytokines) and an increase of IL-6, IL-4 and IL-10 (TH2-cytokines) in stressed BALB/c mice. These effects induced by chronic stress were reverted by administration of copaxone (100ug per injection s.c. to four times during three weeks). These results indicate that copaxone is able to reverse both the memory impairment and the TH1/ TH2 cytokine balance. These results suggest that TH1 response could constitute a protective mechanism preventing behaviour impairment.</p>	<p>OIII-18 SHIFT IN THE BAX/BCL-XL BALANCED MAY ACTIVATE CASPASE 3 AND MODULATE APOPTOSIS/NECROSIS ASSOCIATED WITH PROGRESSIVE RENAL DELETION THROUGH INOS, HSP60 AND HIF-1α IN MURINE NEPHROTIC SYNDROME. Stoyanoff T, Todaro J, Aguirre M, Juaristi J, Álvarez M, Ruiz Díaz D, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. UNNE. Moreno 1240 (3400) Corrientes. E-mail: nbrandan@med.unne.edu.ar</p> <p>Adryamicin (ADR) - induced nephropathy in mice is a commonly used experimental model for pharmacological studies of human renal diseases. However, its molecular mechanism remains unclear. The primary aim of this study was to explore the relationship between the nephrotic syndrome with renal Bax/Bcl-xl ratio, Caspase-3, Hsp60, iNOS and HIF-1α expressions following ADR administration along 30 days.</p> <p>CF-1 mice were injected with a single dose of ADR (15 mg/kg, ip). Histological evaluations (PAS/HE) and scanning electronic microscopy were used for morphological descriptions of renal outer cortex. HIF-1α, Bax, Bcl-xl, Caspase-3, Hsp60 and iNOS expressions were determined by western blotting. Blood urea nitrogen (BUN) and Serum Creatinine (sCr) increased by 10 days ($p < 0.01$), indicating severe loss of renal function that was associated with widespread ultrastructural abnormalities. Histological semiquantitative scores showed glomerulosclerosis, tubular damage and interstitial infiltrates ($p < 0.01$). The Bcl-xl/Bax ratio decreased within the first days ($p < 0.01$) accompanied by active caspase-3 expression as a hallmark of apoptotic signalling. iNOS, Hsp60 and HIF-1α were up regulated on day 15.</p> <p>Our findings suggest that changes in the ratio Bcl-xL/Bax triggers caspase-3 activation which modulates renal apoptosis; while iNOS, Hsp60 and HIF-1α are associated with renal inflammation and fibrosis, tubular atrophy; linked to necrosis in this experimental model.</p>
<p>OIII-19 GASTROPROTECTION AND ANTIMICROBIAL ACTIVITY OF <i>Lithraea molleoides</i> AGAINST <i>Helicobacter pylori</i> Garro MF^b, Dalfovo MC^a, Vega AE^a, Cortiñas TI^a, Silva HJ^a, Saad JR^c, María AO^b, Pelzer L^b. Áreas de ^aMicrobiología, ^bFarmacología y Toxicología y ^cQuímica Orgánica. Universidad Nacional de San Luis. San Luis. E-mail: alemaria@unsl.edu.ar</p> <p><i>Lithraea molleoides</i> (Vell.) Engl. (Anacardiaceae) is known popularly as “molle”. <i>L. molleoides</i> is used in folk medicine as a diuretic and digestive. In one study, the antibacterial activity of <i>L. molleoides</i> was assayed on two clinical strains of <i>Helicobacter pylori</i> isolated from gastric biopsies and the reference strain <i>H. pylori</i> NCTC 11638, and was evaluated by agar diffusion method in well. An inoculum of 10⁶ CFU/ml was plated on Mueller-Hinton agar supplemented with 7% horse blood. The aqueous extract of <i>L. molleoides</i> was tested in the following concentrations 10, 100 and 250 mg/ml and 15 μl were added on each well. The plates are incubated at 37°C in microaerophilic conditions for 3-5 d. The MIC was determined by measuring the zone of inhibition at each concentration. <i>L. molleoides</i> exhibited antimicrobial activity in all strains tested with an inhibition zone range of 17-23 mm for 10 mg/ml; 25-33 mm for 100 mg/ml and 24-35 mm for 250 mg/ml. The results indicate that <i>L. molleoides</i> have activity antimicrobial against <i>H. pylori</i> strains.</p> <p>In other study, absolute ethanol was employed as ulcerogenic agent in Wistar rats (Method of Robert y col.). Infusion 20% of <i>L. molleoides</i> reduced ethanol-induced gastric damage in rats ($p < 0.01$). The results presented indicate that <i>L. molleoides</i> prevents the formation of gastric lesions and has significant antimicrobial properties against <i>H. pylori</i>. <i>L. molleoides</i> could represent an useful tool in relieving digestive disorders.</p>	<p>OIII-20 CHEMICAL ASSESSMENT OF THE NEW ANTIMICROBIAL PEPTIDE AP-CECT7121 ^{1,2} Urbizu, L.; ¹ Sparo, M.; ^{1,2} Virkel, G.; ^{1,2} Soraci, A.; ¹ Confalonieri, A.; ^{1,2} Rivulgo M., ^{1,2} Sánchez Bruni, S ¹- Laboratorios de Farmacología y Toxicología, Facultad de Ciencias Veterinarias -UNCPBA, (B7000APA) Tandil – Argentina. ²-CONICET-. e-mail: ssanchez@vet.unicen.edu.ar</p> <p>The emergence of multi-resistant bacteria, involves a serious therapeutic concern in clinical practice. Antimicrobial peptide (AP) CECT7121 was isolated from an environmental strain of <i>Enterococcus faecalis</i> CECT712, showing high <i>in vitro</i> efficacy against most of the pathogens recalcitrant to conventional treatments. The goals of this research work were the isolation, purification and identification by chromatography (RP-HPLC, TLC and HPLC-MS/MS) of the peptide AP-CECT7121. The BHI broth was inoculated with of an overnight culture of <i>E. faecalis</i> CECT7121. After incubating and chemical processes, the active compound obtained, was loaded on C₁₈ cartridges previous to RP-HPLC analysis. AP-CECT7121 was identified as a lipophylic compound by a peak at 24 min of retention time. The same fraction was used for the aminoacidic assessment using TLC, where a sequence of six aminoacids was obtained (proline, treonine, cistine, valine, tirosine y leucine). This antimicrobial compound after HPLC-MS/MS analysis showed a low molecular weight of 910 Da. Developing of AP-CECT7121 may be a potential tool for the treatment of Human and Veterinary multi-resistant bacterial infectious diseases.</p>

POSTERS BLOQUE 1

<p>B1-01 EFFICACY OF AN IMMUNOMODULATOR COMPOUND OBTAINED FROM <i>Enterococcus faecalis</i> CECT7121 CELL WALL ¹Confalonieri A., ¹Sparo M., ^{1,2} Urbizu L., ^{1,2} Rivulgo M., ^{1,2} Sánchez Bruni S</p> <p>1- Laboratorio de Farmacología, Facultad de Ciencias Veterinarias -UNCPBA, (B7000APA) Tandil – Argentina. 2- CONICET-.e-mail: ssanchez@vet.unicen.edu.ar</p> <p>Several studies have demonstrated the utility of the bacterial cell wall extracts (CWE) as immunomodulators on the treatment of some infectious diseases. <i>Enterococcus faecalis</i> (Ef) CECT7121, a probiotic strain, also demonstrated immunomodulation in some animal models. The goal of this work was to obtain an extract of CWE of <i>E. faecalis</i> CECT7121 and to evaluate its efficacy on <i>Salmonella enteritidis</i> (Se) in mice model. Culture died by heat Ef CECT7121 was sonicated during 30 minutes and was put under three successive centrifugations to 27,000g during 1 h. The obtained CWE was freeze-dried. For the efficacy study, thirty Balb-c mice were divided in 3 groups (n=10) and treated as follows: <u>Group I</u> Control: challenged with 2 doses of Se 5×10^7 CFU/ml (LD₉₉) q12 h and 5 doses of physiological solution q 24h. <u>Group II</u>: received only 5 doses of 1000 µg of CWE q 24h. <u>Group III</u>: was challenged as Group II and treated with 1000 µg of CWE q 24h. The survival rate was observed during 15 days post- challenge. Thirty percent of the animals of the Group III survived, compared with those of the Group I Control (100% of death). There was not observed changes on health of animals of the Group II, by which demonstrate the safety of the CWE. We conclude that CWE compound would display some immunomodulator properties responsible of the prolongation of the animal survival after challenging with a DL99 of Se.</p>	<p>B1-02 CHARACTERISATION OF ENTEROCOCCUS RESISTANT TO VANCOMYCIN IN MEAT AND MILK DERIVED ARTISANAL FOOD. ¹Delpech G., ¹Schell C., ²Pourcel G., ¹Sánchez Bruni S., ^{1,3}, ¹Tabera A., ¹de Luca M., ²Basualdo J., ²Sparo M. ^{1,2}</p> <p>1-Universidad Nacional del Centro de la Provincia de Buenos Aires. Escuela Superior de Ciencias de la Salud. 2-Universidad Nacional de La Plata. Facultad de Ciencias Médicas. 3- CONICET e-mail: monicaspapo@speedy.com.ar</p> <p><i>Enterococcus</i> spp usually showed intrinsic antimicrobial resistance to antimicrobials used in clinical practice, like cephalosporins and aminoglycosides. Vancomycin enterococcus resistant (VRE) were reported by CDC as Public Health risk-international emergence. However, the resistance selection pressure exerted for the misuse of antibiotics at hospitals does not explain the emergence of VRE in invasive infectious diseases in susceptible or immune-deficient patients. The main research goal of this study was to investigate the presence of VRE in meat and milk derived-artisanal food. Eighteen salami and 21 cheeses, elaborated in 4 different artisanal meat-milk elaboration units (Tandil) were studied. Each sample was homogenized, processed by duplicate and inoculated in a specific VRE medium BH agar-vancomycin (6 µg mL⁻¹). Phenotypification was assessed by conventional biochemical tests, also using the SDS-PAGE method. Besides, was investigated the associated resistance (agar diffusion) to ampicillin, teicoplanin, imipenem, linezolid, ciprofloxacin and gentamicin. The presence of VRE in artisanal food was demonstrated as follows: six VRE strains were isolated (1 <i>E. faecalis</i>, 3 <i>E. faecium</i>, 1 <i>E. gallinarum</i> 1 <i>E. raffinosus</i>) with associated resistance to ciprofloxacin, gentamicin (higher level of resistance) and linezolid. More regional studies in the search of VRE are required, since the artisanal food may act as reservoir and or vehicle of these strains, establishing an emergent concern in public health.</p>
<p>B1-03 MULTIDOSE PHARMACOKINETIC STUDY OF AZITHROMYCIN IN PNEUMONIC FOALS ^{1,3}Rivulgo V.M., ¹Fumuso E., ¹Sparo M., ^{2,3} Landoni F., ^{1,3}Sánchez Bruni. S.</p> <p>1.Facultad de Ciencias Veterinarias,UNCPBA. Tandil (B7000APA)-2. Facultad de Ciencias Veterinarias, UNLP-.3.CONICET.e-mail:ssanchez@vet.unicen.edu.ar</p> <p>Azithromycin (AZM) is an azalide antibiotic commonly used in Human and Veterinary Medicine, for the treatment of respiratory diseases. <i>Rhodococcus equi</i> is an intracellular facultative Gram positive pathogen that provokes pneumonia in foals. Pharmacokinetics (PK) of AZM in diseased foals has not been still described. The main goal of this study was to evaluate the plasma PK of AZM in a multiple dose regimen in experimentally challenged <i>R. equi</i> -foals-infection model of pneumonia. Five foals of 42 days old were inoculated by intratracheal endoscopy, with 25 mL of a 10^3 <i>R. equi</i> 103+ strain solution. When the disease developed, foals were treated orally with 10 mg/kg of AZM q 24 h for 6 days. Blood samples were obtained from jugular vein. Samples were frozen up to analysis by bioassay method using <i>Kocuria Rhizophila</i>. Cmax was obtained at 2 hours after the first and latest administration. Comparison between values of AUC₀₋₂₄ (14.0 ± 2.95 µg.h/ml) and AUC₁₂₀₋₁₄₄ (18.0 ± 5.00 µg.h/ml) showed no statistical difference. These values pointed out that the steady state was not attained, being 6 days of treatment insufficient to obtain clinical and bacteriological cure.</p>	<p>B1-04 IN VITRO CEPHALEXIN ACTIVITY ON <i>Escherichia coli</i> STRAINS IN BHI, CANINE SERUM AND URINE USING A DYNAMIC MODEL Picco, E.; Cerra, M.; Michel, P.; Stiefel, S.; Formentini, E.</p> <p>Cátedra de Farmacología, Facultad de Ciencias Veterinarias UNL Kreder 2805 (3080) Esperanza eforment@fcv.unl.edu.ar</p> <p>The activity of antibacterial agents is evaluated in standard bacteriological media, therefore the results do not reflect the antibacterial activity in different biological fluids. We studied the activity of Cephalexin on six strains of <i>Escherichia coli</i> in BHI, canine serum and urine. The study was conducted with a simple <i>in vitro</i> model that mimics the plasma disposition of an antibiotic, and allows evaluate the effectiveness of this one respect of the evolution of initial inoculum size versus time and time-dependent concentrations of the antibiotic. The Cephalexin MIC on <i>Escherichia coli</i> was estimated in a previous study and was 16 µg/mL. For each <i>Escherichia coli</i> strain, an inoculum of 1×10^6 CFU/mL in BHI and canine serum was confronted with 64 µg/mL of Cephalexin (4 x MIC). In urine, the strains were confronted with similar concentrations of Cephalexin to those reported in dogs (15 x MIC). Cephalexin concentrations decreased exponentially with a half-life of 1.5 hours. The efficacy expressed as percentage of reduction in initial size of bacterial inoculum in BHI was $47.8 \pm 5.6\%$, from $65.2 \pm 11.1\%$ in canine serum and $59.4 \pm 5.3\%$ in canine urine. The antibacterial activity was enhanced in biological fluids (p < 0.05), and there was no difference between them. These results show the variability of bactericidal activity of Cephalexin in similar environments than those encountered <i>in vivo</i>.</p>

<p>N1-05 IN VITRO CEPHALEXIN ACTIVITY ON <i>Escherichia coli</i> STRAINS IN BHI, CANINE SERUM AND URINE USING A DYNAMIC MODEL Picco, E.; Cerra, M.; Michel, P.; Stiefel, S.; Formentini, E. Cátedra de Farmacología, Facultad de Ciencias Veterinarias UNL Kreder 2805 (3080) Esperanza eforment@fcv.unl.edu.ar</p> <p>The activity of antibacterial agents is evaluated in standard bacteriological media, therefore the results do not reflect the antibacterial activity in different biological fluids. We studied the activity of Cephalexin on six strains of <i>Escherichia coli</i> in BHI, canine serum and urine. The study was conducted with a simple <i>in vitro</i> model that mimics the plasma disposition of an antibiotic, and allows evaluate the effectiveness of this one respect of the evolution of initial inoculums size versus time and time-dependent concentrations of the antibiotic. The Cephalexin MIC on <i>Escherichia coli</i> was estimated in a previous study and was 16 µg/mL. For each <i>Escherichia coli</i> strain, an inoculum of 1×10^6 CFU/mL in BHI and canine serum was confronted with 64 µg/mL of Cephalexin (4 x MIC). In urine, the strains were confronted with similar concentrations of Cephalexin to those reported in dogs (15 x MIC). Cephalexin concentrations decreased exponentially with a half-life of 1.5 hours. The efficacy expressed as percentage of reduction in initial size of bacterial inoculum in BHI was $47.8 \pm 5.6\%$, from $65.2 \pm 11.1\%$ in canine serum and $59.4 \pm 5.3\%$ in canine urine. The antibacterial activity was enhanced in biological fluids ($p < 0.05$), and there was no difference between them. These results show the variability of bactericidal activity of Cephalexin in similar environments than those encountered <i>in vivo</i>.</p>	<p>B1-06 IN VITRO ACTIVITY OF TULATHROMYCIN ON <i>Staphylococcus aureus</i>; EFFECT OF pH, INOCULUM SIZE AND BOVINE SERUM Picco, E.; Baroni, E.; Delgado, A.; Fernández, H.; Formentini, E. Cátedra de Farmacología, Facultad de Ciencias Veterinarias UNL Kreder 2805 (3080) Esperanza eforment@fcv.unl.edu.ar</p> <p>The MIC is a robust pharmacodynamic parameter for quantify the <i>in vitro</i> bactericidal activity of an antibiotic against sensitive bacteria. However, it only quantifies the intrinsic activity of an antibiotic in a standard bacteriological media with a pH similar to physiological values (7.2-7.4), and does not consider the modification of its intrinsic activity due to changes in pH of the medium, the humoral immune response and the inoculum size. We studied the <i>in vitro</i> activity of Tulathromycin on six strains of <i>Staphylococcus aureus</i>. The MIC was estimated by the macrodilution technique in BHI at pH 7.4, 6.5 and 5.5 and BHI/bovine serum 50:50 (pH 7.44). The MIC of Tulathromycin against control strain (ATCC 29213) was studied on different inoculum sizes (UFC/mL): 5×10^3, 1×10^6, 1.5×10^7, 1.5×10^8 and 7.5×10^8. The results of MIC in BHI were: 2-4 µg/mL (pH 7.4), 80-160 µg/mL (pH 6.5) and 800 µg/mL (pH 5.5), MIC in BHI / bovine serum 50:50: 0.25 µg/mL (pH 7.44) and MIC on different inoculum sizes: 4 µg/mL (5×10^3, 1×10^6 UFC/mL) and 8 µg/mL (1.5×10^7, 1.5×10^8 and 7.5×10^8 UFC/mL). Like has been reported for macrolide agents, Tulathromycin reduces its potency at low pH values. An important finding is the increased bactericidal activity in presence of bovine serum, indicating that antibodies and other serum components may have an important role in the <i>in vivo</i> activity of this antibiotic.</p>
<p>B1-07 IN VITRO EFFECT OF THE REDUCED FLUBENDAZOLE METABOLITE AGAINST <i>ECHINOCOCCUS GRANULOSUS</i> PROTOSCOLECES Elisondo, M.C.^{1,2}, Ceballos, L.^{3,2}, Alvarez, L.^{3,2}, Sánchez Bruni, S.^{3,2}, Lanusse, C.^{3,2}, Denegri, G.^{1,2} ¹Lab. Zoonosis Parasitarias, FCEyN, UNMDP; Argentina. ; ²CONICET; ³Lab. Farmacología, FCV, UNCPBA. E-mail: mceliss@mdp.edu.r</p> <p>Flubendazole (FLBZ) showed efficacy against protoescoleces (PSC) and cysts of <i>Echinococcus granulosus</i> <i>in vivo</i> and <i>in vitro</i>. After its oral administration to mice with cystic echinococcosis, equivalent cyst concentrations of the parent drug and its reduced-metabolite (R-FLBZ) were measured. The aim of this work was to point out the <i>in vitro</i> effect of the R-FLBZ metabolite against <i>E. granulosus</i> PSC. PSC were incubated with 11 nmol/ml of FLBZ, R-FLBZ, albendazole (ABZ) or ABZ-sulphoxide (ABZSO). PSC incubated with culture medium containing methanol were used as controls. Vitality was assessed every 6 days using the methylene blue exclusion technique and samples were taken for electron microscopy. As previously shown, the greater effect was produced by FLBZ. R-FLBZ showed a marked effect producing ultrastructural alterations after 6 days post-incubation and reducing the vitality to approximately 27% after 54 days. The outcomes obtained demonstrated the <i>in vitro</i> efficacy of the R-FLBZ against PCS of <i>E. granulosus</i>.</p>	<p>B1-08 IN VITRO ANTIMICROBIAL SUSCEPTIBILITY TEST OF <i>Paenibacillus larvae</i> ISOLATED FROM DISEASE HONEYBEES IN BUENOS AIRES PROVINCE. Huber, B.; Quintero, M.; Marchetti, M.L.; Errecalde, J.; Mestorino, N. Cátedra de Farmacología. Facultad de Cs. Veterinarias. Universidad Nacional de La Plata. CC 296, 1900 La Plata. e-mail: barhuber@gmail.com</p> <p>The goal of this <i>in vitro</i> test was to provide a reliable predictor to continue with pharmacokinetic/pharmacodynamic studies in the infected host. <i>P. larvae</i> spores were obtained from several diseased colonies by collecting scales of dried larvae. Identification of selected strains was confirmed by microscopic and biochemical techniques. Susceptibility patterns of isolates were assessed by the disk diffusion method following the general guidelines of CLSI, using MYPGP agar. MICs were determined by the agar dilution method. Tylosin was tested in serial twofold dilutions ranging from 2 to 0.0003 µg/mL. The 11 strains isolated were highly susceptible to β lactams, macrolides and rifampicin. Aminoglycosides and trimethoprim/sulfamethoxazole performed very poorly. Given the demonstrated <i>in vitro</i> and field activity, macrolides were chosen for further work. Tylosin was highly active with MIC values ranging from 0.03125 to 0.0625 µg/mL. Previously, we observed that pharmacokinetics parameters were substantially conditional by seasonality, productive level and sanitary state; therefore we considered pharmacokinetic-pharmacodynamic future studies taking account these conditioners to ensure a correct therapeutic strategy in this type of exploitation.</p>

<p>B1-09 ANTIMICROBIAL RESISTANCE IN COMMERCIAL FARMS OF BUENOS AIRES FROM FAECAL SAMPLES USING <i>Escherichia coli</i> AS AN INDICATOR Marchetti, M.L., Lucas M., Lambertini, A., Quintero, M., Errecalde J., Mestorino, N. <i>Cátedra de Farmacología, Facultad de Ciencias Veterinarias, UNLP, 60 y 118, CC 296, 1900. La Plata, Bs.As, Argentina. mlauramarchetti@yahoo.com.ar</i></p> <p>The objective of this research was to evaluate commensal <i>E. coli</i> strains' resistance profiles in vitro, among animals-humans-environment. A survey protocol to obtain information about the use of antimicrobial (ATM) products was design. Samples were collected from Tandil, San Vicente and Lujan. Strains were isolated from faeces samples of dairy cows, calves, pets and septic human's tanks. Water samples were obtained from different sources (house, effluents, milking shed). Faecal samples were cultured in EMB agar, colored by Gram and typificated by biochemical tests. Water samples were tested by Most Probable Numbers method. Sensitivity profiles for 8 ATM agents were tested by disk diffusion method using <i>E. coli</i> ATCC 25922 for quality control (CLSI 2008). ATM agents were chosen based on treatments of humans and animals' diseases, surveys results and food additives usage. Isolates had high level of tetracycline and ampicillin resistance. In every multiresistance profile, resistance to tetracycline was expressed.</p>	<p>B1-10 EFFECT OF pH ON THE ANTIBACTERIAL ACTIVITY OF DANOFLOXACIN AGAINST <i>Staphylococcus aureus</i> Moncada Cárdenas, L.A.; Daniele M; Quintero M.; Errecalde, J.O.; Mestorino, N. <i>Cátedra de Farmacología, Facultad de Ciencias Veterinarias, UNLP, 60 y 118 CC 296, 1900 La Plata. e-mail noram@fcv.unlp.edu.ar- jerrecal@fcv.unlp.edu.ar</i></p> <p>Danofloxacin (DAN) is a fluoroquinolone developed for use in veterinary medicine with rapid bactericidal activity against a broad range of pathogens included most gram-negative bacteria and some gram-positive bacteria, mycoplasmas, and intracellular pathogens. The purpose of this study was to evaluate through bacterial killing curves the effect of the pH variation on the antibacterial activity of DAN against strains of <i>S. aureus</i> isolated of mastitic quarters. <i>S. aureus</i> strains isolated (N = 6) and <i>S. aureus</i> ATCC 25923 were tested through bacterial killing curves, changing the pH of the broth at 7.4, 6.5, and 5.0, in order to simulate the conditions of acidity of subcellular structures which are commonly associated with <i>S. aureus</i> intracellular persistence. DAN showed bactericidal effect concentration-dependent (8x MIC) at different pHs tested which was evident after 6 h of exposure. DAN presents greater union to its target enzyme and exhibits a cellular penetration 70 times more than common quinolones. These data coincide with previous results that were obtained in vivo, where DAN had an excellent efficacy against subclinical mastitis caused by <i>S. aureus</i>.</p>
<p>B1-11 ALTERATIONS IN THE BACTERIAL MEMBRANE INTEGRITY INDUCED BY EU-CI-OFLO ENHANCE THE BACTERICIDAL ACTION OF OFLOXACIN. Romero V¹., Sanchez N¹., Pons, P³., Bocco, J.L²., Manzo R¹., Alovero F¹. Dptos. de ¹Farmacia y ²Bioquímica Clínica, FCQ y ³Centro de Microscopia Electrónica, FCM; UNC. Cdad Universitaria 5016. Córdoba. Argentina. E-mail: fallover@fcq.unc.edu.ar.</p> <p>The search for new more effective Fluoroquinolones is a constant challenge to overcome the resistance issue. The development of new delivery systems is an alternative tool to preserve the utility of old antimicrobials. Eudragit E100 (Eu) is a cationic polyelectrolyte able to react with the acidic group of drugs. Complexes Eu with Ofloxacin (OFLO) and other counterion, Cl⁻, which turns the complexes water soluble were prepared, giving clear dispersions (Eu-Cl₅₀-OFLO₂₀) with positive electrokinetic potential and pHs 6.4-6.5. The killing rate and bactericidal action exhibited by OFLO against <i>P.aeruginosa</i> is enhanced in Eu-Cl₅₀-OFLO₂₀. The bacteria were processed for electron microscopy. Those treated with Eu-Cl₅₀-OFLO₂₀ showed damage of bacterial envelope and the cytoplasm was less electrondense. Flow cytometry with nucleic acid-binding fluorescent probes show lost membrane integrity. This additional mechanism of action coupled with the own of the FQ could explain the enhancement of the bactericidal action.</p>	<p>B1-12 HEMATOLOGICAL AND BIOCHEMICAL PROFILE OF TRIFLURALIN-TREATED GOATS Villagra S¹, Manilla G², Lacchini R², Zaidenberg A^{1,3}, Martins E¹, Rule R^{3,4} ¹IDIP CICPBA "Dr. Fernando Viteri"; ²Zootecnia, FCA; ³Farmacología, FCM UNLP; ⁴CIC PBA. Calle 60 y 120, 1900, La Plata. sergionicvillagra@yahoo.com.ar</p> <p>Trifluralin (2,6,6 dinitropropyl-p-toluidine, TFL) presents anti-<i>Trypanozoma cruzi</i> activity during the chronic phase of the disease in mice. The aim of this study was to evaluate the hematological and biochemical behavior of TFL -prepared in peanut oil as solvent- in goats. The effects of this formulation on plasma activity values of creatine kinase (CK) were also determined as indicators of tissue damage. Creole goats (n=10) were intramuscularly (IM) administered TFL (20 mg/kg/day for six days). Blood samples were collected at different times before and after TFL administration to determine hematological and biochemical profile. Results showed that biochemical and hematological parameters were not significantly different among the different blood sampling times in TFL-treated goats as compared to controls. CK activity after IM TFL administration did not result in tissue damage provoked by the pharmaceutical preparations at the injection site.</p> <p><i>This study was supported by a grant provided by the Commission of Scientific Research of the Province of Buenos Aires, Argentina.</i></p>

B1-13

LEVEL OF TUMOR NECROSIS FACTOR ALFA (TNF- α) IN SEPSIS

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Sepsis is the presence of viable microorganisms in the blood that causes a clinical picture of inflammatory response, oxygenation imbalances and organ dysfunction. The main inflammatory markers involved include TNF alpha, interleukin-1 and interleukin-6.

Aims: To correlate the values of Tumor Necrosis Factor alfa (TNF - α) in septic patients with mortality and clinical development.

Methods: Serum of 16 patients with sepsis criteria. The level of TNF.alfa was measured by immunoanalysis. Were followed up patients for a month.

Results: Patients who died had on average higher levels of TNF alpha to patients who survived (416.14 vs 287.06 pg / ml) $p < 0.01$, while those who developed septic shock on average exceeded those without did (439.03 vs 102.11 pg / ml) $p < 0.01$.

Discussion: The study showed that TNF alpha is higher in patients with sepsis and is an indicator of poor prognosis and unfavorable outcome.

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B2-14

ANTIPROLIFERATIVE ACTION OF LIMONENE ON A LYMPHOMA CELL LINE: RELATION BETWEEN NITRIC OXIDE AND REACTIVE SPECIES OF OXYGEN

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Limonene (L) exerts antiproliferative effect on a lymphoma cell line (BW5147) increasing nitric oxide (NO). H₂O₂ is related to cell proliferation and NO modulation. The aim of the study was to analyze the participation of H₂O₂ and superoxide anion (O₂⁻) in the effect of limonene. The enzymes involved in H₂O₂ modulation such as catalase (CAT), superoxide dismutase (SOD) and peroxidase (Px) were studied by a spectroscopy assay. Results were expressed as Mean ± SEM of three experiments made by triplicate: [&]P<0.05 (respect to L) * P<0.05 (Respect to Basal) (Student's t test). **H₂O₂** (mM/10⁶ cells): Basal: 0.0578 ± 0.0088; L 40 µg/ml: 0.085 ± 0.005 *, L 100 µg/ml: 0.0580 ± 0.004, L 40 µg/ml + MEK 1/2 inhibitor: 0.055 ± 0.0050[&], L 100 µg/ml + MEK 1/2 inhibitor: 0.056 ± 0.005. **O₂⁻** (nmol of reduced NBT /10⁶ cells): Basal: 21.53 ± 0.054, L 100 µg/ml: 27.11 ± 0.52 **, L 100 µg/ml + mevalonic acid: 18.08 ± 1.49 [&]. **SOD activity** (U/ml/ 10⁶ cells): Basal: 0.66 ± 0.060, L 40 µg/ml: 0.77 ± 0.075*, L 100 µg/ml: 0.20 ± 0.02**. **PER activity** (U/ml/10⁶ cells): 3x10⁻⁴ ± 5x10⁻⁵, L 40 µg/ml: 1.3x10⁻⁴ ± 1x10⁻⁵**, L 100 µg/ml: 1.5x10⁻⁴ ± 2x10⁻⁵**. At low concentration, L via ERK increased H₂O₂ level by SOD activation and inhibition of Px. At high concentration, L increased O₂⁻ by inhibition of farnesylation and SOD inhibition. Oxidative stress is implicated in L antiproliferative action.

B2-15

“IN VITRO” COMPARATIVE EFFECT OF AN AQUEOUS EXTRACT OF *LARREA DIVARICATA* CAV. AND NDGA ON H₂O₂ METABOLISM OF NORMAL RATS SUBMANDIBULARY GLANDS.

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L. divaricata possesses anti-inflammatory and antioxidant actions. The effect of *L. divaricata* aqueous extract (LAE, 1-1000 µg/ml) and NDGA (0.084-3.41µg/ml, concentrations present in the extract) on hydrogen peroxide (H₂O₂) level and on superoxide dismutase (SOD), catalase (CAT), and peroxidase (Px), in submandibulary gland of normal Sprague Dawley rats was studied. Results were expressed as X ± SEM of eight determinations performed by duplicate: **H₂O₂** (mM/ g gland), control (C) (4.56 ± 0.4); **LAE 500 µg/ml** (2.5 ± 0.2 [&]). **Px** (U/ml/g gland) C: 0.0086 ± 0.0008, **LAE: 10 µg/ml:** 0.0087 ± 0.0008; **100 µg/ml:** 0.0088 ± 0.0009; **500 µg/ml:** 0.026 ± 0.0010**; **1000 µg/ml:** 0.080 ± 0.0080**; **CAT** (U/ml/g gland) C: 25.82 ± 2; **LAE 10 µg/ml:** 27 ± 2; **100 µg/ml:** 18.74 ± 1*; **500 µg/ml:** 10.96 ± 0.8*; **1000 µg/ml:** 13 ± 1**. **SOD** (U/ml/g gland), C: 6.57 ± 0.6; **LAE 10 µg/ml:** 5.87 ± 0.5; **100 µg/ml:** 6.57 ± 0.6; **500 µg/ml:** 4 ± 0.38**; **1000 µg/ml:** 2.80 ± 0.28**. **NDGA: Px: 0.084 µg/ml:** 0.0050 ± 0.0005*; **0.34 µg/ml:** 0.011 ± 0.001; **3.41 µg/ml:** 0.019 ± 0.0019**. **CAT: 0.084 µg/ml:** 27.97 ± 2; **0.34 µg/ml:** 19.2 ± 2*; **3.41 µg/ml:** 28.8 ± 2. **SOD 0.084 µg/ml:** 6.4 ± 0.7; **0.34 µg/ml:** 0.17 ± 0.01**; **3.41 µg/ml:** 0.15 ± 0.01. LAE decreased H₂O₂ level through an increase of Px activity and a decrease of SOD activity both effects were related to the presence of NDGA and other compounds.

B2-16

STUDY OF DIURETIC EFFECT OF *Artemisia douglasiana* Besser IN RATSGil L, Garcia Aseff S, Wendel G, Pelzer L. Farmacología. Fac Qca, Bioqca y Fcia, UNSL. Chacabuco y Pedernera, San Luis 5700. E-mail: aseff@unsl.edu.ar

Artemisia douglasiana Besser (*Ad*) is popularly known as “matico”, has been used in folk medicine as panacea for a great diversity of health problems. In this study we investigated the diuretic effect of aqueous infusions at 10% and 15 % of the aerial parts of *Ad*. Thirty male Wistar rats (150-200 g) were divided in five groups (n: 6): the treated group received 10% or 15% infusion of *Ad* (p.o.); the reference groups received Furosemide (20 mg/kg, i.p.) and Hydrochlorothiazide (25 mg/kg, p.o.); and the control group received saline solution (50 ml/kg, p.o.). Urinary volumetric excretion (UVE) was measured at 15 min intervals in 4 hours diuresis (Lipschitz, 1943). Electrolytes concentrations (Na⁺, K⁺, Cl⁻; Ion Selective Electrode), pH and density were estimated. *Ad* treated rats showed significant diuretic effect at both doses levels between 30 min and 105 min. UVE 10 %: 71.80 ± 2.284; UVE 15 %: 74.31 ± 3.225, vs UVE control: 56.66 ± 2.797, (p < 0.001; Student's t-test). *Ad* induced an increase in K⁺ and Cl⁻ excretion respect to saline solution. *Ad* 10 % K⁺: 0.86 ± 0.13 vs 0.37 ± 0.06 mEq/kg (p < 0.05); Cl⁻: 0.65 ± 0.09 vs 0.31 ± 0.05 mEq/kg (p < 0.05). *Ad* 15 % K⁺: 0.75 ± 0.08 vs 0.37 ± 0.06 mEq/kg (p < 0.05); Cl⁻: 0.53 ± 0.06 vs 0.31 ± 0.05 mEq/kg (p < 0.05). There were no changes in other parameters. These results indicate that *Ad* show a Furosemide-like activity respect to the onset and duration time of its diuretic effect.

B2-17

POTENTIAL ROLE OF OPIOID RECEPTORS ON THE EFFECTS OF HESPERIDIN AND ITS AGLYCON HESPERETIN.

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Hesperidin (HN, hesperetin-7-rhamnoglucoside) is a glycosylated flavanone present in *Valeriana wallichii*, *V. officinalis*, and Citrus species. Previous reports from our laboratory described the sedative and antinociceptive effects of HN in mice and the possible participation of the opioid system in these activities. In the present work we examined the involvement of 5-HT_{2A/C}, α₁ and α₂-adrenergic and opioid receptors on the effect of HN in the hole board, locomotor activity and writhing tests. In order to advance in the study of the mechanism of action of HN, the capacity of this flavonoid, hesperetin (HN aglycone) and a set of natural and synthetic related compounds to bind to the µ opioid receptor was investigated. Additionally, the effect of HN and hesperetin on µ opioid receptor and GIRK1/2 channels co-expressed in *Xenopus laevis* oocytes was evaluated in electrophysiological experiments.

The results indicated that HN is not a ligand for the µ opioid receptor but its *in vivo* effects are blocked by naltrexone (an opioid receptor antagonist). Hesperetin and other related flavonoids bind to the µ opioid receptor with Ki values between 1 to 120 µM. These findings suggest an interaction between flavonoids and opioid receptors.

<p>B2-18 SPRAY DRYING OF RHAMNUS PURSHIANA EXTRACT FOR DIRECT COMPRESSION AND EVALUATION OF LAXATIVE EFFECT ^{1,2}Gallo.L., ²Bucciarelli A., ³Bianchi M., ²Skliar M., ¹Allemandi D. ¹Dpto.de Farmacia. Univ. Nac. de Córdoba., (5000) Córdoba. ²Dpto.de B., B. y Farmacia., San Juan 670.³Dpto.de Ing. Qca., La Carrindanga Km.7.²⁻³Univ. Nac. del Sur (8000) Ba. Bca, Bs. As. CONICET. E-mail: loreana.gallo@uns.edu.ar</p> <p>During the last years, a notable increment in the use of the phytomedicines has been observed. Dry plant extracts (DPE) are generally used as active ingredients for the formulation of phytomedicines in the form of tablets. <i>Rhamnus purshiana</i> (Rhamnaceae) is one of the most used plants due to its effective, economic and natural laxative action.</p> <p>The optimization of a spray drying process for the production of DPEs of <i>R. purshiana</i> is proposed in order to obtain DPEs with appropriated quality for direct compression (DC). A 2⁵⁻¹ fractional factorial statistical design was selected to study the effect of the processing variables on the DPEs quality. Physical and mechanical properties, hygroscopicity and process yielding of DPEs were studied. The fluid plant extract and colloidal silicon dioxide were the ingredients to be spray dried. Spray drying process was performed in a laboratory scale Mini Spray Dryer. Operative conditions affected the spray dried powders properties. DPEs with good flowability were obtained and a selected sample with these characteristics was used for laxative effect evaluation on CF-1 albino mice. A DPE with good flow properties for DC and significant ($P<0.05$) laxative effect on mice was observed.</p>	<p>B2-19 EFFECT ON GASTRIC ACID SECRETION OF METHANOLIC EXTRACT OF LARREA DIVARICATA CAV IN RAT Pedernera AM¹, Guardia T¹, Guardia Calderón CE², Pelzer LE¹ ¹Farmacología, ²Bromatología. Fac Qca, Bqca y Fcia Univ Nac San Luis. 5.700 San Luis. Email: tguardia@unsl.edu.ar</p> <p>In previous studies we showed for leaves methanolic extract of <i>Larrea divaricata</i> Cav (Zigophyllaceae) (<i>LdMEL</i>) (J. of Ethnopharmacology Vol.105: 415-420, 2006) antiulcerous gastric activity against different necrotizing agents and elevated free radical scavenging capacity. The aim of this study was to assess the effect of <i>LdMEL</i> on gastric acid secretion in rat (Shay et al.,1945). Female Wistar rats, (160-200g) with water <i>ad libitum</i> and deprived of food for 24 h were anesthetized, the ligature was performed 0,5-0,7 mm below the pylorus. Rats were divided into three groups and orally treated as follows: G1control (saline), G2 <i>LdMEL</i> 300 mg/kg and G3 ranitidine (reference) 50 mg/kg. All animals were deprived of water and food for the rest of the experiment. Animals were killed 4 h later, a ligature placed at the esophago-cardiac junction was performed and their stomachs removed. The gastric content was collected and centrifuged, supernatant volumes were measured and acid concentration was estimated by titration to pH 7 with 0.1 NaOH using an automatic titrator. Statistical by ANOVA test. Acidity was expressed as $\mu\text{Eq/ml}$. <i>LdMEL</i> at the dose effective as anti-ulcerogenic in rats, did not inhibit the gastric acid secretion. The volume of gastric content did not show significative difference compared to the control group. These results suggest that <i>LdMEL</i> exert an effective antiulcerous activity without modifying gastric acid secretion.</p>
<p>B2-20 ANTIOXIDANT ACTIVITY AND TOTAL PHENOLIC CONTENT OF 21 ARGENTINEAN MEDICINAL PLANT EXTRACTS. Tournier, H., Fioravanti, D., Dadé, M. and Schinella, G. Cátedra de Farmacología Básica. Facultad de Cs. Médicas, UNLP- CIC Peia de Bs As, La Plata, Argentina. E-mail: schinell@uv.es</p> <p>The use of medicinal herbs is an alternative to conventional medicine to treat diseases associated with oxidative stress. In this study we assess the antioxidant capacity (AC) and the total phenolic (TP) and flavonoid content of 21 extracts obtained from commercially available supplies of native plants of Traslasierra valley, Córdoba: <i>Hedeoma multiflorum</i>, <i>Mintostachys mollis</i>, <i>Lippia turbinata</i>, <i>Satureja parvifolia</i>, <i>Aloysia triphylla</i>, <i>Aloysia gratissima</i>, <i>Aloysia polystachya</i>, <i>Heterothalamus allienus</i>, <i>Xanthium spinosum</i>, <i>Gnaphalium gaudichaidianum</i>, <i>Flaveria bidentis</i>, <i>Hypericum connatum</i>, <i>Larrea divaricata</i>, <i>Aristolochia macroura</i>, <i>Erythraea quitensis</i>, <i>Geoffroea decorticans</i>, <i>Solanum rutilum</i>, <i>Urtica dioica</i>, <i>Usnea gracilis</i>, <i>Anemia tomentosa</i> and <i>Lycopodium saururus</i>. AC was assessed on the basis of different methods: scavenging of stable ABTS and DPPH free radicals, ability to reduce Fe⁺³ in the FRAP assay, and capacity to inhibit the lipid peroxidation of copper-induced human plasma oxidation. All extracts were able to bleach the radicals in the range of 0.03- 4.48 $\mu\text{mol eq. Trolox/mg dry extract}$. <i>S. parvifolia</i> and <i>H. connatum</i> extracts exhibited the highest AC for DPPH (1.48 and 1.77 $\mu\text{mol eq. Tx/mg}$) and ABTS (3.20 and 4.48 $\mu\text{mol Tx eq./mg}$). <i>S. parvifolia</i>, <i>L. divaricata</i> and <i>H. connatum</i> showed the highest reducing capacity (8.89, 8.44 and 7.72 $\mu\text{mol eq. of ascorbic acid/mg dry extract}$). There was a good correlation between the TP content and the AC ($P<0.01$). At 100 $\mu\text{g/ml}$, <i>S. parvifolia</i> and <i>H. connatum</i> also showed a very high capacity (> 85%) to inhibit human plasma peroxidation. These two plants may be important sources for the isolation of compounds with potential use as pharmacological tools.</p>	<p>B2-21 BIOGUIDED PURIFICATION AND PHARMACOLOGICAL CHARACTERIZATION OF NEUROACTIVE COMPOUNDS PRESENT IN ALOYSIA VIRGATA. Wasowski C., Marder M. IQUIFIB (UBA-CONICET), Facultad de Farmacia y Bioquímica, Junín 956 (C1113AAD), Buenos Aires, Argentina. mmarder@qb.ffyb.uba.ar</p> <p>Using the guide of a competitive assay for the benzodiazepine binding site (BDZ-bs) in the GABA_A receptor two active diterpenes were isolated from the aerial parts of <i>Aloysia virgata</i> (Ruiz & Pavón). These compounds; identified as (16R)-16, 17, 18-trihydroxyphyllolcladan-3-one (1) and (16R)-16, 17-dihydroxyphyllolcladan-3-one (2) on the basis of spectral data; competitively inhibited the binding of [³H]-FNZ to the BDZ-bs with $K_i \pm \text{SEM}$ values of $56 \pm 19 \mu\text{M}$ and $111 \pm 13 \mu\text{M}$, respectively. The behavioral actions of these diterpenes, i.p. administered in mice, were examined in the plus maze, hole board, locomotor activity and light/dark tests. Compound 1 exhibited anxiolytic-like effects in mice evidenced by a significant increase of the parameters measured in the hole board test (number of head dips at 0.3 mg/kg and 3 mg/kg, rears at 1 mg/kg and time spent head dipping at 3 mg/kg), in the plus maze assay (percentage of open arm entries at 1 mg/kg) and in the light/dark test (time in light and the number of transitions at 1 mg/kg). Compound 2 augmented the number of rearings in the hole board apparatus (at 0.3 and 1 mg/kg) and the locomotor activity (at 1 mg/kg). These results reveal the presence of neuroactive compounds in <i>Aloysia virgata</i>.</p>

<p>B2-22 GASTROINTESTINAL EFFECTS OF <i>Solidago chilensis</i> AND DEVELOPMENT OF A DRY PLANT EXTRACT WITH ADEQUATE PHYSICO-MECHANICAL PROPERTIES Bucciarelli A, Gallo L, Milczakowsky MC, Skliar MI. Dpto. de Biología, Bioquímica y Farmacia, San Juan 670, UNS, (8000) Bahía Blanca. E-mail: mskliar@uns.edu.ar <i>Solidago chilensis</i> Meyen (Asteraceae) is a native species from South America, widely used in the popular medicine of different countries as an anti-inflammatory, diuretic and to treat gastrointestinal disorders. Despite its traditional uses, pharmacological and toxicological investigations are rather scarce. Gastroprotective effect on ethanol-induced gastric ulcer model and gastrointestinal transit on charcoal meal test of the aqueous plant extract were evaluated in mice. <i>S. chilensis</i> extract exhibited a significant reduction in both gastric ulceration and gastrointestinal transit at 1000 and 2000 mg/kg doses ($P < 0.05$). Acute toxicity by means of a functional observational battery and by assessing the motor activity in an open field was evaluated in mice. No toxic effects were observed for exposure to the extract. Taking into account the possible therapeutical use of the plant, a novel dry plant extract (NDPE) of <i>S. chilensis</i> was developed and physico-mechanical properties were studied. NDPE showed acceptable flow properties for direct compression (DC). Pharmacological results and physico-mechanical properties exhibited by NDPE might be useful in the development of a suitable oral dosage form towards the treatment of gastric ulcers and related disorders by means of DC technology.</p>	<p>B2-23 IN VITRO ANTIMICROBIAL ACTIVITY OF PROPOLIS EXTRACTS AGAINST MICROORGANISMS ISOLATED FROM THE EXTERNAL AUDITORY CANAL OF CANINE ¹Lozina, L.A.; ¹Peichoto, M.E., ²Granero, G., ¹Acosta, O. ¹Facultad de Ciencias Veterinarias - UNNE. Sgto. Cabral 2139 (3400) Corrientes, Argentina e-mail: lozina@vet.unne.edu.ar ² Facultad de Ciencias Químicas. UNC, Córdoba, Argentina</p> <p>Argentine propolis from Mendoza was extracted by maceration using ethanol/water mixtures in different concentrations. The obtained extracts were analyzed by chromatographic methods. Several microbiological methods were used to evaluate which of them can properly determine the antimicrobial activity of the propolis extracts against microorganisms isolated from exudates obtained from the external auditory canal of dogs with otitis. Serial Dilution in Tubes yielded the most consistent results. The results of the Agar Plate Diffusion were directly proportional to the hydrosolubility of the extracts. Therefore, this method did not correctly determine the activity of propolis. Bioautobiographic assays are suitable alternatives to evaluate the antimicrobial activity of a complex mixture containing many antimicrobial components of varying polarity such as propolis. It should be highlighted the importance of using the correct combination of microbiological methods and chromatographic analysis to determine the compounds responsible for biological activity of propolis. This natural product could be used as a topical antimicrobial in canine otitis.</p>
<p>B2-24 EFFECTS OF THE PHYTOESTROGEN GENISTEINE ON THE ISCHEMIA-REPERFUSION IN ISOLATED GUINEA-PIG HEARTS. Colareda, G., Ragone, M.I., Consolini, A.E. Cátedra de Farmacología, Dpto Cs. Biológicas, Fac. Cs Exactas, UNLP, La Plata, Argentina. dinamia@biol.unlp.edu.ar The phytoestrogen genistein (Gen), a component from soy beans, was evaluated as cardioprotective on rats and guinea-pigs. It was reported that Gen can reduce the $I_{Ca,L}$ but also to increase the shortening of cardiomyocytes in guinea-pigs (Liew 2003, Li 2008). Our last results in rat hearts exposed to 20 μM Gen previous to ischemia-reperfusion (I/R) showed that Gen did not improve contractile recovery (%P) in females and decreased it in males (SAFE 2008). Now, we evaluated whether Gen can protect guinea-pig hearts from the contractile failure associated to I/R. Hearts were isolated from anesthetized guinea-pigs (150-300 g, both sex) and aortically perfused with Krebs (C, Ca^{2+} 2 mM) at 30°C. The intraventricular pressure (P) and total heat rate (H_t) were simultaneously measured in a flow-calorimeter. The hearts were pretreated with C (C group, n=6) or C+Gen 20 μM (Gen-I/R group, n=4) by 20 min before exposing to I/R (30 min/45 min). In another group, a period of 3 min I was applied during the Gen pretreatment (pre-conditioning, PC group, n=6). Before I, Gen increased P to 139 \pm 13% of pre-I but not H_t, suggesting that muscle improved the economy. During R, Gen induced an increase in P recovery only in the PC group, at the start (to 81.8\pm16% vs. 54.7\pm8% in C and 25 \pm0.8% in Gen-I/R, $p < 0.05$) and at the end of R (104\pm11% in PC vs. 63\pm8% in C and 49\pm13% in Gen-I/R, $p < 0.05$) with a similar increase in H_t (120 to 148%, NS among the 3 groups). Results suggest that Gen could protect the guinea-pig hearts by increasing a pre-conditioning way.</p> <p><i>Grants: X-513 UNLP-2009/11 PIP 6024/05</i></p>	<p>B2-25 THE ANTISPASMODIC EFFECTS OF ALOYSIA POLYSTACHYA AND A. GRATISSIMA TINCTURES ARE NOT DUE TO K^+ CHANNELS ACTIVATION NOR Ca^{2+} CHANNELS INHIBITION ON ISOLATED RAT INTESTINE. Berardi, A. and Consolini, A.E Cátedra de farmacología, área farmacia, dpto cs. Biológicas, fac. Cs exactas, unlp. La plata, arg. Dinamia@biol.unlp.edu.ar Plants from the genus <i>Aloysia</i> are commonly used in folk medicine as euphetics. In previous works we showed that the aqueous extracts from <i>A. polystachya</i> (burrito, B) and <i>A. gratissima</i> (palo amarillo, PA) were non-competitive inhibitors of acetylcholine (Ach) in rat duodenum. Now we compared the effects of tinctures (TM, macerated in ethanol 70°, 200mg drug/ml) on isolated rat ileons at 37°C, by measuring the longitudinal force by isometric transducers. The dose-response curves (DRC) of Ach (pD_2: 6.08\pm 0.95) were non-competitively inhibited by TM of B and PA (IC50: 3.1\pm0.6 and 6.5 \pm2.2 mg/ml, resp., n=8 and 7). To assay whether this effect was due to activation of K^+ channels (I_K) there were done: a) relaxant DRC of TM on the tonic contraction of Ach or high-$[K^+]_o$ in the absence or presence of 40 mM TEA; b) DRC of Ach in the presence of 10 mM TEA and/or B & PA-TM. B and PA relaxed the Ach tonic contracture (but not that of high-$[K^+]_o$) and the I_{K+}-blocker TEA did not significantly avoided it. The TM also relaxed the TEA contracture but potentiated the non-competitive antagonism of TEA on the Ach-DRC, "apparently" increasing its affinity pD_2 from 1.66\pm0.12 to 2.66\pm0.32 and 2.16\pm0.11 for B and PA, resp. Results suggest that: a) the antispasmodic effect of these <i>Aloysia</i>'s is not due to K^+ channels activation nor to Ca^{2+} channels inhibition; b) it may be due to an interference with another mechanism triggered by the M3 receptor but not by depolarization. UNLP X-513-2009/11.</p>

<p>B2-26 ANTIINFLAMMATORY ACTIVITY OF A PARTIALLY PURIFIED EXTRACT FROM <i>Bromelia hieronymi</i> FRUITS Errasti ME¹, Bruno MA¹, Rotelli AE², Caffini NO¹, Pelzer LE². ¹LIProVe, Dpto Cs Biológicas, FCE, U.N. de La Plata, 115 y 47, (1900) La Plata, Argentina. ²Lab. de Farmacología, FQByF, U.N. de San Luis, Chacabuco y Pedernera, (5700) San Luis, Argentina. E-mail: arotelli@unsl.edu.ar.</p> <p><i>Bromelia hieronymi</i> Mez is a plant extended from Paraguay and Bolivia to the NW of Argentina. The ethanol precipitate from a crude extract of <i>B. hieronymi</i> fruits redissolved in 0.1 M phosphate buffer, pH 6.0 (PER) showed a high proteolytic activity. The lyophilized PER contained 2% of proteins and a proteolytic activity of 0.17 Ucas/mg. PER proteases are cysteine-endopeptidases, as those of bromelain, a reknown phytotherapeutic used as antiinflammatory. The aim was to evaluate the anti-inflammatory activity of PER at different doses. Paw edema was utilized to evaluate the anti-inflammatory activity. Wistar rats (180-200 g), divided into groups, received by ip: saline (control), phenylbutazone (75 mg/kg) or 50 mg/kg, 100 mg/kg and 200 mg/kg of PER. One hour later, all animals were injected in left paw with 2 % carrageenan suspension. Edema was measured at 1, 3, 5 and 7 h using a plethysmometer. PER inhibited the paw edema at doses evaluated, being 200 mg/kg the more effective one and the highest antiinflammatory activity was noted at 5 h. The results demonstrated that the proteolytic preparation from <i>B. hieronymi</i> fruits can act like anti-inflammatory agent on acute processes.</p>	<p>B2-27 EFFECTS OF <i>Medicago sativa</i> ETHANOL EXTRACT ON MICE AND RAT INTESTINAL TRACT Wendel G^a, Toso R^b, Boeirs M^b, Mitjans N^a, Pelzer L^a. ^aFarmacología, FQBF, UNSL; ^bCentro de Investigación y Desarrollo de Fármacos, FCV, UNLPam. Chacabuco y Pedernera. San Luis. 5700. E-mail: gwendel@unsl.edu.ar</p> <p><i>Medicago sativa</i> (alfalfa) has been used for thousands of years in many parts of the world, as a source of food for people and livestock and as a medicinal herb to treat digestive problems. The aim of the present study was to evaluate the effect of the ethanol extract on small intestinal transit and experimentally induced diarrhea in mice, intestinal fluid accumulation in rats and the acute toxicity in mice. In control animals, 20 min after its intragastric administration, the charcoal meal traversed 55.6±1.09% of the total length of the small intestine. Oral administration of the extract (resulting of 1 and 2 g of aerial parts) reduced small intestinal transit in mice: 31.5±0.8%, 26.8±1.9%, respectively ($p<0.001$). During the 2 h after castor oil administration, mice produced copious diarrhea, the maximum score achieved being 24. The extract also significantly reduced the diarrhea score to 6 and 5 respectively ($p<0.01$). Intraluminal fluid accumulation was determined by enteropooling in Wistar rats. The pretreatment with the extract had no effect on the volume of intestinal fluid secretion induced by castor oil. There were no death during the toxicity test. The extract did not induce change on the spontaneous activity in mice. In conclusion, the present results suggest that <i>Medicago sativa</i> produce an inhibitory effect on intestinal transit and the severity of diarrhea.</p>
<p>B2-28 URTICA CIRCULARIS: ANTINOCICEPTIVE AND ANTI-INFLAMMATORY EFFECTS ON EXPERIMENTAL MODELS Marrassini C.¹, Miño J.², Acevedo C.², Ferraro G.¹ and Gorzalczy S.³, ¹Cátedra de Farmacognosia, ²Cátedra de Farmacología IQUIMEFA (UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. <i>Junin</i> 956 (1113), Buenos Aires, Argentina. sgorza@ffyb.uba.ar</p> <p><i>Urtica circularis</i> (Hicken) Sorarú (Uc) belongs to the Urticaceae family and is known with the common names of “ortiga”, “ortiga crespa”, “caá poropí” and “urtiginha miúda”. This is an Argentinean native herb and is widely distributed in Paraguay, Uruguay and Brazil. Several species of <i>Urtica</i> are used in the folk medicine as antipyretic and anti-inflammatory agents and for pain relief. In addition, nettles are considered to be a very nutritious food, they are easily digested and are high in minerals (especially iron), vitamin C and pro-vitamin A. For this study, Uc was collected in Estancia “La Merced”, Corrientes, Argentina. The dried aerial parts were ground to a fine powder and it was extracted by maceration with 80% ethanol. The antinociceptive activity of Uc was analyzed with the writhing, formalin and hot-plate tests in mice. A dose-related antinociceptive response was obtained in the writhing test at doses between 30 - 500 mg/kg i.p. and 100 mg/kg p.o. (inhibition: between 52% to 96%). The extract also inhibited the formalin test's second phase at doses of 30 mg/kg i.p. and 250 mg/kg p.o. (inhibition: 78% and 88%, respectively). Furthermore, no significant effect was obtained in the hot-plate test. The anti-inflammatory activity was analyzed with the carrageenan-induced paw edema in rats at doses of 100 and 300 mg/kg i.p. A significant antiedematogenic effect was obtained at doses of 300 mg/kg (40 % of inhibition) and no effect was seen in the ear edema test induced by TPA in mice. On the other hand Uc didn't induce gastric ulceration at dose of 100 mg/kg i.p., but at 300 mg/kg, it produced a slight gastric lesion (petechial points), which was lesser than the one produced by indomethacin 10 mg/kg i.p. These results indicate that Uc have analgesic and anti-inflammatory activities that could support the folk medicinal use of the plant.</p>	

POSTERS BLOQUE 3 – PRIMERA SECCION

B3-29**EFFECT OF VANADIUM ON ANXIETY-LIKE BEHAVIOR IN WISTAR RATS**Cuesta S., Cholich V.¹ and García G.

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Oxidative stress has been shown to be associated with anxiety in different behavioral models. Vanadium (V), as a transition metal element which occurs in various oxidative states, may participate in the reactions involving formation of free radicals. We have shown that i.p. administration of V(+5) to adult rats resulted in decreased locomotor and exploratory activity in the open field and lipid peroxidation in some brain areas. The present study was conducted to evaluate the effects of V(+5) on anxiety-like behavior in Wistar rats. To evaluate states of anxiety elevated T-maze test was carried out. 36 male adult rats were randomly distributed into 3 groups and for 5 consecutive days: 12 were i.p. injected with 3 mg/kg body weight (bw) of sodium metavanadate (NaVO₃) (**V₁ group**); 12 were injected with 7.2 mg/kg bw of NaVO₃ (**V₂ group**) and 12 were injected with saline solution (**C group**). Although a significant difference between V₂ and control group in baseline was observed (p < 0.05), no difference was detected either in inhibitory avoidance 1 or in escape. Those differences could be explained through the diminished locomotion already detected with other tests (open field).

B3-30**ROS GENERATION AND ANTIOXIDANT STATUS IN RATS' BRAIN AREAS AFTER EXPOSURE TO SODIUM METAVANADATE**Cuesta S., Frances D.¹, Pochettino A.², Quiroga A.¹, Martínez A., García G.

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In this work, *in vivo* ROS formation and antioxidant status in sodium metavanadate (NaVO₃) treated rats' brain areas were studied. 60 rats were randomly distributed into 3 groups and, for 5 consecutive days, 20 were i.p. injected with 3 mg/kg body weight (bw) of NaVO₃ (**V₁ group**); 20 were injected with 7.2 mg/kg bw of NaVO₃ (**V₂ group**) and 20 were injected with saline (**C group**). Rats were guillotined and cerebellum (Cer) and hippocampus (Hc) were removed and processed for: CuZn superoxide dismutase (SOD) (Beauchamp and Fridovich-1971) and catalase (Beers and Sizer-1952) activities as well as hydroxyl radical (OH) (Floyd et al. -1984) and total and oxidized glutation (Tietze-1983) levels. Histochemical studies for *in situ* ROS (Kerver et al, 1997) and SOD detection (Viggiano y col., 2003) in entire brains were done. OH levels were significantly increased and *in situ* ROS histochemical staining was positive in V₂ group Cer. GSH/GSSG ratio was significantly decreased in V₁ and V₂ groups while neither Catalase nor Cu-Zn SOD activity shown any change in both brain areas. Vanadium-induced OH production was detected in Cer with the highest dose and an impaired antioxidant defence in both brain areas was also observed.

B3-31**"WNT FACTORS AND NEURONAL POLARITY: INVOLVEMENT OF PI3K PATHWAY".**

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Neuronal development, from the establishment of neuronal polarity to axon guidance and maturation are controlled by a combination of an intrinsic program of gene expression and by extrinsic factors (such as Wnts, BMPs, IGF-1, BDNF, and NGF). Wnt factors are secreted signalling molecules implicated in important developmental processes, as embryonic patterning, tissue polarity and cell movement. Recent works have shown that Wnts also regulate neuronal maturation as they have been implicated in axon guidance, dendritogenesis and synapses formation. Wnts through Frizzled (Fz) receptor activate Dishevelled (DVL), a first effector. Wnt-DVL signalling can signal through three different pathways: the canonical or β -catenin pathway, the planar cell polarity pathway and the calcium pathway. In this work, we study the role of WNT-DVL signalling during neuronal differentiation, particularly during axon outgrowth and the establishment of neuronal polarity. Neurons cultured in the presence of Wnt3a or expressing DVL show multiple and more complex axons. Wnt3a seems to regulate axon formation through a non-canonical pathway and this effect is blocked by sFRP (a Wnt antagonist). Importantly, Wnt3a activates PI3K in neurons and in purified growth cones particles suggesting that Wnt3a may act through the same pathway as IGF-1 (previously defined as an essential for neuronal polarity). In addition, we found that Wnt3a cross-activates the receptor of IGF-1 in neurons and in growth cones and this effect is blocked by an IGF-1R blocking antibody. These findings suggest that Wnt proteins are essential for neuronal polarity and suggest a possible parallelism between the two signalling systems: Wnt-Fz-DVL and IGF-1-IGFR-PI3K on axon formation.

B3-32**IMPACT OF LOUD NOISE ON ASSOCIATIVE MEMORY. RAT HIPPOCAMPAL NEURONAL ALTERATION AND OXIDATIVE STATUS IMBALANCE.**URAN¹ S.L., AÓN² L., CACERES¹ L.G., CAPANI² F., GUELMAN¹ L.R.

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Central Nervous System (CNS) is vulnerable to reactive oxygen species (ROS). The aim of the present work was to test if loud noise exposure can affect hippocampal-related memory, histology and oxidative status.

15-days-old male Wistar rats were exposed to white noise (100dB) and separated into acute (2h/day) and chronic exposure (2h/day for 15d). Passive avoidance test (PA), hippocampal ROS levels, antioxidant enzymes activities (SOD/CAT) as well as histological assessments were performed at 30 and 90-days-old rats.

Results show a decreased latency to enter the dark compartment in PA only at 30 days when compared to control animals. ROS levels were decreased, while antioxidant enzymes activities were increased after noise exposure in 30 days-old-rats. Histological abnormalities were found only at 30 days in CA1 and dentate gyrus.

Data suggest that loud noise is capable of inducing temporary memory impairments. The increase in CAT and SOD activities could be triggered as a compensatory response to hippocampal noise-induced damage, leading to a decrease in ROS levels at 30 days. The improvement in the performance at 90 days could be related to the lack of damage in hippocampus at this age.

<p>B3-33 PARTICIPATION OF THE OXIDATIVE STRESS IN THE IMMUNE ALTERATION IN BALB/C AND C57 DIABETIC MICE.</p> <p>Rubinstein R, Albarracín R, Genaro AM y Wald MR CEFYBO-UBA-CONICET. Paraguay 2155. Bs As. Argentina. roxirubin@yahoo.com.ar</p> <p>An increased susceptibility to infection was described in diabetic patients suggesting an immunosuppression, being hyperglycemia the main factor involved. However, there are diabetic patients with normal evolution after an infection challenge. Among the factors that can regulate this susceptibility is the balance between pro- and anti-inflammatory cytokines, type TH1 and TH2 respectively. Here we studied the effect of diabetic state in the immune response in TH1-biased C57Bl/6 (C57) and TH2-biased BALB/c mice. Diabetes resulted in a decrease of Con A T-cell and LPS B-cell stimulated proliferation in BALB/c but not in C57 mice. However, glucose levels in diabetic mice were significantly higher in C57 than in BALB/c. The direct effect of elevated extracellular glucose on lymphoid cells by culturing T and B lymphocytes was investigated. Results indicate that T and B-cell proliferation in BALB/c was decreased by high concentration of glucose (HG) but not in C57. HG diminished cell viability and increased apoptosis of BALB/c lymphocytes but not in C57. Along with this decrease in lymphocyte proliferation, an increase in oxidative stress was observed, suggesting its participation in the observed effects. Moreover, antioxidants reverted HG actions on cell viability and T and B proliferative response. These results indicate that genetic control of TH1-TH2 balance could affect the evolution of infection in subject with diabetes.</p>	<p>B3-34 ANTICONVULSANT SULFAMIDES WITH AFFINITY FOR THE GABA_A RECEPTOR AND ANXIOLYTIC ACTIVITY IN MICE.</p> <p>Wasowski C.^a, Gavernet L.^b, Barrios I.A.^b, Bruno-Blanch L.E.^b, Marder M.^a</p> <p>^a IQUIFIB (UBA-CONICET), Facultad de Farmacia y Bioquímica, Junín 956 (C1113AAD), Buenos Aires, Argentina. ^b Química Medicinal, Departamento de Ciencias Biológicas, UNLP, calle 47 y 115 (B1900BJW), La Plata, Argentina. mmarder@qb.ffyb.uba.ar</p> <p>A set of sulfamates and sulfamides designed, synthesized and evaluated against MES and PTZ tests with promising results were tested for their affinity for the benzodiazepine binding site (BDZ-bs) in the GABA_A receptor. The most active compounds found; <i>N,N'</i>-dicyclohexylsulfamide (1) and <i>N,N'</i>-diphenethylsulfamide (2), competitively inhibited the binding of [³H]-FNZ to the BDZ-bs with <i>K_i</i> ± SEM values of 27.7 ± 4.5 μM (n= 3) and 6.0 ± 1.2 μM (n= 3), respectively. The behavioral actions of these sulfamides, i.p. administered in mice, were examined in the plus maze, hole board and locomotor activity assays. Compound 1 exhibited anxiolytic-like effects in mice evidenced by a significant increase of the parameters measured in the hole board test (at 0.3, 1 and 3 mg/kg) and the plus maze assay (at 1 mg/kg). Compound 2 evidenced anxiolytic activity in the plus maze test at 1 mg/kg. Locomotor activity of mice was not modified by compound 1 or 2 at the doses tested. Anxiety represents a major problem for people with epilepsy. The use of these anticonvulsant sulfamides would be beneficial to individuals who suffer from both disorders.</p>
<p>B3-35 MONOSODIUM GLUTAMATE (MSG): NEONATAL HYPOTHALAMIC IN MALE RATS</p> <p>Cardamone L, Mahieu S, Millen N, Contini M de C. LIFE. FBCB. UNL. Santa Fe. Argentina. Ciudad Universitaria. Paraje El Pozo. CC 242. mcontini@fcb.unl.edu.ar</p> <p>The aim of this work was to evaluate the effects of MSG in neonatal hypothalamic model. Male Wistar rats were housed at a temperature of 23° C ± 2° C and a daily cycle of 12 h light and dark. They were given ad libitum water and standard diet. For hypothalamic lesion-induced obesity, newborn rats were subcutaneously injected with MSG (4 mg/g body weight) at 2, 4, 7 and 9 days after birth and saline solution was also administered to control rats at similar days. Lee index (body weight (g)^{1/3}/nasal-anal length (cm) x 100) was calculated as a predictor of obesity in MSG-rodents. At the age of 7 month the following assessment were carried out: basal glycaemia, glucose tolerance (K glc.), insulin tolerance test (K ins.), retroperitoneal fatty weight (RFW), cholesterol, HDL, LDL, triglycerides (TG) and BSP clearance. Data is express as mean ± SEM (standard error of the mean). [G]: C: 0,909 ± 0,058; MSG: 1,107 ± 0,050*. K ins.: C: 0,62 ± 0,06; MSG: 0,412± 0,03*. Lee Index: C: 0,304 ± 0,002; MSG: 0,312 ± 0,003*. Tail length (mm) C: 201 ± 2,97; MSG: 180 ± 5,81*. RFW (g)/100g weight: C: 1,87± 1,12; MSG: 2,47 ± 0,21*.TG: C:0,633±0,052; MSG: 1,217±0,185. Lee index in MSG rats was increased. MSG-treated rats had about 11% shorter tail length compared to the control, this is related to a smaller growth. K ins. is altered thus suggesting insulin resistance in MSG rats. This could be associated with increased retroperitoneal fatty weight and also with the existence of obesity. Additionally, BSP clearance is decreased in MSG rats implying that hepatic functions involved might be affected.</p>	<p>B3-36 ACUTE AND CHRONIC POSTNATAL STRESS ALTERS GLUTAMATE TRANSPORTER AND BEHAVIORAL STRESS RESPONSE.</p> <p>MM Odeón, AE Salatino, ML Orta, GB Acosta. ININFA- (CONICET-UBA). Junín 956. 5th floor, C1113AAD, Buenos Aires. E-mail: merodeon@hotmail.com</p> <p>The aim of this study was to evaluate the consequences of acute and chronic early life environmental manipulations on adult brain on glutamate transporter (GluT), evaluating the uptake of [³H]Glu by synaptosomes-enriched fractions isolated from cerebral frontal cortex (FC) and hippocampus (HIC) by kinetic parameters. Also we investigated the possibility of relations between GluT and anxiety. In acute stress, control rats were moved to a separated cage while stressed rats were exposed to cold stress (4°C) during 1 h. In repeated stress the rats were separated from their mothers and exposed to cold stress (4°C) for 1 h at postnatal days during 20 days. These animals were allowed to a 30 days recovery period until adulthood. FC and HIC were dissected to study GluT and trunk blood samples were collected to determinate corticosterone levels. Acute stress in CF decreased the uptake while increased <i>K_m</i> and <i>V_{max}</i> in all ages studied. Repeated chronic stress did not change in uptake levels in both areas whereas kinetics parameters were modified. The levels of corticosterone increased on acute stress and unchanged on chronic stress. In chronic stress we found an increment in time spent in the illuminated site of the dark/light transition test. In summary, we have observed regional changes in GluT produced by stress. Chronic stress increased the time spent in the adverse environment. These results suggest that a exposure to postnatal stress at different periods after birth modifies GluT, affects hypothalamic-pituitary-adrenal (HPA) axis, which could be relevant to function of GluT in the adult rat brain and induces anxiolytic-like action in an animal model of anxiety.</p> <p>Supported by UBACYT B019</p>

B3-37**HIGH AFFINITY [³H]-OUABAIN BINDING TO CEREBRAL CORTEX MEMBRANES. CHARACTERIZATION OF INHIBITORY EFFECT OF PEPTIDE NEUROTENSIN**

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Neurotensin inhibits Na⁺, K⁺-ATPase activity present in synaptosomal membranes isolated from rat cerebral cortex. This effect occurs through high affinity neurotensin receptor (NTS1). The presence of neurotensin (agonist) or SR 48692 (Sanofi-Aventis, U.S., Inc.), a non-peptidic antagonist for high affinity neurotensin receptor (NTS1) in the incubation medium decrease high affinity [³H]-ouabain binding to CNS membranes (SAFE, 2008). In order to explore potential participation of NTS1 receptor activation on such effect, assays were carried out in vitro and after administration of the antagonist. Rat cerebral cortex membranes were incubated with [³H]-ouabain in the presence of neurotensin and / or SR 48692 solutions, to obtain additive or synergic effects, according to the concentration employed. Lots of rats were administered i.p. with SR 48692 (dissolved in saline solution with 0.01% Tween 80) and were decapitated 30 min later. Rats injected with vehicle were processed in parallel to serve as controls. [³H]-ouabain binding was statistically significantly decreased after administration of 250 µg / kg SR 48692. In cortical membranes isolated from rats previously injected with SR 48692, neurotensin added during [³H]-ouabain binding assay decreased binding in a way similar to that recorded in the vehicle injected controls. Saturation assays followed by Scatchard analyses showed increase in Kd value but no change in Bmax value. Results suggested that neurotensin acts as a competitive inhibitor of high affinity [³H]-ouabain binding. The antagonist for NTS1 receptor not only failed to block neurotensin effect but also produced an inhibitory effect itself on [³H]-ouabain binding to CNS membranes.

B3-38**PREVIOUS STRESS ATTENUATES THE SUECEPTIBILITY TO MIDAZOLAM'S DISRUPTIVE EFFECT ON FEAR MEMORY RECONSOLIDATION: INLUENCE OF D-CYCLOSERINE.**

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The retrieval of a consolidated memory results into a labile phase, vulnerable to interference by benzodiazepines. The aims of the present study was to assess MDZ vulnerability after reactivation of recent and remote contextual fear memories in animals that had experienced a stressful situation prior to acquisition. Male Wistar rats were subjected on day 1 to a stressful session and on day 2 submitted to a contextual fear conditioning paradigm and 1, 7 or 21 days after training re-exposed to the training context (A) for 3 or 5 min. Immediately after retrieval rats were administered (i.p.) either with SAL, MDZ 1.5 mg/kg, or MDZ 3 mg/kg. One day later, rats were tested in A. The results showed that MDZ does not affect reconsolidation of a 7-day and 21-day fear memory in stressed animals regardless of the duration of the re-exposure period and the MDZ doses used. In addition, we tested the influence of pre-activation D-cycloserine (DCS) on MDZ's effect on fear memory reconsolidation in stressed animals. Our evidence showed that: a) Previous stress prevents MDZ's disruptive effect on memory reconsolidation of a fear memory and b). DCS prior to reactivation promotes retrieval-induced lability in resistant memory traces.

POSTERS BLOQUE 3 – SEGUNDA SECCION

B3-71-

THE REACTIVATION OF A CONSOLIDATED FEAR MEMORY INCORPORATES NEW AVERSIVE INFORMATION FROM A STRESSFUL SITUATION.

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Consolidated memories may result into a labile one after retrieval, requiring a re-stabilization process, defined as reconsolidation, which is dependent on protein synthesis. The functional significance of this process remains unknown; one hypothesis proposes that this phase is essential to incorporate new environmental experiences to the original memory, a process defined as memory updating. Adult male Wistar rats were subjected to a contextual fear conditioning paradigm using a single footshock (weak training session). One day after training, rats were subjected to a stressful situation (restraint for 30 min.) and another group remained in their home cage without manipulation. Half of the rats were re-exposed to the original context of conditioning (test 1) for 3 minutes one day after the stress. There was an increase of freezing only in those animals re-exposed to the associated context, which was maintained for 10 days during the re-exposure to the training context (test 2). Pharmacological manipulations (benzodiazepines and NMDA antagonists) that attenuates the stress consequence or prevents the fear memory reconsolidation, as well as very short period of re-exposure to the associated context, prevented stress-induced increase in freezing. We conclude that the reactivation session allows the updating of new environmental information corresponding to a traumatic event (inescapable stress) into an already consolidated fear memory.

B3-72

GLUTAMATERGIC ROL IN THE LIGHT NEUROFILAMENT DECREASE IN CA3 HIPPOCAMPAL NEURONS OF ANIMALS EXPOSED TO INESCAPABLE STRESS

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The main goal of this work was to investigate the signal transduction pathway associated with the decrease of the light neurofilament subunit (NFL) in CA3 hippocampal neurons of animals exposed to inescapable stress. Male adult rats were injected with an antagonist of NMDA receptor (MK-801 0.1mg/kg i.p.), an antagonist of AMPA (CNQX 0.75 mg/kg i.p.) receptor or vehicle 30 minutes before exposure to a protocol of inescapable shocks (I) (one session of 60 footshocks lasting 15 sec each during 1 hour). Control group (C) consisted of rats not exposed to stress. One hour or four days later the animals were sacrificed for 1) PKA and PKC activity measurement in hippocampus extracts; 2) immunohistochemistry of NFL in slices of brain. Results: 1) No differences were found in PKA or PKC activity between C and I animals. 2) I-vehicle animals showed a significant decrement compared with C-vehicle animals ($p < 0.05$) in NFL relative area. The antagonist MK-801 prevented this reduction (I-MK-801 vs I-vehicle, $p < 0.05$). Similarly, CNQX prevented NFL diminution in I animals ($p < 0.001$). No differences were found in C-MK-801 or C-CNQX in comparison with C-vehicle ($p > 0.05$). We conclude that glutamate is implicated in the decrease of NFL in CA3 hippocampal neurons of stressed animals. PKA and PKC seem not participate in the above mentioned NFL decrement. Supported by: PICT 31953 and UBACYT M073.

B3-73

FLUOXETINE EFFECTS ON THE ALTERED SIGNAL TRANSDUCTION OF CRF1 IN AN ANIMAL MODEL OF DEPRESSION.

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In previous works we demonstrated that in the hippocampus of animals exposed to the learned helplessness paradigm (LH) the expression of CRF1 and the MAPK signaling triggered by CRF are reduced. In order to study the pharmacological effect of fluoxetine in these parameters, we evaluated the behavioural response, the levels of CRF1 by in situ hybridization using a cRNA digoxigenin-labeled probe and the activation of ERK1/2 (pERK1/2) by immunofluorescence in the hippocampus of LH rats after 21 days of fluoxetine administration (10mg/kg/day; i.p.). We compared four groups: C FLX (rats not exposed to stress that received fluoxetine), C SF (rats not exposed to stress that received physiological solution), LH FLX (rats that develop the behavioural despair after exposure to stress and received fluoxetine) and LH SF (rats that develop the behavioural despair after exposure to stress and received physiological solution). LH FLX showed the reversion of the behavioural despair in comparison with LH SF ($p < 0.05$). LH FLX showed no difference with the C FLX group in the mRNA CRF1 expression while LH SF showed a decrease versus C SF ($p < 0.05$). When we measured the levels of activation of ERK1/2 we found that LH FLX and LH SF showed a decrease versus C FLX and C SF ($p < 0.05$ and $p < 0.01$). We conclude that chronic treatment with fluoxetine reverses the behavioural despair as well as the CRF1 decrement, while fails to exert any effect on pERK1/2 changes. Supported by: PICT 31953, UBACYT M073.

B3-74

EXPLORING MODAFINIL NEUROPROTECTIVE EFFECTS ON METHAMPHETAMINE ACUTE TOXIC DOSE

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Acute toxic dosing models (ATD) of methamphetamine (METH) have previously shown to affect dopaminergic and/or serotonergic systems in the rodent brain. In order to explore potential neuroprotective effects of modafinil, a vigilance enhancer/antinarcoleptic drug, Swiss Webster mice were injected with a METH ATD protocol (3 X 7 mg/kg, i.p. injections, 3 hour apart), modafinil (180 mg/kg, 2 i.p. injections, 1h before first METH injection and 1h before third injection) or METH+modafinil; control group received vehicles. As expected, METH induced hyperthermia, but modafinil did not block the effect. We then measured monoamine striatal content by HPLC 6 days after METH ATD. The group that received METH showed depletion on both DA and dopaminergic metabolites; no serotonergic depletion was observed. However, the group that received the co-administration of modafinil and METH showed similar dopaminergic content values to the control (vehicle-vehicle) group suggesting a modafinil protective effect against METH-induced dopaminergic depletion. Also, we performed behavioral analysis of mice spontaneous exploratory activity and we found a subtle decrease of total locomotion and velocity in METH treated groups (6 days after last METH injection), modafinil co-administration was not able to modulate this effect. Supported by Grants from: ANPCyT PICT 2007-01009 (to Dr. Urbano), and ANPCyT PICT 2005-31953 and UBACYT M073 (to Dr. Wikinski).

<p>B3-75 EFFECTS OF EARLY ADVERSE LIFE EVENTS ON GABAERGIC NEURONS Salatino AE, Odeón MM, Orta ML, Acosta GB. ININFA-(CONICET-UBA). Junín 956. 5th floor, C1113AAD, Buenos Aires. E-mail: adrian86@gmail.com</p> <p>Neonatal period may be an especially high risk period given the continued proliferation of neuronal cells and developmental of neuronal pathways. We investigate the consequences of repeated maternal separation and exposed to cold stress on brain development in order to determinate if the effects on GABAergic function were age-specific. Rats' pups were separated from their mother plus cold exposure (4°C) for 1h at postnatal (PD) 5, 7, 13 and 21 during 20 days (wash-out period: 30d). The rats were killed by decapitation and trunk blood samples were collected to measure corticosterone levels. Frontal cortex (FC) and hippocampus (HIC) were dissected in order to study GABA uptake. Also we used Western blotting to evaluate the alterations in the expression of HIC and FC GAT-1. Our results shows that the time course of repeated stress decreased GABA uptake in FC at PD5 and HIC at PD13. At PD5 we found a decreased GAT-1 level in HIC and increased in FC. Chronic stress altered the basal levels of corticosterone at the different ages studied. These results support the notion that the development of the FC is affected by stressors during early life. The findings are in agreement with the hypothesis of compensatory changes development in response to repeated stress, we would propose a FC as key in the development of adaptative mechanisms.</p> <p>Supported by UBACYT B019</p>	<p>B3-76 SEX DIFFERENCES IN THE MODULATION BY BACLOFEN OF ANXIETY-LIKE BEHAVIOUR ASSOCIATED TO NICOTINE WITHDRAWAL SYNDROME Calvo M¹, Varani A¹, Induni A^{1,2} and Balerio G^{1,2} ¹ININFA (CONICET) y ²Cát. de Farmacología (FFyB, UBA) Junín 956, 5°Piso. Buenos Aires. E-mail: gbalerio@ffyb.uba.ar</p> <p>Increased anxiety is one of the motivational aspects of NIC withdrawal. We have previously demonstrated that baclofen (BAC), GABA_B receptor agonist, was able to decreased somatic expression of NIC and morphine withdrawal syndrome. The aims of the present study were: a) to analyze if the anxiogenic effect associated to NIC withdrawal is influenced by sex, b) to evaluate the effect of BAC on the anxiety-like behaviour, in NIC abstinent mice of either sex. Swiss Webster albino mice received NIC (2.5 mg/kg; sc) 4 times daily, for 7 consecutive days. On day 8th, dependent mice received the nicotinic receptor antagonist mecamylamine (MEC; 2 mg/kg; sc) 1h after the last dose of NIC. A second group of dependent mice received BAC (2 mg/kg; ip) 45 min before MEC precipitated abstinence. Immediately the anxiety-like behavior was measured for 15 min in the elevated plus maze test. NIC withdrawal significantly decreased the percentage of time spent and the percentage of entries in the open arms (p<0.001) in male as well as in female mice. This effect was prevented by BAC pretreatment in male (p<0.001) but not in female mice. Our results demonstrate that: a) the anxiogenic response associated to NIC withdrawal is not influenced by sex, b) BAC prevented this anxiogenic effect associated to NIC withdrawal only in male mice. In conclusion, our results suggest a sexual dimorphism in the involvement of GABAergic system in the anxiety-like behaviour during NIC withdrawal. <i>Supported by UBACYT B016</i></p>
<p>B3-77 SEXUALLY DIMORPHIC ANXIETY-LIKE BEHAVIOR DURING MORPHINE WITHDRAWAL SYNDROME ^{1,2}Induni, A S, ¹Varani, A, ¹Machado, L, ¹Calvo, M, and ^{1,2}Balerio G. ¹ININFA (CONICET), ²Cát. de Farmacología, FFyB (UBA). Junín 956 5° piso (1113), Buenos Aires. E-mail: gbalerio@ffyb.uba.ar</p> <p>We have previously demonstrated sex differences during morphine (MOR) withdrawal. We have also shown that the GABA_B receptor agonist baclofen (BAC) was able to prevent the MOR withdrawal in male as well as female mice. The aim of the present study was to evaluate the anxiety-like behavior in mice of either sex during naloxone (NAL)-precipitated withdrawal and its prevention with BAC in the elevated plus maze (EPM). Swiss-Webster prepubertal mice were rendered dependent by i.p. injection of MOR (2 mg/kg), twice daily for 9 days. On the 10th day, dependent mice were divided into two groups: withdrawal group received NAL (6 mg/kg, i.p.) after the last dose of MOR, while prevention group received BAC (2 mg/kg, i.p.) before NAL injection. Animals were placed in the center of the EPM facing towards an open arm and recorded for 15 min. Our results showed a significant increase in the percentage of entries (p<0.05) and time (p<0.01) in the open arms of MOR withdrawn males vs control group. Conversely, the percentage of entries and time in the open arms were not modified in withdrawn females. The pretreatment with BAC did not modify the anxiety-like behavior in MOR withdrawn animals. The greater sensitivity of males in response to MOR confirms our previous observations showing a sexual dimorphism during MOR withdrawal syndrome. The lack of BAC effect suggests that the anxiety-like behavior associated to MOR withdrawal signs would not be related to the GABAergic system. <i>Supported by UBACYT B016</i></p>	<p>B3-78 FLUOXETINE EFFECTS ON HIPPOCAMPAL SYNAPTIC CONNECTIVITY AND PSA-NCAM DEPENDENT REMODELLING IN AN EXPERIMENTAL MODEL OF DEPRESSION. Podestá MF, Lorenzo Lopez JR, Codagnone M, López M, Brusco A, Wikinski S, Reinés, A. Instituto de Investigaciones Farmacológicas (CONICET-UBA). Email: podestamf@ffyb.uba.ar</p> <p>Dysfunction of hippocampal plasticity and excessive glutamate (GLU) release has been proposed to play a critical role in the pathophysiology of depression. We examined the synapse morphology and cell adhesion molecule (CAM) expression in the learned helplessness (LH) paradigm, with and without fluoxetine (FLX) treatment. CA3 synapses of LH animals showed increased synaptic cleft width, postsynaptic density (PSD) remodelling and modified synaptic vesicles number compatible with plastic and synaptic connectivity alterations. CA3 NCAM and PSA-NCAM levels diminished in LH rats. GLU hyperstimulation of hippocampal neurons in culture decreased NCAM and PSA-NCAM immunostaining, diminished PSD-95(+) and SYN(+) synapse number and increased SYN(+) individual synapse area, changes that resemble those observed in LH animals. FLX treatment of LH rats recovered synaptic cleft width values, increased reserved synaptic vesicle number, strongly reduced NCAM and increased PSA-NCAM levels in CA3. Results support the hypothesis that GLU hyperactivity in the CA3 of LH rats could reduce CAM expression and that FLX action could involve PSA-NCAM dependent synaptic remodelling that might lead to neuronal connectivity normalization. Grants PICT34397, UBACYT B422</p>

B3-79

BACLOFEN REESTABLISHES C-FOS EXPRESSION DURING NICOTINE WITHDRAWAL SYNDROME IN MICE

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C-Fos, a member of Fos family of transcription factors, is implicated in behavioural responses and synaptic plasticity induced by abused drugs. Our previous studies demonstrated that baclofen (BAC), GABA_B receptor agonist, was able to prevent the somatic expression and reestablish the dopaminergic and serotonergic activity during NIC withdrawal syndrome in mice. The aim of the present study was to evaluate the immediate early gene c-Fos expression in various brain areas in mice during NIC withdrawal syndrome and its prevention with BAC. Swiss mice received NIC (2.5 mg/kg, sc) 4 times daily, for 7 days. On day 8th, dependent mice received the NIC receptor antagonist mecamylamine (MEC; 2 mg/kg, ip) 1h after the last dose of NIC. A second group of dependent mice received BAC (2 mg/kg, ip) before MEC-precipitated abstinence. Animals were anesthetized and transcardially perfused with paraformaldehyde. Brains were removed and cut to perform immunohistochemical studies. Our results showed a significant decrease in c-Fos expression in the dentate gyrus of hippocampus ($p < 0.05$) and the bed nucleus of the stria terminalis ($p < 0.001$) of NIC withdrawn mice vs control group. Conversely, the number of Fos-positive nuclei was significantly increased in the cingulate cortex. BAC was able to reestablish the expression of c-Fos in these brain areas of NIC withdrawal animals. In conclusion, the effect of BAC in preventing the somatic signs of NIC withdrawal could be related with changes in c-Fos expression. *Supported by UBACYT B016*

POSTERS BLOQUE 4 – PRIMERA SECCION

B4-39

PHARMACOKINETIC STUDY OF TOPOTECAN IN A SWINE MODEL AFTER INTRA-ARTERIAL (OPHTHALMIC) ADMINISTRATION. POTENTIAL IMPLICATION IN RETINOBLASTOMA TREATMENT.

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Retinoblastoma is a tumor of childhood. Enucleation is usually the treatment of choice for unilateral disease; however, bilateral retinoblastoma is more challenging. Systemic chemotherapy followed by local therapies is given to reduce tumor burden but hematological toxicity and secondary leukemias are usual. To improve the vitreous delivery of drugs that yield local therapeutic concentrations while attaining low systemic toxicity, we studied a new technique of administration by selective ophthalmic artery drug infusion in a swine model and characterized topotecan (TPT) pharmacokinetics. Under general anesthesia, the sheath of a 5-F/3-F outer guiding arterial catheter was placed in the femoral artery. An arteriogram was performed to visualize the cerebral vasculature and the eye for guiding TPT administration *via* the internal maxillary artery. TPT (0.5 mg/30 ml) was infused over 30 min. TPT vitreous humor penetration was assessed using micro dialysis. Dialysates and plasma samples were analyzed for TPT by HPLC. Negligible systemic absorption was observed with detectable TPT plasma concentrations up to 30 min after the end of infusion (AEI). TPT vitreous humor levels were about 30 ng/ml up to 2 h AEI. Despite low systemic TPT levels, vitreous humor drug concentrations were substantial. We present the development of a novel technique for local chemotherapy delivery to the vitreous humor with future implications in advanced retinoblastoma.

B-4-40

CEPHALEXIN TISSUE CONCENTRATIONS AFTER INTRAVENOUS, INTRAMUSCULAR AND SUBCUTANEOUS ADMINISTRATION TO DOMESTIC CATS.

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Introduction: Cephalexin (CFX) is a first generation cephalosporin widely used in domestic animals for the treatment of grampositive (*Staphylococcus* spp., *Streptococcus* spp.) and gramnegative (*Escherichia coli*, *Proteus* spp) infections. The aim of this study was to compare CFX tissue concentrations after intravenous (IV), intramuscular hydro soluble formulation (IMsol), sustained release formulation (IMdepo), and subcutaneous (SC) administration to cats.

Materials and Methods: 7, 6, 11 and 7 adult cats received 10 mg/kg of CFX by IV, IMsol, IMdepo and SC administration, respectively. Blood and tissue samples (obtained from standard surgeries) were withdrawn at pre-determined times over an 8 h period. CFX concentrations were determined by microbiological assay. Plasma disposition curves were analyzed by non linear methods.

Results: maximum and minimum tissue concentrations after IV, IMsol, IMdepo and SC administration were respectively: 10.58±4.34 µg/ml (uterus) and 1.75± 0.92 (muscle) µg/ml; 10.13±4.76 µg/ml (uterus) and 0.96±0.06 µg/ml (subcutaneous); 3.74±1.83 µg/ml (uterus) and 0.87±0.02 µg/ml (testicles); and 5.76±6.70 µg/ml (skin) and 1.38±2.76 µg/ml (muscle).

B4-41

RENAL EXPRESSION AND URINARY EXCRETION OF OAT5 IN RATS WITH ACUTE BILIARY OBSTRUCTION (ABO).

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Oat5 has been characterized as an organic anion/dicarboxylate exchanger. Oat5 interacts with chemically heterogeneous anionic compounds, such as non-steroidal anti-inflammatory drugs, diuretics, penicillin G and steroids sulfate conjugates. This protein is localized in the kidney at the brush border of proximal tubule straight segment. From studies performed in our laboratory it was demonstrated, for the first time, the presence of Oat5 in urine. The aim of this study was to examine the renal expression and urinary excretion of Oat5 in rats with ABO (n=4). A parallel group of sham rats (S, n=4) was employed. Oat5 abundance (%) was evaluated in renal homogenates (h), renal brush border membranes (m) and in urine (u) by Western blotting technique. Urine abundance was related to urinary creatinine levels. Oat5(h): S= 100 ± 3; ABO= 133 ± 7*; Oat5(m): S= 100 ± 3; ABO= 110 ± 3. Oat5(u): S= 100 ± 6; ABO= 56 ± 5* (*p<0.05). High plasma levels of biliary compounds existing in cholestatic rats determine an enhanced fraction of unbound anionic substances to plasma proteins, increasing their glomerular filtration. The fall in Oat5 renal excretion in addition to the increase in renal Oat5(h) show a preservation of Oat5 levels in renal tissue. This mechanism would be directed towards improving the reabsorption of filtered compounds of special importance such as steroids sulfate conjugates and pharmacological agents.

B4-42

NaDC1 RENAL EXPRESSION AND URINARY EXCRETION IN RATS EXPOSED TO MERCURIC CHLORIDE (HgCl₂).

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HgCl₂ is an established environmental pollutant that accumulates preferentially in kidneys, affecting the proximal tubules and causing acute renal failure (ARF). The sodium-dicarboxylate cotransporter 1 (NaDC1) is located in the apical membrane of proximal tubular cells. Its primary function is to reabsorb filtered Krebs cycle intermediates. The aim of the present study was to evaluate the renal expression (in homogenates (H) and apical membranes (M)) and the urinary excretion (U) of NaDC1 by immunoblotting technique in a nephrotoxic model of ARF. Four groups of male Wistar rats were treated with different doses of HgCl₂ 18 h before the experiments: 0(C, n=4), 0.2(Hg0.2, n=4), 1(Hg1, n=4), 5(Hg5, n=4) mg/kg b.w., s.c.

NaDC1	C	Hg0.2	Hg1	Hg5
H (%)	100±8	94±4	83±5	90±3
M (%)	100±5	91±5 ^{c,d}	69±6 ^{a,b}	56±4 ^{a,b}
U (%)	100±6	134±18 ^d	227±19 ^d	1470±180 ^{a,b}

ANOVA plus Newman-Keuls (P<0.05) *avs*C, *bvs*Hg0.2, *cvs*Hg1, *dvs*Hg5.

A HgCl₂ dose-dependent decrease in NaDC1 expression in M and a HgCl₂ dose-dependent increase in U were observed. It has been proposed that Hg²⁺ enters into proximal tubular cells via basolateral transporters using the outward gradient of α-ketoglutarate. The decrease in NaDC1 abundance might help to prevent the uptake of mercury by declining this gradient.

<p>B4-43 INDUCTION BY ETHANOL OF NIFURTIMOX AND BENZNIDAZOLE BIOTRANSFORMATION CATALYZED BY RAT HEPATIC MICROSOMES. Bartel LC, Montalto de Mecca M, Castro JA Centro de Investigaciones Toxicológicas (CEITOX) CITEFA-CONICET. J B de La Salle 4397. Villa Martelli, Prov Bs As. jcastro@citefa.gov.ar</p> <p>There are available two drugs for the etiological treatment of Chagas' disease, Nifurtimox (Nfx) and Benznidazole (Bz). Both nitroheterocyclic drugs have serious toxic side effects associated with their nitroreduction to reactive metabolites. The aim of this work was to study whether Nfx or Bz metabolisms, by liver microsomes from rat receiving ethanol, were altered. Sprague Dawley male and female rats (125-150 g bw) were fed a standard Lieber and De Carli liquid diet for 28 days. Controls were pair-fed with a diet, in which ethanol was isocalorically replaced with carbohydrate. The NADPH-dependent liver microsomal nitroreductase activities of Nfx and Bz were determined in control and alcohol treated animals. Results obtained in ethanol drinking livers of male rats evidenced a significant inductive effect of the microsomal nitroreductase activity of both drugs. Similarly, increases in the activity of Bz nitroreductase by female livers were obtained. Experiments on Nfx nitroreductase activity for females are in course. These observations suggest that at least part of the undesirable effects observed, when ethanol drinking interacts with either Nfx or Bz use, could be due to their enhanced biotransformation to reactive metabolites. The potential therapeutic implication should be taken into account considering that not only they are being used in the acute phase but also in the indeterminate phase of the disease.</p>	<p>B4-44 THERAPEUTIC NIFURTIMOX AND BENZNIDAZOLE MONITORING IN BLOOD Bulffer, R.F., Fanelli, S.L., Castro, J. A. Centro de Investigaciones Toxicológicas (CEITOX) CITEFA-CONICET. J B de La Salle 4397. Villa Martelli, Prov. Bs. As. jcastro@citefa.gov.ar</p> <p>There are two drugs accepted for the etiological treatment of Chagas' disease, Nifurtimox (Nfx) and Benznidazole (Bz). Both have serious toxic side effects so it is necessary to have an appropriate methodology for their therapeutic monitoring. In this study we analyzed the use of HPLC and UV-Visible methods for the drugs determination in blood. Animals were given a single intragastric dose of Bz or Nfx (100 mg/kg in 1 % carboxymethylcellulose). Rats were killed at different times (1h, 3h, 6h or 24h). Blood samples were extracted with dichloromethane in Extrelut® columns. The solvent was evaporated to dryness under nitrogen and the extracts were further analyzed by HPLC (C₁₈ ODS Hypersil column, 20 cm x 2.1 mm ID, 5 µm particle size and diode array detector) or in a Spectrophotometer Shimadzu 2550 at 320 nm (Bz) or 400 nm (Nfx). The efficiency of recovery of Bz or Nfx added to blood were 90.6 % and 52 % respectively. Plots of peak areas against concentration were linear over the concentration ranges studied. Maximum blood level was found after 3 h of treatment for both antichagasic, while after 24 h of treatment the drugs were not detected. Although HPLC-UV method was more sensitive, both methodologies would be applicable for therapeutic monitoring according to instruments availability.</p>
<p>B4-45 NANOSTRUCTURES BASED ON ALKYL VITAMIN C DERIVATIVES (ASC_n) AND EX VIVO SKIN PERMEATION. Saino V^a, Chetoni^b P, Monti D^b, Buralassi S^b, Tampucci S^b, Palma S^a and Allemandi D^a. ^aDepartamento de Farmacia, Fac. de Ciencias Químicas, Haya de la Torre and Medina Allende, UNC, Córdoba, Argentina. ^bDipartimento di Scienze Farmaceutiche, Via Bonanno 33, University of Pisa, Pisa, Italy. e-mail: vsaino@gmail.com</p> <p>The purpose of the present investigation was to study ASC₁₂ and ASC₁₆, able to form liquid-crystal structures (coagel), for their capacity to promote the cutaneous permeation of ibuprofen (IBU) through hairless rat skin. Two coagel formulations (ASC₁₂/C and ASC₁₆/C), and the same coagels added of polyethylene glycol (PEG-400) were tested choosing a commercial product (Arfen®) as reference. The ASC₁₆ and ASC₁₂ derivatives formed stable supramolecular assemblies in water and in water/PEG mixtures (coagels), allowing the solubilisation of IBU (0.85%) and producing a controlled IBU release rate system as evidenced by the dynamic dialysis <i>in vitro</i> test. The <i>n</i> values were indicative of a linear kinetic for all coagel formulations, while Arfen® demonstrated an anomalous drug release. Both coagels and in particular those vehicles containing PEG showed a higher amount of permeated drug through the skin compared to Arfen®. They had a high enhancement factor (EF) value in spite of a low relative release rates RR value. Our results evidenced both the enhancement role of the ASC_n coagels and the synergic effect of the combination ASC_n/PEG.</p>	<p>B4-46 PHARMACOKINETICS OF CEPHALEXIN IN NON LACTATING AND LACTATING GOATS Ambros, L.; Tarragona, L.; Monfrinotti, A.; Prados, A.P.; Hallu, R.; Rebuerto, M. (UBACYT V 026) Farmacología FCV, UBA. Chorroarín 280 (1427), Buenos Aires. e-mail: ambros@fvet.uba.ar</p> <p>The aim of this study was to compare the pharmacokinetics of cephalexin after the intravenous (i.v.) administration to non lactating and lactating goats. Six female (2 – 3 years old) goats received an i.v. dose of 10mg/kg of cephalexin lysine during anestrus (non lactating, experience I) and 25-28 days after the parturition (lactating, experience II). Blood samples were withdrawn at pre-determined times. Cephalexin concentrations were determined by microbiological assay using <i>Micrococcus luteus</i> ATCC 9341 as test microorganism. Plasma disposition curves for each animal were analyzed by non linear methods applying PcNonlin software. plasma cephalexin concentrations were detected for 2 hours after the administration in all animals. Pharmacokinetic parameters calculated for experiences I and II were compared using the Wilcoxon test (p<0.05). Results of the relevant parameters were (mean ± standard deviation): elimination half-life 0.42 ± 0.21 and 0.37 ± 0.15 h; AUC_{0-inf} 28.70 ± 5.97 µg·h/mL and 24.82 ± 4.71 µg·h/mL volume of distribution 0.21 ± 0.06 l/kg and 0.22 ± 0.08 l/kg; clearance 0.47 ± 0.26 l/kg·h and 0.42 ± 0.09 l/kg·h, in non lactating and lactating goats, respectively. These results show that lactation does not modify the pharmacokinetics of cephalexin in goats.</p>

<p>B4-47 PLASMA DISPOSITION KINETICS OF ALBENDAZOLE AND ITS METABOLITES IN LAYING HENS Bistoletti M, Moreno L, Ferreira R, Alvarez L, Lanusse C <i>Laboratorio de Farmacología, Facultad de Ciencias Veterinarias, UNCPBA, Tandil; CONICET, Argentina.</i> Endoparasites are a common and frequently underestimated problem, in avian production systems. Flubendazole is the only benzimidazole (BZD) anthelmintic licensed for use in poultry. However, other BZD drugs such as albendazole (ABZ) are “extra-labeled” used in poultry. The available information on BZD pharmacokinetic (PK) properties in poultry is scarce. The aim of the current work was to evaluate the plasma disposition kinetics of ABZ and its sulphoxide (ABZSO) and sulphone (ABZSO₂) metabolites after intravenous (iv) administration to laying hens. Six (6) hens were iv treated with ABZ (10 mg/kg). Blood samples were taken up to 72 h post-treatment and plasma analyzed by HPLC. ABZ showed an initial concentration (C₀) of 15.2 µg/mL, which rapidly decreased until the lowest concentration (0.107 µg/mL) attained at 12 h post-administration. The ABZ AUC value was 10.2 µg.h/mL and T_{1/2el} was 3.85 h. ABZSO and ABZSO₂ reached peak concentration of 3.21 and 0.34 µg/mL, respectively. ABZSO and ABZSO₂ plasma concentration profiles were higher than those of ABZ parent drug, with AUC values of 26.3 µg.h/mL (ABZSO) and 15.6 µg.h/mL (ABZSO₂). The work contributes with basic PK information useful to assess the potential therapeutic use of ABZ in laying hens.</p>	<p>B4-48 PHARMACOKINETICS OF CEFQUINOME IN LLAMAS (<i>Lama glama</i>) AFTER AN INTRAVENOUS ADMINISTRATION Himelfarb M¹, Lorenzutti M¹, Zarazaga P¹, Aguilar S², Litterio NJ¹, Boggio JC¹. ¹Cát de Farmacología y Toxicología. ²Cát Clínica de Grandes Animales. Universidad Católica de Córdoba. Ob. Trejo 323. 5000. Córdoba, Argentina. martinhim@hotmail.com The objective of this study is to perform a pharmacokinetic (PK) analysis of cefquinome in llamas, after an IV administration. Our experience is based in 6 adult healthy female. It has been administrated 2 mg/kg of cefquinome (Cobactan[®] 4,5%, Intervet, Germany) in the right jugular vein. The blood samples were collected at regular intervals. Cefquinome was quantified by HPLC/uv. For the validation of the technique was determinate, linearity, accuracy, precision, inter-day and intra-day variation, quantification limit and recovery. This data was analyzed with PCNONLIN v 4.0, and a non compartmental model was selected. The quantification limit was 0,07 µg/ml. Pharmacokinetic parameters were: t_{1/2λ}: 2,58 ± 0,77 hs; Cl_i: 0,059 ± 0,013 L/Kg; V_d: 0,21 ± 0,037 L/Kg. We could agree that the developed chromatographic technique is valid for the proposed objectives and allows to quantify amounts of cefquinome, in serum, in the intervals of 29,33 µg/ml and 0,070 µg/ml. Furthermore there should be a quantification of several CIMs for local pathogens in llamas, to be able to perform a full pharmacokinetic/pharmacodynamic study.</p>
<p>B4-49 PHARMACOKINETIC INTERACTION BETWEEN MARBOFLOXACIN AND FLUNIXIN MEGGLUMINE OR DEXAMETHASONE, AFTER INTRAVENOUS ADMINISTRATION IN GOATS. Lorenzutti M¹, Himelfarb M¹, Zarazaga P¹, Auad J², Boggio JC¹, Litterio NJ¹. ¹Universidad Católica de Córdoba. Cát. de Farmacología y Toxicología. ²Cat. Enf Infecciosas. Obispo Trejo 323. 5000. Córdoba. Argentina. matiaslorenzutti@hotmail.com. The objective of this study is to determine a possible pharmacokinetic interaction between marbofloxacin (MFX) and flunixin meglumine (FM) or dexamethasone (DXM), respectively after intravenous administration in goats. Six healthy goats were used, and a cross-over experimental design has been performed. The doses used were 5mg/Kg, 2 mg/Kg and 0.1 mg/Kg for MFX, FM and DXM, respectively. MFX and FM were administered intravenously and DXM intramuscularly. The blood samples were collected at regular intervals. MFX was quantified by HPLC. The data were analyzed by a bi-compartmental model. A Wilcoxon test was performed. No differences were observed on the selected pharmacokinetics parameters between MFX and FM or MFX and DXM neither. Based in these results, we can conclude there is no pharmacokinetic interaction between MFX and FM or DXM, and changes in dosage regimen is not needed. However, more studies with different physiologic and pathologic states will be necessary.</p>	<p>B4-50 ABSENCE OF PHARMACOKINETIC INTERACTION BETWEEN MELOXICAM AND PHENOBARBITAL IN HEALTHY DOGS. Montoya, L.; Kreil, V.; Monfrinotti, A.; Tarragona, L.; Ambros, L.; Reuelto, M. Farmacología. Facultad de Ciencias Veterinarias, UBA. Chorroarín 280. (1427) Buenos Aires, Argentina. lmontoya@fvvet.uba.ar. Therapeutic treatments may combine different drugs. Meloxicam (MEL) is an NSAID which is biotransformed mostly in the liver. Phenobarbital (FNB) could produce enzymatic induction. The pharmacokinetic interactions between FNB and MEL in healthy dogs were investigated in this study. Six beagle adult dogs received 0.1 mg/kg MEL (group 1) or the same dose after a 30-day treatment with 2,5 mg/kg of oral FNB every 12 h (group 2). Blood samples were collected in predetermined times after drug administration. Concentrations of MEL were determined by HPLC. Data were analyzed by noncompartmental methods using the PCNONLIN software. Results are reported as mean ± standard deviation. No statistical differences (Willcoxon Test, p≤0.05) between group 1 and group 2 in pharmacokinetic parameters were found for elimination rate constant (0.029±0.009 vs 0.03±0.004 h⁻¹), terminal half life (26.3±9.5 vs 23.4±4.5 h), volume of distribution (292.3±92.6 vs 410.6±150 ml/kg) volume of distribution at the steady state (197.2±54.0 vs 430±210 ml/kg), total clearance (7.99±2.4 vs 12,4±4,9 l/kg/h) and area under the curve (13.45±3.7 vs 7,07±2,70 µg.h/ml). These results suggest the absence of pharmacokinetic interactions in MEL distribution and elimination when is administered after a long FNB treatment.</p>

POSTERS 4–SEGUNDA SECCION

B4-80**PHARMACOKINETICS OF ORAL AMOXICILLIN AFTER METOCLOPRAMIDE ADMINISTRATION IN DOGS**

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The purpose of the present study was to investigate if previous administration of metoclopramide affects amoxicillin pharmacokinetics after its oral administration to healthy dogs. Seven adult healthy dogs were included in this study. Each dog was fasted for 8 h previous the oral administration of an amoxicillin suspension (25 mg/kg; group 1) or amoxicillin suspension following intravenous metoclopramide (0.5 mg/kg; group 2), with a 2 week wash out period. Amoxicillin plasma concentrations were determined by microbiological assay. Disposition curves were analyzed by a non compartmental model (PcNonlin software). Pharmacokinetic parameters were compared performing Wilcoxon's paired *t* test ($p \leq 0.05$). Results are reported as mean \pm standard deviation. Group 1: peak concentration (C_{max}): 15.2 ± 3.6 $\mu\text{g/ml}$; time to C_{max} (t_{max}): 1.6 ± 0.5 h; terminal half-life ($t_{1/2\alpha}$) = 1.3 ± 0.4 h, mean residence time (MRT) = 2.9 ± 0.6 h, area under the curve extrapolated to infinity ($AUC_{0-\infty}$) = 48.1 ± 15.0 $\mu\text{g}\cdot\text{h/mL}$. Group 2: C_{max} : 16.0 ± 4.3 $\mu\text{g/ml}$; t_{max} : 1.1 ± 0.4 h; $t_{1/2\alpha}$ = 1.4 ± 0.4 h, MRT = 2.7 ± 0.4 h, $AUC_{0-\infty}$ = 49.0 ± 12.0 $\mu\text{g}\cdot\text{h/mL}$. No statistical differences were found in amoxicillin pharmacokinetic parameters between groups. Consequently, no dose adjustment should be required in amoxicillin treatments in dogs when metoclopramide is previously administered.

B4-81**Plasma pharmacokinetics and milk penetration of amoxicillin in lactating goats.**

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The aims of this study were to describe the pharmacokinetics of amoxicillin formulated as a long acting solution in lactating goats administered by the intramuscular (i.m.) route, and to determine the penetration of this drug into the milk. Between 28 and 31 days after the parturition, six lactating goats received an i.m. dose of 15 mg/kg of amoxicillin long acting solution. Blood and milk samples were withdrawn at pre-determined times. Plasma and milk amoxicillin concentrations were determined by the microbiological assay using *Micrococcus luteus* ATCC 9341 as test microorganism. Plasma disposition curves were analyzed by non linear methods applying PcNonlin software. The plasma pharmacokinetic behavior was analyzed by a non compartmental model. Low plasma concentrations were found in all animals. The maximum plasma concentration was 1.23 ± 0.52 $\mu\text{g/ml}$, the time to reach the maximum concentration was 1.23 ± 0.52 h and the elimination half life was 6.39 ± 2.35 h. Amoxicillin was not detected in milk. These results show an acceptable plasma pharmacokinetic profile only for very susceptible microorganisms in goats. The intramuscular administration of long acting formulations of amoxicillin is not a good option for the treatment of mastitis in these animals.

B4-82**THIOESTERIFICATION OF R(-) FENOPROFEN ENANTIOMER IN HEALTHY CATS. AN IN VITRO STUDY.**

Castro, E., Soraci, A., Tapia, O., Solana, H., Fogel, F., Franci, R. Departamentos de Fisiopatología, Clínica, y Cs Biológicas, FCV, UNCPBA, Tandil, Argentina, *Campus Universitario, Pje Arroyo Seco s/n. E-mail: edcast@vet.unicen.edu.ar*

The chiral inversion process is a characteristic metabolic pathway for different aryl-2-propionic acids or profens. Important variations have been observed between these individual compounds as well as between species. The molecular development of the chiral inversion mechanism has been described by several authors (Wechter et al., 1974; Nakamura et al., 1981; Knihinicki et al 1989; Menzel et al., 1994). Three steps are involved in this process: (i) activation of the R(-)-profen by formation of acyl-coenzyme A thioester, (ii) Enzymatic epimerization of the R-thioester to the S thioester/or hydrolysis to regenerate the R enantiomer, and in the final step, (iii) hydrolysis of S thioester completes the inversion process. The aim of this *in vitro* study was to determine the formation of coenzyme A thioester from R(-)-FPF using liver microsomes obtained from experiments with healthy cats. V_{max} values (130 ± 49 nmol/min/mg) for the thioesterification of R(-) FPF were, to our knowledge, the highest reported of all the investigated species. K_m values (μM) were 157 ± 23 . These values are consistent with the percentage of chiral inversion observed in studies *in vivo*. The calculated stereoconversion rate was 93.20 ± 13.7 (Castro et al, 2001)

B4-83**ENHANCE OF TRASCORNEAL PERMEATION USING NOVEL EUDRAGIT-FLURBIPROFEN COMPLEXES**

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In this study we evaluated the transcorneal permeation in rabbits of novel Eudragit-Flurbiprofen (Eu-FI) complexes. Two Eu-FI formulations, 0,1% of FI in 5% dextrose and saline solutions, were assayed. A commercial product (Tolerane®) and 0,01% of FI aqueous solution (control) were comparatively studied. We corroborated that a high proportion of FI was attached to Eu by means of ionic interactions. As consequence of this behaviour, an increase in apparent aqueous solubility of FI was observed, even at pHs where its solubility is low. Regarding transcorneal permeation experiments, Eu-FI solutions permeated at slower rate when the acceptor medium was dextrose solution, whereas the permeation rate was higher in saline solution. This was owed to the ion exchange produced as consequence of the replacement of FI by Cl^- that diffused from saline solution. FI, dissolved in the control solution, permeated the cornea at high rate comparatively to the former, owed mainly to high Eu-FI affinity in Eu-FI solutions. In addition, FI permeation from the later was higher than the commercial formulation. The increase in aqueous compatibility of FI through the dispersion of complexes seemed to improve the drug permeation through rabbit cornea in "ex vivo" experiments. This could be advantageous in the formulation of ophthalmic solutions containing anti-inflammatory drugs.

<p>B4-84 IMPACT OF IVERMECTIN AND TRICLABENDAZOLE RESIDUES ON MILK PROCESSING. Iezzi, S.; Imperiale, F; Farias, C, Lifschitz, A.; Sallovitz, J.; Lanusse, C. Laboratorio de Farmacología, FCV-UNCPBA, Tandil, Argentina. Email: fernanda@vet.unicen.edu.ar Ivermectin (IVM) is a broad-spectrum antiparasitic macrocyclic lactone (ML) extensively used in food-producing animals. Triclabendazole (TCBZ) is an halogenated benzimidazole (BZD) compound worldwide used to control immature and adult stages of liver fluke (<i>F. hepatica</i>). The patterns of milk residue excretion for different ML and BZD compounds have been recently determined in our laboratory. The current trial addressed the evaluation of the stability of IVM and TCBZ residual concentrations in milk under heating conditions as those reached during milk processing. IVM and TCBZ concentrations were measured in milk using HPLC-based methodology with fluorescence detection for IVM and UV detection for TCBZ. IVM (0.1-20ng/ml) and TCBZ (0.1-20µg/ml) were added to drug-free milk samples collected from untreated lactating cows. Drug-spiked milk samples were heated at 65°C for 30 minutes (pasteurization). IVM and TCBZ concentrations were measured prior and after the heating process. Results obtained indicate that no significant changes in the IVM and TCBZ residue profiles take place after heating. Variation observed in residual concentrations in heated milk was within the range of the analytical method. The “yoghurt test” was used to determine any inhibition effect of IVM and TCBZ residues on lactic bacteria. Concentrations studied caused no bacterial inhibition. The impact of these residual drugs concentrations in milk-derived product on human safety and industrial processing are under further evaluation.</p>	<p>B4-85 DEVELOPMENT OF AN HPLC ASSAY TO DETERMINE CLOSANTEL IN GOAT MILK. Imperiale, F.; Farias, C.; Iezzi, S; Sallovitz, J.; Lanusse, C. Lab. Farmacología, FCV-UNCPBA. Tandil, Argentina. E-mail: fernanda@vet.unicen.edu.ar Closantel is an antiparasitic drug used to treat the liver fluke trematode (<i>F. hepatica</i>) and some nematode (<i>Haemonchus contortus</i>) infections in ruminant species. Development of an adequate analytical methodology is required to assess closantel residues in milk obtained from treated animals intended for human consumption. A simple reversed-phase HPLC analytical method with fluorescence detection was developed, validated and applied to quantitatively determine closantel in goat milk. Linearity, precision, recovery and limit of quantification of the method were determined. Drug extraction from samples was effectively performed using a double liquid-liquid extraction and clean up by solid phase extraction. Regression analyses were linear over the concentration range examined (from 50 to 400 ng/ml) and correlation coefficient of the calibration line was 0.9981. The developed HPLC method allowed the quantification of closantel up to 50 ng/ml within internationally accepted coefficient of variations (<20%). The accuracy of the test procedures obtained showed a CV=4.2%, being considered analytically satisfactory. Recovery values were higher than 70%. The analytical method described here is a useful tool for detecting residues of this antiparasitic drug in goat milk.</p>
<p>B4-86 INTERACTION BETWEEN THE EFFLUX TRANSPORTER BCRP (ABCG2) AND THE ANTI-HIV DRUG EFAVIRENZ IN RATS. Peroni RN^{1,2}, Di Gennaro SS¹, Hocht C², Chiappetta DA³, Sosnik A³, Rubio MC^{1,2}, Bramuglia GF². ¹ININFA (CONICET-UBA); ²Farmacología (FFyB-UBA); ³Farmacotecnia (FFyB-UBA). Breast cancer resistant protein (BCRP/ABCG2) is an efflux transporter expressed in organs that influence the absorption and distribution of drugs, as the small intestine and the blood-brain barrier (BBB). The non-nucleoside reverse transcriptase inhibitor efavirenz (EFV) is an anti-HIV drug that inhibits BCRP in vitro (Weiss et al., 2007) and chronic treatment with EFV increases BCRP expression in small intestine and BBB in rats (Peroni et al., 2008). This study was conducted to investigate the role of BCRP in the intestinal absorption and in the delivery to the central nervous system (CNS) of EFV and the influence of the chronic treatment with EFV on the expression of BCRP in adult male rats. Adult male Sprague-Dawley rats were used to perform all the experiments. The intestinal permeation rate was investigated in ileum everted sacs and the delivery to CNS of EFV was studied by microdialysis into the CNS. EFV was measured by HPLC-UV. In control rats, the concentration-dependent efflux of EFV (1-10 mM) observed in ileum everted sacs was almost completely blocked by pretreatment with the specific BCRP inhibitor fumitremorgin C (10 µM). Moreover, the delivery of EFV to CNS after a single i.v. administration of (20 mg/kg solved in Pluronic F127 10%, pH 5) was two-fold increased in rats pretreated with the BCRP inhibitor gefitinib (20 mg/kg, i.p.). The intestinal absorption and the distribution into the CNS of EFV were modulated by BCRP in rats. Since, EFV itself could modulate BCRP expression could, in turn, influence the bioavailability and the delivery of this drug to target or sanctuary HIV-sites.</p>	<p>B4-87 PERMEABILITY STUDY OF CIPROFLOXACIN AND CIPROFLOXACIN ALUMINUM COMPLEX THROUGH THE RAT SMALL INTESTINE IN SIDE-BY-SIDE DIFFUSION CHAMBERS Guzman M¹, Ballent M², Lifschitz A², Lanusse C.², Breda S¹, Manzo R¹, Olivera M¹ ¹Depto de Farmacia, Facultad de Ciencias Químicas, UNC, Córdoba, Argentina. meoliver@fcq.unc.edu.ar ²Facultad de Ciencias Veterinarias, UNCPBA, Tandil, Argentina The purpose of this study was to investigate the in vitro intestinal absorption process of ciprofloxacin hydrochloride (CIP) and CIP-aluminum complex (CIP-Al). The permeability was determined in side-by-side diffusion chambers in different regions of the rat small intestine. The permeability class was ascertained by comparing drug tested with the low permeability internal standard, fluorescein. The apical to basolateral (AP-BL) and the BL-AP transport of the compounds was also investigated. All compounds were detected by fluorescence detector (275nm, 491nm (excitation) and 443nm, 515nm (emission) for CIP and fluorescein, respectively. CIP and CIP-Al exhibited no segmental dependent permeability through the gut wall (p=0,05). Both drugs exhibited significantly greater BL-AP than AP-BL permeability (p=0,05), indicative of net mucosal secretion, which significantly increased in the distal ileum in comparison to the proximal regions of the intestine (p=0,05). Based on comparison to fluorescein, CIP and CIP-Al were classified as low permeability drugs. The results demonstrate that aluminum complexation does not limit in vitro intestinal absorption. However, the in vivo comparative bioavailabilities obtained in mice, showed that the higher solubility of CIP-Al would play a major role in CIP-Al bioavailability.</p>

<p>B4-88 ENHANCED ACTIVITY OF GLUTATHION-S-TRANSFERASE IN THE FLUKE <i>FASCIOLA HEPATICA</i> RESISTANT AT TRICLABENDAZOLE Scarcella S¹, Alzola P², Alzola R., Solana H³. ¹Becaria ANPCyT, ²Becaria CIC BA, ³Prof. Principal CIC BA Lab. Biol. Cel. y Mol. Dpto. Cs. Biológicas – FCV-UNCPBA (7000) Tandil-ARGENTINA</p> <p>Fasciolosis is a zoonotic parasitic disease caused by <i>Fasciola hepatica</i>. Its control is mainly based on the use of triclabendazole (TCBZ), a halogenated benzimidazole thiol derivative that shows excellent efficacy against both juvenile (immature) and adult stages. The helminth parasites possess different biochemical mechanisms for detoxification; the over-expression of metabolic enzymatic systems is one of them. The resistance of <i>F. hepatica</i> to TCBZ is growing worldwide. Hence, the knowledge of detoxification and resistance mechanisms in <i>F. hepatica</i> is needed. This preliminary work was aimed to assess the cytosolic enzymatic activity of Glutathion-S-Transferase (GST) in adult <i>F. hepatica</i> specimens, susceptible (<i>Cullomptom strain</i>) and resistant (<i>Sligo</i> and <i>Oberon strains</i>) to TCBZ. Both resistant strains expressed significant major metabolic activity compared to that measured in the cytosolic fraction obtained from susceptible flukes. GST catalyzes nucleophilic attack by reduced glutathione to a wide array of compounds, including toxic products of lipid peroxidation. TCBZ action may induce secondary oxidative stress in <i>F. hepatica</i>, which may explain the observed increment in GST activities as a defensive mechanism. These preliminary results may be useful to further understand the mechanisms underlying the drug metabolism/disposition and activity in target helminth parasites.</p>	<p>B4-89 HEPATIC CYTOCHROME P450 AND FLAVIN-CONTAINING MONOOXYGENASE METABOLIC ACTIVITIES IN MALE AND FEMALE SHEEP Maté, L.⁽¹⁾; Virkel, G.⁽¹⁾; Lifschitz, A.⁽¹⁾; Ballent, M.⁽¹⁾; Sallovitz, J.^(1,2); Lanusse, C.⁽¹⁾ ⁽¹⁾ Laboratorio Farmacología, FCV-UNCPBA - CONICET (ARGENTINA). ⁽²⁾ CICPBA (ARGENTINA). e-mail: gvirkel@vet.unicen.edu.ar</p> <p>Xenobiotic metabolizing enzymes play a major role in determining the persistence of therapeutically used drugs in target tissues. Phase I oxidative reactions are catalyzed by the cytochrome P450 (CYP) superfamily and the flavin-containing monooxygenase (FMO) system, the most important membrane-bound mixed function oxidases in mammals. The objective of this work was to evaluate CYP- and FMO-dependent activities in liver microsomes obtained from male and female Romney Marsh sheep aged 8-10 months. The involvement of both enzyme systems on the hepatic enantioselective sulphoxidation of the benzimidazole anthelmintic albendazole (ABZ) was also characterized. CYP- and FMO-dependent metabolic activities were measured by using known marker substrates. The total CYP contents in the hepatic microsomes were 0.51±0.18 (males) and 0.53±0.08 (females) nmol/mg of microsomal protein. No gender differences were observed in CYP1A-, CYP2B-, CYP2C-, CYP3A- and FMO-dependent activities. The metabolic ratios FMO/CYP for the total sulphoxidation of ABZ were 3.35 and 3.58 in male and female sheep, respectively. This finding also indicates no gender differences on the contribution of both enzyme systems to the hepatic metabolism of this anthelmintic. Overall, male and female Romney Marsh sheep displayed similar phase I metabolic activities in the liver.</p>
<p>B4-90 PK MODEL CONTRIBUTION TO VANCOMYCIN DOSAGE ADJUSTMENT IN RENAL PATIENTS Miceli M. B., Serra H. A. ¹ª Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. Paraguay 2155 piso 15 1121 Buenos Aires, Argentina. E-Mail: haserrafarmaco@gmail.com</p> <p>Vancomycin dose adjustment in renal patients must be performed in order to avoid more damage of the kidney. Usually, it is done by empirical methods, like Lake & Peterson (Pharmacotherapy 1987; 7: 69-72) and others.</p> <p>Here, we propose the Giusti-Hayton adjustment method (Drug Intel Clin Pharm 1973; 7: 382-7) to acquire the vancomycin dose interval (tau). Such method is based exclusively on each patient estimated creatinine clearance (ClCr) and easily runs in MS Excel® for Windows®.</p> <p>Using a sample of patients with moderate renal insufficiency from a published results (Antimicrob Agents Chemother 1984; 25: 433-7), we obtained the following relationship between tau (h) and ClCr (mL/min/1.73 m²):</p> $\tau = 592.76 \times \text{ClCr}^{-0.788} \quad r^2 = 0.9969.$ <p>To validate the model we compared this method with others and obtained similar results.</p> <p>Conclusions, this method provides an easy way to know the correct tau for vancomycin to be applied in each patient. Further experience could demonstrate if this approach would reduce the renal damage and health costs in vancomycin treated patients.</p>	<p>B4-91 ACETAZOLAMIDE CORNEAL PERMEATION FROM INTERPOLYELECTROLITE-DRUG COMPLEXES. Palena, M., Tártara, I., Quinteros, D., Palma, S., Allemandi, D., Manzo, R. Jimenez-Kairuz, A.¹. Dpto. de Farmacia, Fac. de Cs. Químicas, UNC. Ciudad Universitaria, X5000HUA Córdoba. E-mail: alvaro@fcaq.unc.edu.ar</p> <p>Acetazolamide (ACZ) is an inhibitor of carbonic anhydrase used mainly in the management of glaucoma by oral route. Due to its low solubility and poor corneal permeability there is no ocular formulation available. In this work we present interpolyelectrolyte/drug complexes (DIPEC) using two opposite charged polyelectrolytes, Eudragit E100 (EE) and Eudragit L100 (EL) as ACZ potential carriers. Different EE:EL stoichiometric composition in aqueous dispersion were prepared: EE:ACZ:EL (1:0,07:x), where x=0 to 0,5.</p> <p>The influence of EE:EL ratio on turbidity, particle size, electrokinetic potential (ζ) and <i>in vitro</i> release characteristics of the particles were investigated. <i>In vitro</i> release using Franz cells with synthetic membranes, phosphate buffer (pH 7,4) and simulated lachrymal fluid as receptor media were performed. Additionally, permeability assay through rabbit cornea using ringer solution as receptor media was carried out.</p> <p>As the proportion of EL increased an increment in relative turbidity and a smooth decrease of ζ were observed. Particle size was dependent on EE:EL ratio, varying between 50 and 1500 nm. These facts could be related to nanoparticles formation. ACZ release rate decreased from 32 to 18 $\mu\text{g}\cdot\text{sec}^{-0.5}\cdot\text{cm}^{-2}$ with the increase of EL proportion and release profiles did not show any difference between both receptor media. Corneal permeability of ACZ from EE:ACZ:EL (1:0,07:0,05) was studied and yielded five folds higher than that from ACZ solution.</p> <p>DIPEC could be considered as an interesting ACZ carrier to improve glaucoma treatment by ocular controlled delivery. Additionally <i>in vivo</i> studies should be performed in order to evaluate efficacy and pharmacokinetic.</p>

POSTERS BLOQUE 5 – PRIMERA SECCION

<p>B5-51 INCREASED NITRIC OXIDE SYNTHASE ACTIVITY IN THE PAROTID GLAND FROM RATS WITH EXPERIMENTAL PERIODONTITIS. Miozza V, Borda E, Sterin Borda L, Busch L. Cátedra de Farmacología. Facultad de Odontología. U BA. Excessive production of nitric oxide (NO) has been implicated in various inflammatory conditions. In the present study we investigated the activity of the nitric oxide synthase (NOS) in parotid glands from rats with experimental periodontitis and controls. Periodontitis was produced by a ligature of black thread placed around the cervix of the tow lower first molar. Experiments were carried out 22 days after the ligature. Results showed that ligation caused a significant increase in parotid NOS activity with a different predominant isoform. In controls NOS activity was inhibited by the selective nNOS and eNOS inhibitors while in ligated rats it was inhibited by a selective iNOS inhibitor. NOS activity in rats with ligation was inhibited in the presence of SQ 22536, an adenylyl cyclase inhibitor, but was not affected by the calcium chelator EGTA. Conversely, EGTA inhibited NOS activity in the control group. Prostaglandin E₂ (PGE₂) concentration was increased in parotid gland from rats with ligation. The increment was abolished in the presence of indomethacin and the selective COX-1 inhibitor, FR 122047. NOS activity in parotid gland from rats with ligation was also inhibited in the presence of indomethacin and FR 122047. In rats with ligation unstimulated amylase release was increased. Inhibition of both, PGs and NO production, diminished the increment in amylase release. Conclusion: in parotid glands from ligated rats PGE₂ production is increased and induces an increase in cAMP accumulation which in turn activates the inducible NOS isoform. The increment of NO production participates in the increase in basal amylase release.</p>	<p>B5-52 ^{99m}Tc-SESTAMIBI UPTAKE FOR THE DIAGNOSIS AND FOLLOW-UP OF SKIN TUMORS INDUCED IN MICE. Collia N¹, Salgueiro MJ¹, Tesán F¹, Palmieri M², Durán H³, Medina V¹, Leonardi N^{1,4}, Goldman C¹, Boccio J¹ y Zubillaga M¹. ¹FFyB, UBA; ²FCEN, UBA; ³CONICET, USAM, CNEA; ⁴Laboratorios BACON SAIC, Argentina. <i>Junín 956 Piso Bajo – (1113) CABA. jsalgueiro@ffyb.uba.ar</i> The objective of the study was to evaluate ^{99m}Tc-Sestamibi as a potential radiopharmaceutical (RP) for the diagnosis and follow up of chemically induced skin tumors in mice. Twenty Sencar mice carrying visible and palpable tumors were included in this study and divided in 2 groups according to the route of administration of the RP: intravenous (IV) or subcutaneous (SC). Sestamibi was labeled with 30 mCi of ^{99m}TcO₄⁻ and 1 mCi of the RP was administered IV or SC to each animal. The animals were sacrificed 15 and 30 min after the administration in each group (IV15, IV30, SC15, SC30). Tumors, healthy skin, blood, liver, kidneys, heart, lungs, colon and pancreas were dissected, weighed and measured in a solid scintillation counter. Tumors and healthy skin were prepared for histopathological analysis. Statistical analyses showed no differences in the biodistribution of the radiopharmaceutical according to the route of administration or the time of biodistribution. Paradoxically, there was not a differential uptake between tumors and healthy skin owing to the fact that at the time of evaluation this experimental model generates more papilomas than carcinomas.</p>
<p>B5-53 APOPTOTIC ACTIVITY OF ISOESPINTANOL AND RELATED COMPOUNDS IN HUMAN POLYMORPHONUCLEAR CELLS Dade, M¹; Rojano, B²; Tournier, H¹; Schinella, G¹. ¹Cátedra de Farmacología Básica. Facultad de Cs Médicas-UNLP. CIC-Pcia. Buenos Aires, La Plata, Argentina. ²Lab. de Ciencias de los Alimentos. Universidad Nacional de Colombia (sede Medellín), Colombia. <i>martindade26@hotmail.com.ar</i> Spontaneous apoptosis of human polymorphonuclear cells (PMN) is fundamental for maintaining a normal level of circulating cells and ensuring the rapid resolution of inflammatory responses. Recently, we had demonstrated that isoespintanol (2-isopropyl-3,6-dimethoxy-5-methylphenol), isolated from leaves of <i>Oxandra cf. xylopioides</i>, has anti-inflammatory activity probably by inhibition of IL-1β production. The cytotoxicity of isoespintanol (1) and two derivatives, bromide isoespintanol (2) and demethylated isoespintanol (3) was assessed on PMN by the MTT and propidium iodide (PI) exclusion assays. (2) and (3) (100μM) decreased cell viability by 40% and 25% respectively after 3 h of incubation. In PI exclusion assay only (3) showed necrotic activity (PI⁺: 31% vs. 7% of the control, P<0.01). The nature of cytotoxicity was evaluated using different flow cytometry methods: a) the exposure of membrane phosphatidylserine by the binding of Annexin V-FITC, and b) the development of hypodiploid nuclei by PI. While only a small proportion of PMN untreated or treated with (1) underwent apoptosis, the proportion was much greater for those treated with (2) (An⁺/PI: 62% vs. 2% of the control, P<0.01). (2) was able to increase the development of apoptotic nuclei (39% vs. 12% of the control, P<0.01). When treated in the presence of a caspase inhibitor (z-VAD-fmk) the degradation of DNA was significantly reduced. We conclude that (2) induce an apoptotic process on PMN partially mediated by caspases activation.</p>	<p>B5-54 EFFECT OF PRENATAL ACE INHIBITION ON MEDIATORS OF APOPTOTIC SIGNALLING DURING POSTNATAL LUNG DEVELOPMENT Capelari DN, Fuentes LB, Ciuffo GM. Area de Farmacología. IMIBIO SL – CONICET. UNSL. 5700. San Luis. E-mail: lfuen@unsl.edu.ar Apoptosis or programmed cell death is an important component of different processes including normal cell turnover, proper development and chemical-induced cell death. Apoptosis is a process characterized by a set of morphologic changes and energy-dependent biochemical mechanisms. Bcl-2 family members determine cell death and survival by controlling mitochondrial membrane ion permeability, cytochrome c release, and the subsequent activation of caspase. The aim of this study was to investigate the effect of prenatal ACE inhibition on mediators of apoptotic signalling in postnatal lung tissue development. Mini-osmotic pumps with enalapril or saline solution were implanted in pregnant Wistar rats during the last week of pregnancy. Pup's lungs at four different ages: PND0, PND8, PND15 and PND30 were evaluated. The expression of anti-apoptotic Bcl2 or pro-apoptotic BAX gene was analysed by RT-PCR, and caspase-3 activity was confirmed by Western blot analysis. Semi-quantitative assessment in both groups indicated similar result with significant up-regulation of Bcl2 expression (ANOVA, P<0.001) at PND8 and PND15 respect to PND0 and PND30. Moreover, we found high and constitutive BAX expression with no significant differences during development. Proteolysis of procaspase-3 was detected with high activation at PND0 and PND30. Hoechst staining demonstrated presence of apoptotic cells. In conclusion, the observations suggest that occurrence of apoptosis plays an important role in lung morphogenesis.</p>

<p>B5-55 STRUCTURAL VARIATION OF QUERCETIN IMPROVES INHIBITORY ACTIVITY ON LPS-STIMULATED INDUCIBLE NITRIC OXIDE SYNTHASE (iNOS) EXPRESSION IN J774 CELLS Ortega, M.G¹, Saragusti, A.² Chiabrando, G.² y Cabrera, J.¹ ¹Dpto. de Farmacia. Fac. de Cs. Qcas. UNC-IMBIV-CONICET ²Dpto de Bioquímica Clínica .Fac. de Cs. Qcas. UNC. CIBICI-CONICET. Medina Allende y Haya de la Torre. Ciudad Universitaria, Córdoba 5000 gortega@fcq.unc.edu.ar</p> <p>In inflammation, bacterial products and proinflammatory cytokines induce the formation of large amounts of nitric oxide (NO) by inducible nitric oxide synthase (iNOS), and compounds that inhibit NO production could be potential anti-inflammatory agents. Flavonoids are polyphenolic compounds with a wide range of biological activities found in the Plant Kingdom. Quercetin is one of the most common flavonoids found in the human diet, which possesses anti-inflammatory, anti-oxidant, and anti-tumoral properties. The aim of this job was to investigate a quercetin tetraacetyl derivate (TAQt) in order to analyze if structural variation improves the inhibitory activity on iNOS expression in LPS-stimulated J774 cell line from mouse macrophages. Previously we informed the important inhibition of TAQt on NO production (CI₅₀=21.01±1.03 μM). Subsequently, we evaluate the putative molecular mechanism involved in this inhibition by analyzing the protein and transcriptional expression of iNOS and the NF-κβ translocation to the nucleus. Finally, our results show that semi-synthetic Qt derivate improves the inhibition on NO production via inhibition of iNOS synthesis by blocking translocation of NF-κ B to the nucleus.</p>	<p>B5-56 EFFECT OF PRENATAL STRESS ON LYMPHOCYTE PROLIFERATIVE RESPONSE. PARTICIPATION OF CATECHOLAMINES AND CORTICOSTERONA. Pascuán C, Wald M, Palumbo ML and Genaro AM. CEFYBO-Dto Farmacología, CONICET-UBA. Facultad de Medicina. Paraguay 2155. ceciliapascuan@gmail.com</p> <p>Prenatal Stress has been associated with changes in immune response but the mechanism involved has not been fully elucidated. Over the last years considerable evidence showed a dynamic interaction between the brain and the immune system. The aim of this work was investigate alterations in neuroimmune interaction in adults animals subjected to PS. For this purpose, pregnant mice were individually restrained 2 hour a day, since gestational day 14, until delivery. Stressed offspring mice were tested at 2-months of age together with control matched mice. A group of animals were submitted to acute or chronic stress. Results shown that PS was not induce significant changes in proliferative response, corticosterona or catecholamines levels. However, these animals have a lower proliferative response respect to control mice when were submitted to acute and chronic stress. Moreover, PS animals respond to acute stress with lower levels of corticosterone. But, not significant changes were observed under chronic stress. On the other hand, PS animals respond to both acute and chronic stress with a similar changes of catecholamines levels than control animals. In addition an increased sensitivity of inhibitory effect of corticosterona were found in lymphocytes from PS animals. These results indicate that PS induce a disruption in hypothalamic-pituitary-adrenal axis (HPA)-immune interaction.</p>
<p>B5-57 ASSOCIATION OF STRESS, SLEEP, HABITS WITH FIBROMYALGIA Castagnino J, Rodríguez López E, Garce S, , Fleitas Rumak P, Maritano J, Steimberg J, Lipszyc P, Genaro AM, Scublinsky D. Cátedra I Farmacología, Facultad Medicina. U.B.A. Paraguay 2155, piso 15, Buenos Aires, Argentina. jcastagnino@hotmail.com</p> <p>Fibromyalgia (FM) is an enigmatic entity that consists in a chronic pain syndrome which has been associated with sleep disorders and stress. We developed this study to clarify if this association is due to chronic pain or FM. The main objective of our study was: to determine the association between perceived stress, sleep disorders, habits in fibromyalgia and chronic pain controls (CPC). There were recruited 54 cases (81.5% women, 18.5% men) that fulfilled FM ACR 1990 criteria, 164 controls (78.7% women, 21.3% men) with pain but without the disease and 190 healthy controls. Age of patients was between 18 and 65 years old, both women and men. All patients received a four pages questionnaire. It included nine items as follows: 1) Personal data 2) Medication (including self-medication) 3) Alcoholism CAGE questionnaire 4) Smoking Fagerström Test 5) Diseases history 6) Fibromyalgia history 7) Chronic pain history 8) Sleep Questionnaire and 9) Perceived Stress Questionnaire</p> <p>FM patients showed a significantly higher level of perceived stress than CPC (p < 0.0001). Alcohol intake was significantly higher in CPC than FM (p < 0.004). There was no difference between CPC and FM in smoking. Self-medication was higher in CPC than FM (p < 0.014). There was no difference in the sleep lost days in CPC respect to FM. However the vast majority of FM patients felt that they had not gotten a restful sleep. These results showed that fibromyalgia is a specific syndrome strongly connected with stress that involves more than just pain.</p>	<p>B5-58 UP REGULATION OF NIACINE RECEPTOR IN MOUSE MACROPHAGES BY IN VIVO LPS INOCULATION. POTENTIAL ROLE IN LPS-INDUCED ENDOTOXIC SHOCK. Zorrilla Zubilete M, Cremaschi G, Genaro A, Wald M, Lipszyc P. School of Med, Bs As, Argentina. mariazorillaz@gmail.com</p> <p>Niacin is known to improve lipid metabolism and exert antioxidant/anti-inflammatory actions. The tissue damage that occurs during sepsis is largely mediated by macrophages. Our aim was to investigate if niacin may improve the evolution of LPS-induced septic shock. Moreover the participation of macrophage niacin receptor and pro-inflammatory cytokine production was also analyzed. To this end, C57Bl/6 mice were randomly assigned to niacin-treated (250 mg/Kg/day in drinking water) and untreated groups. Animals began the treatment 24h before the LPS (500 ug/mice) inoculation and continued until the end of the experiment and the survival was determined. Our results indicated that niacin-treated mice showed an increase in survival after endotoxic shock induction. The characterization of niacin receptor in macrophage by binding with [³H]-nicotinic acid showed an increase in the receptor number in macrophages from LPS-treated mice. Macrophages of normal animals stimulated in vitro with LPS showed an increase of IL-6 and TNF-α production, but not of IFN-γ. Addition of niacin did not modify cytokine production. It is probably that in vivo LPS induce INF-γ production by T-lymphocyte that in turn induces up regulation of niacin receptors in macrophage. Under in vivo condition the regulation of pro-inflammatory cytokine production in macrophages by niacin could be possible. The involvement of this cytokine network is now under study.</p>

B5-59

VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN RAT HEART DEVELOPMENT

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Vascular endothelial growth factor (VEGF) is a mitogen factor essential in vasculogenesis and angiogenesis. VEGF regulates survival, migration and differentiation of vascular endothelium, endocardium and cardiac valves. The *vegfa* gene is alternatively spliced to create isoforms designated according to their number of amino acids: VEGF₁₂₀, VEGF₁₄₄, VEGF₁₆₄, VEGF₁₈₈. The aim of this study was to analyze the VEGF isoforms expression during postnatal development in the rat heart. Wistar rat at different postnatal days: PND0, PND8, PND15, PND30 and PND60 were evaluated. The four splice variants of VEGF were assayed by semi-quantitative RT-PCR. VEGF₁₈₈ and VEGF₁₆₄ isoforms were mainly expressed in postnatal stages, especially VEGF₁₈₈. We observed significant increase in the VEGF₁₈₈ isoform expression with age, PND0 and PND8 respect to PND30 and PND60 (ANOVA, P<0.001). The VEGF₁₆₄ isoform expression was lower than VEGF₁₈₈ and no significant changes during the stages studied were detected. The VEGF₁₄₄ and VEGF₁₂₀ isoforms were expressed only during the first week of development (P<0.05). Our results show that several different VEGF mRNA splice variants are expressed in the rat heart. Thus, the differential expression of VEGF isoforms in cardiac tissue at early and late development may be critical in angiogenesis and vasculogenesis processes.

BLOQUE 5 – SEGUNDA SECCION**B5-92****MPAIRED BLOOD BRAIN BARRIER PERMEABILITY IN SEVERE CHOLESTASIS IN A RAT ANIMAL MODEL.**

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The blood brain barrier (BBB) is a physical barrier and a system of cellular transport mechanisms. Common duct ligated rats (CDL) constitute an attractive model to study the mechanism of cholestasis and its injurious actions. The aim of this work was to study BBB integrity and function in CDL rats. **Material and Methods:** Male Wistar rats were divided in two groups: CDL rats (n=24) and sham-operated rats (n=24); 8 rats from each group were perfused transcatheterially with a trypan blue (TB) solution at the time of sacrifice; 4 rats from each group were used for the Evans Blue Test (EB); samples of cerebrospinal fluid were obtained by cisternal puncture for protein and glucose determination and blood samples were collected for biochemical determinations: ALT, AST, ALP, lactate dehydrogenase, albumin, bilirubin, ammonia concentration and total proteins were determined in 8 rats. **Results:** TB was positive in CDL rats and negative in Sham group. The brain tissue of CDL rats showed a significant increase of EB (8,71± 0,51 ug/ g) against Sham group (5,90±0,25 ug/gr). We observed that biochemical determinations increased significantly in the CDL, meanwhile total proteins and albumin tended to decrease in the same group. Ammonia blood concentrations showed a significant increase in CDL rats (0,51±0,08 mg/dl) against Sham rats (0,24±0,06 mg/dl). **Conclusions:** in CDL rats cholestasis was associated with increased permeability of BBB.

B5-93**ENDOTHELIUM-DEPENDENT RESPONSE TO ANGIOTENSIN II AND NORADRENALINE IN RABBITS FEED ON A HIGH FAT DIET**

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The aim of this work was to study the role of endothelium in the contractile response to angiotensin II (Ang II) and noradrenaline (NA) in rabbits feed on a high fat diet. Rabbits were feed with either normal rabbit chow (CD) or a high fat diet containing 6,67% corn oil and 3,33% lard (FD) ad libitum for 12 weeks. Thoracic aorta was excised, rings were cut and mounted in an organ bath to register isometric contractions in endothelium intact (E+) or endothelium removed (E-) arteries. One cumulative dose response curves (CDRC) to acetylcholine (ACh) was performed. After washing, one CDRC to NA or AngII was performed in E(+) and E(-) arteries. In other groups, E(+) arteries were incubated with indomethacin 10^{-5} M or miconazol 10^{-6} M or L-NAME 10^{-4} M before CDRC to NA or Ang II. Results: affinity to ACh was lower (pD₂: 6.82±0.14 vs 7.08±0.09, p<0.05; n=12) and maximal contractile response (E_{max}) was unchanged in FD arteries. E_{max} to AngII (FD: 2877±452 vs CD: 5282±269 mg) and NA (FD: 7630±798 vs CD: 11675±804 mg) was blunted in (E+) but not in E(-) arteries (AngII-FD: 4250±550 vs CD: 4293±431 mg; NA-FD: 13361F±1257 vs CD:11970±571 mg). Shift to the right of CDRC to Ang II and NA was observed both in E(+) and E(-) in FD with respect to CD. L-NAME prevented the decrease in E_{max} (FD: 12041±250 mg) and affinity to NA. However, neither indomethacin nor miconazol nor L-NAME prevented the decrease on Ang II response. Conclusions: high fat diet blunted NA and AngII contractile response. This phenomenon was endothelium dependent. Mechanism of NA-decreased response depends on NO release but mechanism of Ang II remains to be elucidated.

B5-94**HIGH FAT DIETS MODIFY PLASMA LIPID LEVELS AND INTERACTION BETWEEN NORADRENALINE- AND ANGIOTENSIN II-RESPONSES IN RABBITS.**

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Alterations in plasma lipid levels exert an important impact on vascular function. The aim of this work was to study the effect of different high fat diets on the plasma lipid levels and vascular interactions between angiotensin II (Ang II) and noradrenaline (NA) in rabbit aortic rings. Rabbits were feed with either normal rabbit chow (CD) or a diet containing 1% cholesterol for 6 weeks (HD) or a fat diet for 12 weeks (FD). CT, LDL, HDL, TG and free fat acids were measured. Thoracic aorta was excised. Rings were cut and mounted in an organ bath to register isometric contractions. One cumulative dose response curves (CDRC) to Ang II or NA were performed. Arteries were washing and a CDRC to NA or Ang II was performed in the ring previously treated with either Ang II or NA CDRC respectively. Results: CT and LDL were higher in HD. Arachidonic acid was higher in FD and HD. Maximal contractile response (E_{max}) to Ang II was improved in HD (6124±469mg) and decreased in FD (2877±456mg) with respect to controls (4604±574 mg, p<0.05). E_{max} to NA was unmodified in HD and reduced in FD (FD: 7975±768 vs CD: 11675±804 mg, p<0.01). In control rabbits, Ang II desensitizes NA-response (pD₂ 6.26±0.06 vs 4.75±0.14; p<0.001) but NA does not modify Ang II-response. In HD but not in FD, Ang II sensitizes NA-response (pD₂: 6.28 ±0.08 vs 6.55±0.04; p<0.05). However, both in HD and FD, NA desensitizes Ang II-response (pD₂ HD: 7.89±0.06 vs 7.63±0.07; FD: -7.60±0.10 vs -7.03±0.16; p<0.05). Conclusions: high fat diets modify plasma lipid levels and vascular interactions between Ang II- and NA-responses. This would be a regulatory mechanism to maintain the vascular tone.

B5-95**PRELIMINARY STUDIES ABOUT MONOSODIUM GLUTAMATE (MSG) INTAKE AND RENAL FUNCTIONS**

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Distribution of glutamate receptors in the juxtaglomerular apparatus (JGA) and proximal tubules suggest that these receptors may be involved in the regulation of kidney functions. We examined the effect of MSG ingestion (0.12 mg/100 g peso/day) during 7 months in male Wistar rats (T) on some kidney functions. Control rats (C) received a daily dose of sodium (NaCl) similar to the eaten by the MSG group through the glutamate. Body weight gain (BWG), kidney weight (KW) and retroperitoneal fatty weight (RFW) were obtained at 7^o month. Lee index was calculated as a predictor of obesity. At the age of 7 months, water and Na balances and urine concentration test were realized. P-aminohippurate renal clearance (CIPAH ml/min. 100g), glomerular filtration rate (GFR, ml/min.100 g), fractional excretion of water (FE%_{H₂O}), sodium (FE%_{Na}), potassium (FE%_K) were determined by conventional clearances techniques. Data is express as mean±SEM. We observed an increase in BWG, KW, RFW, and Lee I. associated to a reduction in tail length suggesting a metabolic disorder. Sodium and water balances were similar in both groups. T group were unable to maintain the osmolality as C in hydropenic conditions. GFR: C: 0,67± 0,02, T: 0,44±0,04*, CIPAH C:3,17±0,04, T: 2,26±0,19*, FF: C:21,7%, T:20,3% (*p<0,05). The FE%_{H₂O}, Na and K were no different between groups. The drop of CIPAH justifies the lower GFR in T. The proportional reduction in both parameters could be explained by an effect of MSG on the JGA, although any linkage to the MSG-induced metabolic changes is not excluded.

<p>B5-96 SEROTONIN TRANSPORTER PROMOTER POLYMORPHISM IN ARGENTINEAN POPULATION. ¹Errasti A, ¹Armesto A, ¹Daray F, ²Faccione D, ²Giron S, ^{1,2}Maffia P. ¹III Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. ²Laboratorio de Estudios Genéticos Aplicados (EGA), Universidad Nacional de Quilmes (UNQ). farmaco3@fmed.uba.ar</p> <p>Introduction: the promoter region of serotonin transporter gene contains a functional polymorphism with two alleles that have been designated the short (S) and long (L) alleles. The serotonin transporter is the target of selective serotonin re-uptake inhibitors (SSRI) and several studies have found that the L allele is associated with better response to SSRI treatment than the S allele. The aim of this study was to evaluate the genotype and allelic frequencies in the Argentinean population to assess possible implications for treatment. Methods: genomic DNA samples from 145 individuals were isolated from whole blood or buccal swabs after written consent to perform genetic tests accordingly to standard procedures at the EGA laboratory, UNQ. Genetic allelic variation was determined by PCR amplification with specific primers. Alleles were designated S (375 bp) and L (419 bp). Results: observed genotypes were: SS (37%), LS (38%) and LL (25%) giving allele frequencies S (0.56) and L (0.44) in Hardy-Weinberg equilibrium ($\chi^2=7.637$, dF=1, p<0.005). Conclusions: serotonin transporter promoter polymorphism was evaluated in a randomized Argentinean population. The frequencies calculated herein differ from other countries, suggesting that future studies considering the impact of these alleles on treatment response in Argentinean population should be performed.</p>	<p>B5-97 POTENTIATION OF 5-HYDROXYTRYPTAMINE (5-HT) RESPONSES BY A 5-HT UPTAKE INHIBITOR, CITALOPRAM, IN HUMAN UMBILICAL ARTERY. Errasti A, Armesto A, Del Rey G, <u>Rothlin R</u>. <i>III Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires. farmaco3@fmed.uba.ar</i></p> <p>Introduction: 5-HT contracts the human umbilical artery (HUA) and mediates its effects through 5-HT_{2A} and 5-HT_{1B} receptors. 5-HT is taken up into cells via the specific serotonin transporter (SERT); therefore, the aim was to evaluate the effects of the SERT inhibitor, citalopram, on contractions to 5-HT in HUA. Methods: HUA rings were mounted in isolated organ baths and after 2hs equilibration period, were incubated with or without citalopram for 30 min. Then, concentration response-curves (CRC) to 5-HT were constructed. Results: citalopram (10 nM) increased the potency of CCR to 5-HT (<i>control</i>, 7.76 ± 0.01; <i>treated</i>, 8.12 ± 0.01, n=7, p<0.05) without modification of maximal response (<i>control</i>, 3.62 ± 0.48g; <i>treated</i>, 3.27 ± 0.46). Citalopram (100 nM) caused no further increase either in potency or efficacy. On the other hand, citalopram (1 µM) induced a parallel rightward shift without modification of maximal response of the CCR to 5-HT (7.27 ± 0.01, n=7, p<0.05, pK_B=6.33 ± 0.11). Conclusion: the lower concentration of citalopram increases the potency of 5-HT compatible with its 5-HT re-uptake inhibitory value (IC₅₀: 1.8 nM) indicating that SERT inhibition could be involved in HUA. The higher concentration of citalopram inhibits 5-HT responses in HUA with an estimated pK_B of 6.33, probably due to citalopram inhibiting 5-HT_{2A} receptor at this concentration (pK_i=5.25).</p>
<p>B5-98 INCREASED LEVEL OF CYTOKINES AND ATRIX METALLOPROTEINASES IN OSTEOARTHRITIC Ricarte Bratti, JP, Montrull, HL, Demurtas, S, Meirovich, CI and Brizuela NY. Dpto. de Farmacología. FCM. Universidad Nacional de Córdoba. Santa Rosa 1085. Córdoba, Argentina. nildabrizuela@hotmail.com</p> <p>The osteoarthritis (OA) is a chronic articular disease of the locomotive device that compromises both, the synovial and the subcondral bone</p> <p>Objective: The aim of this study was to investigate the expression of several cytokines and matrix metalloproteinases (MMPs) in osteoarthritis (OA) and control sera and different joint tissues. Methods: Serum, synovial fluid, cartilage and subchondral bone tissues were examined in OA and control subjects. The level of tumor necrosis factor (TNF)-α and interleukin (IL)-1α and MMP-3, were measured by immunoanalysis.</p> <p>Results: Serum levels of TNF-α, MMP-3 were significantly higher in OA patients than in controls.</p> <p>CRP was elevated when compared to healthy controls. In contrast to control samples, OA cartilage revealed significantly higher MMP-3 and TNF-α.</p> <p>IL-1α was significantly higher in OA cartilage. MMP-3, (IL)-1α and (TNF)-α were elevated in OA subchondral bone.</p> <p>Conclusion: This study demonstrates pro-inflammatory condition of OA pathology and supports the idea that subchondral region may increase the synthesis of cytokines and MMPs leading to degradation of adjacent cartilage.</p>	<p>B5-99 A MODEL OF EXPERIMENTALLY INDUCED OCULAR HYPERTENSION IN RABBITS THROUGH CAUTERIZATION OF EPISCLERAL VEIN Tártara LI., Llabot JM., Allemandi DA., and Palma SD. Laboratorio de Farmacotecnia. Departamento de Farmacia, Facultad de Ciencias Químicas, Haya de la Torre and Medina Allende, UNC, Córdoba, Argentina. CONICET</p> <p>The aim of the present report was to study the effect of deep episcleral veins cauterization on long-term increase in intraocular pressure (IOP) in animals. Materials and methods: 6 rabbits (New Zealand, 2-3 kg weight) were anesthetized. 3 or 4 right eye (RE) episcleral veins were isolated and cauterized, the fellow eye was used as control. IOP was measured before cauterization (normal RE IOP 11,8 mm Hg±1,8) and every week after, for 2 month, with a tonometer of aplanation (Perkins). Results: IOP increase in RE was 46,6% (average of IOP: 17,3 mm Hg±5,5). No correlation was found between IOP and the number of cauterized episcleral veins. In all cases, an increase in IOP was observed after 14 days. 33,3% of eyes did not show significative IOP variation and intraocular complications (hyphema, corneal descompensation, growth corneal size). Conclusion: the cauterization of episcleral veins demonstrated to be an effective method to cause a moderate and controlled increase in IOP which remained above normal values along the time. This model could be used for the evaluation of effectiveness of new ocular drug delivery systems.</p>

B5-100**USE OF PERTECNETATE ($^{99m}\text{TcO}_4^-$) FOR THE IMAGING DIAGNOSIS OF ACUTE OSTEOARTICULAR INFLAMMATION IN MICE**

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The use of a solid scintillation counter adapted for the diagnosis of acute osteoarticular knees inflammation in mice has the disadvantage of not being available in preclinical research facilities. We aimed to adapt this technique to the use of a gamma camera. For this purpose, 120 Swiss mice were divided in 2 groups: experimental (E) and control (C). Inflammation of the right knee was mechanically induced in the experimental group 24 h before the study. Uptake in the Regions of Interest (ROI) was evaluated using a gamma camera 5, 20 and 60 min after IV administration of 10 μCi of the radiopharmaceutical. In addition, knees were dissected, weighed and measured in a solid scintillation counter. Activity concentration ratios (ACr) between both knees of the same animal were compared to the ROI ratios. No correlation was found between ROIr and ACr with the severity of the lesions. Data was confirmed with the histopathological results. Specificity and sensitivity values were 60% and 53.8% respectively. The positive predictive value was 36.8% and the negative predictive value was 25%. These results are in accordance with the unspecific uptake of the $^{99m}\text{TcO}_4^-$ in the lesion. More specific radiopharmaceuticals should be assayed in order to develop a procedure for imaging inflammation in animals.

BLOQUE 6 – PRIMERA SECCION**B6-60****EFFECT OF α -LIPOIC ACID ADMINISTRATION ON ACETYLCHOLINE-INDUCED AORTIC RING RELAXATION IN FRUCTOSE FED RATS.**

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In previous studies we showed that fructose-treated rats (F) (10 % in drinking water) develop metabolic abnormalities such as insulin resistance, and dyslipidemia. Endothelial dysfunction (ED) is one of the key vascular alterations found in this situation, and recent studies suggest that pro-oxidative and pro-inflammatory processes play a significant role in its development. We hereby investigate the effect of α -lipoic acid (ALA) administration on acetylcholine-induced relaxation (Ach-IR) of aortic rings of rats turned intolerant to carbohydrates. ALA is an antioxidant that combines free radical scavenging with the ability to regenerate other antioxidants. Subgroups of control (C) and F rats were chronically treated during 15 weeks with ALA (50 mg/day per os). Thiobarbituric acid reactive substances (TBARS) were evaluated in heart and liver homogenates. Dose-response curves for Ach-IR were conducted in a high-glucose medium. F treatment increased TBARS and decreased Ach-IR when compared with C rats ($P < 0.001$). Both effects were prevented in F-ALA rats: (vs C $P > 0.05$; vs F $P < 0.01$ ANOVA). These results suggest that F leads to an excessive generation of O_2^- and consequently peroxynitrite anions, and that this may in turn trigger ED. It also supports evidence about the ability of ALA to restore altered relaxation in F rats, probably through its antioxidant activity.

B6-61**VITAMIN E ADMINISTRATION PARTIALLY RESTORES METABOLIC VARIABLES IN FRUCTOSE FED RATS.**

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Many studies have demonstrated that normal rats fed a fructose-enriched diet (FF) (60 % fructose) develop hypertension accompanied by metabolic abnormalities such as hyperinsulinemia, insulin resistance, and dyslipidemia. This situation is considered to parallel multiple metabolic syndrome observed in humans. Increased reactive oxygen species (ROS) has been suggested as a possible mechanism for the detrimental effects of fructose. We hereby investigate the effect of vitamin E (VE) treatment on plasma thiobarbituric acid reactive substances (TBARS), triglycerides, cholesterol and insulin. Fasting blood glucose and oral glucose tolerance tests (OGTT) were performed. TBARS were also evaluated in heart and liver homogenates at the end of the experimental period. Subgroups of control and FF rats were chronically treated with VE (C-VE and FF-VE) (50 mg/day during 18 weeks). Fructose administration increased significantly TBARS in plasma, heart and liver ($P < 0.001$) and this effect was suppressed by VE treatment. Levels of plasma triglycerides, cholesterol, insulin and glucose were also increased, but only triglycerides and cholesterol were partially reversed in FF-VE rats ($P < 0.001$ and $P < 0.05$ respectively). These results support further evidence about the ability of chronic treatment with VE to counteract oxidative stress through the scavenging of ROS, while the molecular mechanism of the amelioration of dyslipidemia

B6-62**USE OF ANTIHYPERTENSIVE DRUGS AND PHARMACOLOGICAL INTERACTIONS IN DIABETIC PATIENTS IN A PUBLIC HOSPITAL AT ROSARIO**

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Drug utilization research allows estimating its adequate implementation. Objective: To describe the use of antihypertensive drugs (aHD) and potential pharmacological interactions (PFI) among drugs dispensed by pharmacy office to diabetic outpatients from Provincial del Centenario Hospital during the first 6 months of 2008. Methods: Cross sectional study from collected prescriptions that included hypoglycaemic drugs (HGD). Frequencies are expressed in percentages with confidence interval of 95% (CI95). Results: Data were collected from 569 outpatients. The 51,7% (CI95: 47,5-55,8%) took some aHD with its HGD. In this group, outpatients taking enalapril (E): 80,6% (CI95: 75,6-85,0%), atenolol (A): 31,6% (CI95: 26,4-37,3%), furosemide (F): 17,3% (CI95: 13,2-22,2%), and hydrochlorothiazide (HCTZ): 16,3% (CI95: 12,3-21,1%). Among patients that took their oral HGD for 3 or more months, in 467 total prescriptions, 47,8% (CI95: 43,2-52,3%) included more than one drug. There were 37 different PFI. It is worth highlighting: E with acetylsalicylic acid (AAS), ibuprofen (I) and F; glibenclamide (G) with AAS, I and A. Conclusion: A subutilization of E and HCTZ in this population as well as a high use of F is evident. The PFI must be considered as possible sources of complication of treatment and its continuity. These topics should be further investigated.

B6-63**USE OF HYPOGLYCEMIC DRUGS IN A PUBLIC HOSPITAL FROM ROSARIO, SANTA FE.**

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Drugs utilization research allows estimating its adequate implementation. Objective: To evaluate the use of hypoglycemic agents among outpatients from Provincial del Centenario Hospital during the first 6 months of 2008. Methods: Consumption was calculated using defined daily doses (DDD) and prescript DD (PDD) from the dispensations in Hospital pharmacy office. Frequencies are expressed in percentages with confidence interval of 95% (CI95). Results: Prescriptions were collected from 569 patients. The 70,3% (CI95: 66,3-74,0%) of outpatients took some oral hypoglycemic drug (OH) during the studied time. From these, 64,3% took metformin (M) (CI95: 59,3-68,9%) and 59,5% (CI95: 54,5-64,3%) took glybenclamide (G). The 29,7% (CI95: 26,0-34,7%) of outpatients was exclusively insulin dependent (OEDI). Only the 21,9% (CI95: 15,9-28,9%) from these took NPH insulin (NPHI) and regular insulin (RI). Consumption: DDD: M: 10125, G: 13570, INPH: 33310, RI: 3362,5. PDD: M: 1110,3 mg; G: 9,0 mg; NPHI: 69,9 UI, RI: 41,1 UI. The 29,8% (CI95: 25,3-34,2%) of users of OH took drugs 3 or more months in the studied period and the 47,3 % (CI95: 39,8-54,9%) from OEDI. Conclusion: It is known that M is a first choice drug to treat diabetes with requirement of OH, then it is evident a subutilization of M compared to G. It is very limited the use of RI in OEDI. There is a poor continuity of outpatients taking their drugs. These topics should be further investigated.

<p>B6-64 FUNCTIONAL RELEVANCE OF ENDOTHELIAL ANGIOTENSIN-CONVERTING ENZYME (ACE) IN BIOLOGICAL INACTIVATION OF BRADYKININ (BK) IN HUMAN UMBILICAL VEIN (HUV).</p> <p>Nowak W., Ireizo J., Daich M., Migliore D., Rothlin R. 3^o Cátedra de Farmacología. Facultad de Medicina (UBA). Paraguay 2155. Piso 9. CP 1121. farmaco3@fmed.uba.ar.</p> <p>Introduction and goals: ACE is a metallopeptidase that hydrolyze the endogenous BKB2 receptor agonist, BK, in isolated HUV. The aim of the present study was to evaluate the functional relevance of endothelial ACE in the biological modulation of BK responses in HUV.</p> <p>Methods and Results: HUV rings were placed under isometric tension in Krebs solution at 37°C. After 120 min, concentration-response curves (CRC) were obtained to BK. There was a significant leftward shift observed in control HUV rings devoid of endothelium compared with intact tissues (pCE₅₀ E+: 9.12±0.06, pCE₅₀ E-: 9.62±0.04; <i>p</i><0.001). Exposure to Captopril 1µM (ACE inhibitor) potentiated BK-elicited vasoconstrictor responses in HUV rings with endothelium (pCE₅₀ Captopril E+: 9.33±0.04; <i>p</i><0.05), while no such effect was observed in tissues devoid of endothelium (pCE₅₀ Captopril E-: 9.49±0.06; <i>p</i>=NS). No differences were observed in maximal responses. The presence of endothelial layer was confirmed by histological studies.</p> <p>Conclusion: The present results indicate that ACE's activity localized in endothelial HUV cells is functionally relevant in modulating BK vasoconstrictor responses in isolated HUV.</p>	<p>B6-65 EFFECT OF DAILY EXPOSURE TO AROMATIC HYDROCARBONS ON FOLLICULAR GROWTH IN RATS</p> <p>Barreiro KA, Di Yorio MP, Artillo Guida RD, Faletti AG CEFYBO-CONICET, Facultad de Medicina-Universidad de Buenos Aires. Paraguay 2155, CABA. agfaletti@yahoo.com.ar</p> <p>Polycyclic aromatic hydrocarbons produce different toxic responses in reproductive health by activating the arylhydrocarbon receptor (AhR). The aim of this project was to study the action of a repeated exposure of two AhR ligands, β-naphthoflavone (βNF) (an AhR agonist) and α-naphthoflavone (αNF) (an AhR antagonist) on follicular growth by using immature rats daily treated with different doses (0.1-50 mg/kg) of either βNF or αNF. After a 10 day-treatment, the animals were stimulated with gonadotropins (eCG/hCG) to induce ovulation and then killed 20 h after hCG administration. Serum progesterone levels (P), measured by radioimmunoassay, and the developing stages of follicles, determined by histological evaluation, were studied. At high levels, both αNF and βNF increased the number of primordial (αNF: 214%; βNF: 344%; <i>p</i><0.001), primary (αNF: 76%; βNF: 136%; <i>p</i><0.05), antral (αNF: 113%; βNF: 118%; <i>p</i><0.001), and atretic (αNF: 58%; βNF: 39%; <i>p</i><0.05) follicles. Only βNF increased the ovulatory rate by assessing the number of corpora lutea per ovary (84%; <i>p</i><0.01). These effects were consistent with an increase in the serum P expressed as ng/ml (C: 24, αNF: 52, βNF: 56; <i>p</i><0.01). These results demonstrate that repeated daily exposure to aromatic hydrocarbons, even after birth, can alter the primordial follicle reserve and the follicular growth in rats.</p>
<p>B6-66 ANTIHYPERTENSIVE DRUG THERAPY IN ADULT PATIENTS</p> <p>Verdugo R, Wendel G, Trujillo L, Fuentes L. Farmacología.UNSL.5700.San Luis. E-mail:lfuen@unsl.edu.ar</p> <p>Hypertension is one of the most common complex disorders and essential hypertension indicates that no specific medical cause can be found. The aim was to know the antihypertensive drug therapy in patients from our community. Retrospective study of 700 individuals (64.3% women) from private cardiologic institute, > 20 years from middle class of San Luis city, was performed. Age, weight, blood pressure and therapeutics treatment were recorded. The results were analyzed by SPSS (version 12.0). Mean values age: 55.4±13.0yr, weight: 85.9±17.4 kg. Systolic blood pressure >140 mm Hg: 65.3% (61.1% women; 53.0% in the group age: 40-60 yr). Systolic and diastolic blood pressure vs age were positively associated (<i>r</i>=+0.122, <i>p</i>=0.01; <i>r</i>=+0.116, <i>p</i>=0.05 respectively). Commonly used drugs include the typical groups of ACE inhibitors: 59.8% (most used: enalapril, lisinopril); beta blockers: 42.7% (mainly atenolol, carvedilol); calcium channel antagonists: 21.4% (amlodipine, diltiazem); angiotensin II receptor antagonists: 18.1% (losartan, valsartan); diuretics: 12.6% (hydrochlorothiazide, furosemide); combination products: 6.1%, which usually contain hydrochlorothiazide and other drug; additionally less used groups: 1.7%. Several agents may be given simultaneously. The prevalence of hypertension rises as the population grows older, affecting approximately 50% of individuals aged 40 yr or older. ACE inhibitors as first-line therapy followed by beta blockers have been used in our community. Prevent even moderate elevation of arterial blood pressure leads to long life expectancy</p>	<p>B6-67 EFFECT OF XANTHATIN ON GASTRIC MUCOSAL LESIONS INDUCED BY COMPOUND 48/80 IN RATS</p> <p>María AO^a, Wendel GH^a, Favier LS^b, Alvarez ME^b, Piezzi RS^c, Tonn CE^b, Pelzer L^a, Penissi AB^c.ⁱHEM-CONICET, Universidad Nacional de Cuyo. Áreas de ^aFarmacología y ^bQuímica Orgánica. Universidad Nacional de San Luis. Chacabuco y Pedernera. 5700. San Luis. Argentina. E-mail: alemaria@unsl.edu.ar</p> <p>Xanthatin, isolated from <i>Xanthium cavanillesii</i> Schouw, prevents damage induced by several ulcerogenic agents (Favier et al., J. Ethnopharmacol. 2005, 100:260-267). Moreover, we described the mechanism of gastroprotection of xanthatin in a previous study (Favier et al., Biocell 30(1), 2006). Recently we have reported that xanthatin inhibits compound 48/80-induced serotonin release from peritoneal mast cells, acting as mast cell stabilizer (Eur. J.Pharmacol. 2009, 612(1-3):122-30).</p> <p>The aim of this study was investigate the effect of xanthatin on gastric mucosal lesions induced by compound 48/80 in rats. This compound is known to cause degeneration of connective tissue mast cells, with release of serotonin and histamine from the cells. Repeated i. p. administration of compound 48/80 produced damage in the stomach with severe oedema in the submucosa. Gastric lesions were produced according to the method of Yasuhiro et al., 1998. Wistar rats were given compound 48/80 (1 mg/kg, i. p.) once daily for 4 days. The lesions induced by 48/80 were prevented by xanthatin (40 mg/kg, p. o., 60 min before administration of compound 48/80) (<i>p</i><0.05). The present study demonstrates that xanthatin inhibits compound 48/80-induced gastric lesions, acting as mast cell stabilizer in vivo.</p>

<p>B6-68 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D) EFFECTS ON THE PUP RAT BRAINS. MEASURE OF HYDROXYL RADICAL.</p> <p>Biolatto, S.; Pochettino, A.; Duffard, R. and Evangelista, A. LATOEX – Facultad de Ciencias. Bioquímicas y Farmacéuticas UNR – Suipacha 531 - 2000 - Rosario. sbiolatto@gmail.com.</p> <p>2,4-Dichlorophenoxyacetic acid (2,4-D) is a selective herbicide of the phenoxyacetic acid group, with weak aromatic acid properties. It is used to control broad-leaved weeds. In previous studies we demonstrated that 2,4-D induced disparate alterations on enzymatic activities of the defensive mechanism and/or modifications of the reactive oxygen species (ROS) levels in specific neonate rat brain regions. (Bongiovanni et al., 2007; Ferri et al., 2007).</p> <p>We determined in the present study hydroxyl radical by high performance liquid chromatography (HPLC) coupled with an UV detection, indirectly by its reaction products with salicylic acid (SAL), 2,3-dihydroxybenzoic acid (2,3-DHBA), and 2,5-dihydroxybenzoic acid (2,5-DHBA). For this purpose, Wistar rats were made pregnant and exposed to 2,4-D (70 mg/kg/day, sprayed on food) from gestation day 16 onward. On postnatal days (PND) 1, 7 and 14, pups were sacrificed by decapitation and the brain pup's were obtained. We detected a significant decrease in the body weight at PND 14, but there is not difference in brain weight at any age of exposed pups. In addition ROS formation was only observed at PND 14. In conclusion, the exposure to 2,4 D during lactation results in a damage in the pups nutritional status and in the ROS formation on the post natal day 14.</p>	<p>B6-69 SEMI-QUANTIFICATION OF ANDROGEN RECEPTOR MRNA AND DETERMINATION OF HORMONE LEVELS IN MALE RATS BY A PRE-AND POSTNATAL EXPOSURE TO 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D).</p> <p>Pochettino, A.; Hapon, MB. (*); Jahn, G.(*); Duffard, R.; Evangelista, A. LATOEX – Facultad de Ciencias. Bioquímicas y Farmacéuticas UNR – Suipacha 531 - 2000 - Rosario. - (*).IMBECU – CRICYT (CONICET) – MENDOZA aristidespochettino@gmail.com.</p> <p>Chlorophenoxy herbicides are widely used for the control of broadleaved weeds. We previously reported that 2,4-D decreases the height of prostatic epithelial cells and the level androgen receptor (AR) protein in male rats exposed to 2,4-D pre-pubertal and pubertal. The biological function of androgen in the prostate is mediated by AR. The goal of the present work was to assess whether the 2,4-D has any effects on AR mRNA expression and on hormones involved in the development of the prostate. Pregnant Wistar rats were treated with 2,4-D (70 mg/kg/day, sprayed on food) from gestation day 16 onward. On postnatal day 23, pups were weaned and the treated group continued to be fed with 2,4-D until sacrifice by decapitation at 45, 60, 90 or 120 days of age. We studied, serum testosterone (T), dihydrotestosterone (DHT), insulin-like growth factor-1 (IGF-1), growth hormone (GH) and ventral prostate AR mRNA levels. We observed a significant decrease in concentrations of T, DHT, IGF-1 and GH at age 45 (99%, 98%, 70% and 76%) and 60 days (88%, 76%, 41% and 59%) respectively with respect to controls. There was no change in AR mRNA level at any age studied. The low circulating androgens, together with the other parameters previously determined, would be responsible for the lack of development of the glands in exposed pre-pubertal and pubertal rats.</p>
<p>B6-70 EFFECTS OF SWANSONINA ISOLATED FROM IPOMOEA CARNEA ON GUINEA PIGS</p> <p>Cholich L, García E, Teibler G, Lértora J, Acosta O. Cátedra de Farmacología, Facultad de Ciencias Veterinarias, Universidad Nacional del Nordeste, Sargento Cabral 2139, Corrientes 3400. lucianacholic@hotmail.com</p> <p>The toxic principle of <i>Ipomoea carnea</i> is an indolizidine alkaloid named Swainsonine (SW). This is a potent inhibitor of lysosomal α-mannosidase and Golgi α-mannosidase-II, resulting in lysosomal accumulation of incompletely processed oligosaccharides. The intoxication is characterized by cytoplasmic vacuolization of neurons, thyroid, liver, kidneys and pancreas. Also it causes immunodeficiency and animals became susceptible to the occurrence of pneumonia. The main objective of the present study was to evaluate some toxic effects of SW on guinea pigs. Four animals received 0,36mg/kg/day of SW during 42 days. The intoxicated animals were clinically normal. Samples of pancreas and lung were fixed in 10% neutral buffered formalin at room temperature, embedded in paraffin, sectioned at 5 μm thickness, stained with hematoxylin and eosin. Cytoplasmic vacuoles were found in pancreas accompanied by a significant elevation of AST level (p > 0, 0015). Besides it was found alterations in lung compatible with pneumonia as a consequence of acute inflammation. We conclude that the isolated SW from <i>I. carnea</i> induces a cytoplasmic vacuolization of exocrine pancreas and could cause immunosuppression in guinea pigs.</p>	

BLOQUE 6 – SEGUNDA SECCION**B6-101****ALLOPREGNANOLONE ACUTE EFFECT ON THE RAT OVARY FUNCTIONALITY.**

M. Laconi, S. Cerioni, A. Vega, R. Yunes and R. Cabrera. LINCE-IMBECU-CONICET), F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza. Mendoza. Argentina. mlaconi@lab.cricyt.edu.ar

Allopregnanolone (ALL) is one of the best characterized neurosteroids in the brain. Previously we demonstrated that ALL inhibited the apoptotic process in the rat *corpora lutea* and caused a decrease in the β 3 HSD enzyme activity in the medio basal hypothalamus with an increase of this activity in the ovary on rat estrous day. The aim of this work was to study if ALL icv could modify the ovulation rate, ovarian (Pg) levels and ovarian histology during the estrous cycle. On the proestrous morning, Sprague Dawley adult female rats were injected in the third ventricle with ALL 6 μ M or vehicle and sacrificed 24, 48 and 72 hs after that. The ovarian and serum Pg levels were measured by RIA. One ovary was collected to histological studies and the other to Pg measures. The results were analyzed by ANOVA and post hoc-test, vs vehicle. $p < 0.05$ was considered significant. ALL induced an increase in ovarian Pg levels at 48 hs ($p < 0.001$), without significant changes at 24 and 72 hs. An inhibition of the ovulation was observed 24 hs post ALL without modification in the others groups. No significant changes were observed in the ovarian histology at the times of this study. We concluded that ALL would have different central and peripheral modulatory mechanisms of action on the regulation of the physiological reproductive female function, suggesting genomic and non-genomic mechanism in concert.

B6-103**EFFECT OF ALLOPREGNANOLONE ON GLUTAMATE RELEASE IN PUBERTY.**

Giuliani F, García S, Casas S, Escudero C, Nanfaro F, Bazzocchini V and Cabrera R. LINCE-IMBECU-CONICET, F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza. Onset of puberty in female rats, when vaginal opening becomes evident, is produced by a pulsatile GnRH release from hypothalamus. Among factors that regulate this event, Glutamatergic/NMDA system would play an essential role. Moreover, previous results of our laboratory demonstrated that this neurotransmitter system might be modulated by the neurosteroid Allopregnanolone (Allo) in adult rats. The aim of this work was to determine if Allo modify the glutamate release in hypothalamus of peripuberal and puberal rats and if this possible effect would be mediated by modulation of NMDA receptors. K^+ evoked [3H]-glutamate release of medial basal hypothalamus (MBH) and preoptic area (POA) slices of peripuberal (37d approx.) and puberal (55d) rats was carried out by superfusion method. The different treatments were vehicle (KRBG Mg^{2+} free buffer), Allo 120nM, KRBG- Mg^{2+} buffer (to antagonize NMDA receptors) and KRBG- Mg^{2+} buffer + Allo 120nM. Results were analyzed by ANOVA 1 and Turkey's post test ($p < 0.05$ were considered as significant). Allo enhanced [3H]-glutamate release in both stages. The antagonism of NMDA receptors with Mg^{2+} reverted the Allo effect to basal values in both groups. Mg^{2+} alone had not effect "per se" with respect to vehicle groups. Together these data indicate that Allo would regulate glutamate release in peripuberal and puberal rats and that this effect might be mediated by NMDA receptor modulation, showing a possible new role for this neurosteroidal molecule in this important stage of reproductive life of female rats.

B6-102**ALLOPREGNANOLONE HAS MNEMONIC-ENHANCING EFFECTS IN FEMALE RATS.**

Escudero C, Cerioni S, García S, Yunes R and Cabrera R. LINCE-IMBECU-CONICET, F.C.Médicas, U.N.Cuyo. F.C.Salud. U.Mendoza. Learning and memory processes may be influenced by fluctuations in steroid hormones and neurosteroids, such as Allopregnanolone (Allo). In this study, we investigated the effects of the subcutaneous administration of estrogen (E) and progesterone (P) to ovariectomized (OVX) rats, infused in CA1-CA3 hippocampus regions with Allo (6 μ M) or vehicle (30min before training), on the inhibitory avoidance task (Step Down, SD). All groups were trained in SD task and, after 24-h intertrial delay, SD latency was tested. The results were analyzed vs vehicle by t-test ($p < 0.05$ was significant). No differences were observed in SD latencies when OVX rats received hippocampal administration (HA) of Allo. The administration of estradiol (E) (0,1mg/kg, 48h before training), did not modify the SD latency after HA of Allo, but in E-P primed group (0,1mg/kg and 4mg/kg, 48hs and 5hs before training, respectively) Allo increased SD latencies. HA of bicuculine (GABA_A antagonist) prior to Allo had not effect on the increased SD latencies observed in E-P group. The HA of AP-7 (NMDA receptor-antagonist), (2 μ g/ μ l, 60min before training) prior to Allo in E-P rats reversed the increase of SD latencies observed before. Together, these data suggest that Allo would have positive mnemonic effects in the SD task in E-P primed rats and might act through the glutamatergic system.

B6-104**HIGH DOSES OF ALENDRONATE IMPROVES THE PLASTIC COMPONENT OF RESISTANCE OF THE RAT FEMORAL SHAFT FRACTURE, WITHOUT AFFECTING THE MIRENALIZATION AND ELASTIC BEHAVIOR.**

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BP effects on bone post-yield behavior are scarcely studied. We analyzed alendronate effects on rat cortical bone mass, design, "quality" and strength including pre/post-yield behavior avoiding growth and hormonal interactions in female, retired-breeder Sprague-Dawley rats aged 13 mo (bw about 350g) treated with 0 (N=10), 5 (9), 25 (9) or 125 (10) μ g/kg/d of alendronate 2d/wk during 12 weeks. Positive effects of only the highest dose were observed on F_{max} (+27%) and all post-yield properties: d_{max} +31%, EA_f +21%, EA_{fy} +230%, always $p < 0.001$. The parallel, linear correlation curves between the mechanically-assayed F_{max} (y) and the xBSI (x), expression of the predictive value of xBSI which disregards all determinants of cortical micro-structure, showed similar intercepts for 0, 5 and 25 groups and a higher intercept for the 125 group ($p < 0.001$). Results indicate a positive effect of the highest assayed dose of alendronate on ultimate strength and all post-yield properties of bones, with no changes in bone mass, pre-yield properties, or cortical mineralization or stiffness (E). This excludes any effect on bone mass, geometry, material "quality" (as assessed) and resilience. Restriction of effects to post-yield properties, as well as the underestimation of ultimate strength by the BSI at that dose, suggests some positive alendronate effect on some micro-structural determinant(s) of bone toughness. The analysis of the attractive possibility to extrapolate these findings to human skeletons requires further investigation.

<p>B6-105 POTENTIAL PHARMACOLOGICAL USE OF BOTHROPIC PLA₂ IN HEMOSTASIS García Denegri M.E.¹; Bustillo S.¹; Tejada R.^{1,2}; Ponce-Soto L.A.³; Acosta O.¹; Leiva L.¹. ¹Universidad Nacional del Nordeste. Av. Libertad 5400, (3400) Corrientes, Argentina. E-mail: emiliadenegri@hotmail.com. ²Hospital J.R. Vidal, Corrientes, Argentina ³UNICAMP, Brazil. Bothrops snake venoms have been proved toxic to a variety of cell types, in both <i>in vivo</i> and <i>in vitro</i> models. We have previously isolated an acidic phospholipase A₂ from <i>Bothrops alternatus</i> venom. This enzyme did not show myotoxic or lethal activity when it was injected i.m and i.p. respectively in mouse in high doses. However, it exhibited catalytic activity on phospholipids, edema and indirect hemolytic activity. In this work, we examined the cytotoxic activity of the isolated enzyme on different cell types: myoblasts (C2C12), mouse mammary epithelial cells (NMuMG) and murine mammary adenocarcinoma cells (LM3). Cells were exposed to different amounts of PLA₂ for 3 h at 37°C-5% CO₂. Citotoxicity was quantitatively assayed by crystal violet method and the percentage of viable cells was registered. Anticoagulant property was also studied on human citrated plasma pre-incubated for 10 min with different PLA₂ solutions (0.033 to 1.06 mg/mL). The isolated PLA₂ prolonged the clotting time, so concentrations higher than 0.133 mg/mL produced a significant effect (P < 0.05). On the other hand, the purified enzyme did not exhibit damage on any cell line assayed, confirming that it is a low toxic venom component, although it presents an interesting pharmacological activity, and acting on coagulation system. Both pharmacological characteristics revealed a potential use of this enzyme as a promising molecule prototype in hemostasis treatment.</p>	<p>B6-106 DOWN-STREAM ACTION OF EPO-R IN BONE MARROW ERYTHROID COMPARTMENT UNDER PACLITAXEL EFFECT Aguirre M, Todaro J, Juaristi J, Alvarez M, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. Moreno 1240 (3400). Corrientes. UNNE. e-mail: nbrandan@med.unne.edu.ar Paclitaxel (Px), an antitumoral drug, was used in a single dose of 29 mg/kg (ip) as an injury agent for inducing transient suppression of hematopoiesis in mice during 10 days. The aim of this study focuses on EPO-R, GATA-1 and EKLF expressions related to the apoptotic events triggered by Px in bone marrow (BM) and the subsequent <i>in vivo</i> erythropoietic recovery. A transient mild anemia with maximal BM apoptosis (TUNEL), disruptions of BM niche (scanning electronic microscopy), depletion of BM erythroid colonies (clonogenic assays), Bax and caspase-3 over expressions (immunoblottings), high caspase-3 activity (colorimetric assay) and minimal erythroid maturation ([⁵⁹Fe] uptake) were seen within 1-2 days post Px. EPO-R over expression from day 3, prompted the subsequent up-regulations of GATA-1, Bcl-xL and EKLF. CFU-E and BFU-E enhanced from days 5 to 10, whilst normal percentages of [⁵⁹Fe] uptake were noticed since day 6. Proerythroblasts and basophilic erythroblasts reached normality by day 10, suggesting a delay in the erythroid maturation. These findings suggest that the erythroid recovery involves EPO-R expression which might govern the sequential up regulation of GATA-1 and EKLF, crucial factors to accomplish the erythroid program.</p>
<p>B6-107 BONE MARROW AND SPLEEN CELL DEATH FOLLOWING HEMORRHAGIC SHOCK: CRITICAL IMPLICATIONS FOR BAX AND BCL-XL Todaro J, Aguirre M, Stoyanoff T, Juaristi J, Alvarez M, Brandan N. Cátedra de Bioquímica. Facultad de Medicina. Moreno 1240 (3400) Corrientes. UNNE. e-mail: nbrandan@med.unne.edu.ar Hemorrhagic shock (HS) induces profound changes in the physiologic processes of many tissues and activates different stress-induced compensatory and adaptive responses. The aim of this study was to evaluate the effects of acute bleeding and the apoptotic/necrotic events triggered in murine bone marrow (BM) and spleen (SP) during 15 days. Male adult CF-1 mice were submitted to HS with bleeding (10% of blood volume) by retroorbital puncture following resuscitation with sterile saline solution. Hematological parameters, BM and SP hematopoietic precursors, apoptotic indexes, Bcl-x_L/Bax and Caspase 3 expressions were determined over 15 days after HS. Hematological parameters indicated an acute anemia that recovered on day 15. Reticulocyte counts showed an opposite pattern in BM and peripheral blood. Erythroid total precursors decreased in BM at 48 h. BM and SP exhibited enhancement of red cell precursors by 72 h. Bax /Bcl-xL ratio increased from 1 to 10 days in SP, concomitant with the maximal splenic apoptosis (days 7-10). However, BM coexpressed switching cell death from apoptosis to necrosis. These results suggest that HS causes differential adaptive responses to deal with stress- induced erythropoiesis in BM and SP.</p>	<p>B6-108 SUBLETHAL DOSES OF DEHYDROLEUCODINE INDUCE MALFORMATIONS IN RHINELLA ARENARUM (ANURA: BUFONIDAE) EMBRYOS Moreno, LE, Juárez, AO, Pelzer LE Farmacología, Fac. Qca. Bqca. y Fcia. Univ. Nac. San Luis. San Luis 5700. Argentina. lmoreno@unsl.edu.ar Dehydroleucodine (DhL), is a sesquiterpene lactone of the guaianolide type. The literature described toxic effects <i>in-vitro</i> mammalian cell culture test of DhL. As amphibian embryos and larvae are excellent models for studies of development and toxicity tests of chemical compounds, we decided to evaluate the number and type of malformations induced by DhL in embryos of <i>R. arenarum</i> obtained by <i>in-vitro</i> fertilization. Groups of 15 late blastula-stage embryos, developing normally, were selected under stereoscopic microscope and placed in 15 cm diameter glass petridishes by triplicate with : 0,001, 0,030, 0,01 y 0,35 mg/ml of DhL dissolved into 1% (v/v) DMSO followed by dilution in Ringer solution, control groups were also achieved. The assay was conducted for 4 days, solution renewal every 24 h. Surviving embryos were counted, fixed in formalin, and examined by microscopy to determine their developmental stages and malformations. Malformations were found in greater than 73,3% of embryos exposed to 0,1 mg/ml. The most frequent malformations in this concentration were gastrulation achieved with lips abnormal and neurulae with extruding yolk plugs. We conclude that DhL at the doses here assayed exhibit teratogenic effects.</p>

<p>B6-109 CHLORIDE PASSAGE ACROSS THE ISOLATED SKIN OF THE TOAD <i>BUFO ARENARUM</i> Orce G., Castillo G., Chanampa Y. and Razouk G. Inst. of Physiology, Faculty of Medicine, UNT - Dept. Physiology, INSIBIO (UNT-CONICET) Junín 1229, 4000 Tucumán - orcegap@yahoo.com</p> <p>Cl⁻ transport across membranes bears great importance to body fluid management, Cl⁻ being the main anion in the extracellular compartment. We found in the isolated toad skin a Cl⁻ channel whose characteristics set it apart from others described in the literature. The channel is activated by exposure to theophylline or cAMP, but not to oxytocin or norepinephrine. It can be activated in the absence of apical Cl⁻, and supports Cl⁻ flux in either direction, which can be measured when exposed to a [Cl⁻] gradient as a gradient-generated short circuit current (SCCg). It is permeable to Cl⁻, Br⁻, I⁻ and ^{99m}TcO₄⁻ in a different pattern than observed following permeabilization of tight junctions by apical hypertonicity. The channel is inactivated by exposure of the skin to dinitrophenol or rotenone; in the latter case, inhibition is overcome by addition of succinate to the bath, thus confirming dependence on cell metabolism. In the absence of an osmotic gradient, exposure of the theophylline-treated skin to a [Cl⁻] gradient generates a water flow following the gradient. The channel is a high-volume Cl⁻ passage pathway and may be involved in the maintenance of the body's ionic and osmotic balance. The lack of activation by oxytocin or norepinephrine indirectly supports the hypothesis of compartmentalization of cAMP production following receptor stimulation.</p>	<p>B6-110 PHARMACOLOGICAL PROFILE OF SELF-MEDICATION IN ELDERLY Ponce Lucía N. ; Brizuela Nilda Y. Cátedra de Farmacología, Facultad de Ciencias Médicas. Universidad Nacional de Córdoba. Santa Rosa 1085-Córdoba-Argentina-CP5000. E-mail: poncenuri@hotmail.com</p> <p>The number of elderly patients is increasing every day in our society. The present study is prospective in nature, descriptive, cross sectional, carried out between April and May 2007, in a primary care clinic at a senior center in the city of Córdoba, Argentina.</p> <p>The aim of this study was to determine the profile of self-medication in geriatric patients and relate them to polypharmacy usually consumed in this age group, in order to schedule a preventive intervention and reduce risk.</p> <p>Individual interview was conducted using 220 patients and the results showed that 20.9% self-medicated in the pre-consultation, 68,75% were women. The predominant age was between 71 to 76 years, the most consumed drugs were analgesics: 59,37%, the acid secretion inhibitors: 37.5% and 12.5% antibiotics, anti-influenza drugs: 5 (7,81%), Anticholinergics: 5 (7, 81%) .</p> <p>The cause of automedication was: 34 by advice of the pharmacist (53,12%), 17 by pairs or relatives (26.56%), 6 to repeat prescription (9.37%) and 7 by above the line (10.9%)</p> <p>Conclusion: The automedication is dangerously installed and it's control is shared responsibility of doctors, patients, and pharmaceuticals . Health care education programs should be developed with the aim of making the public aware of the negative effects of automedication.</p>
<p>B6-111 LYMPHOCYTE FUNCTION IN TRANSGENIC MICE OVER EXPRESSING THE TRH GENE. A Klecha^{1,2}, ML Barreiro Arco², S Garcia³, C Pirola³, A Genaro^{1,2}, G Cremaschi^{1,2}. ¹CEFYO-CONICET, ²Fac Farmacia y Bioquímica, UBA e IDIM-CONICET. alijut@ffyb.uba.ar</p> <p>We have previously demonstrated that thyroid axis status is able to modulate immunity. Thus, hypothyroidism induced in mice by propylthiouracil administration lead to a decrease in lymphocyte reactivity and in the secretion of the Th1 cytokines interferon-γ (IFN-γ) e interleukin-2 (IL-2). To investigate the participation of the different components of the axis, namely thyroid hormones (T3 and T4), thyrotropin (TSH) or thyrotropin realizing hormone, transgenic mice over-expressing the TRH gene (tm-TRH) were used to analyze lymphocyte activity. These animals were obtained by pronuclear injection of a gene construct containing the TRH precursor cDNA under the action of the CMV promoter and the polyadenylation signal of bovine growth hormone. The tm-TRH displayed higher diencephalic levels of TRH, but similar serum levels of TSH and thyroid hormones than control mice. TRH levels as well as TSH correlates with a higher T and B lymphocyte proliferative responses in response to selective mitogen stimulation. Additionally, these effects were accompanied by an increment in the release of Th1 cytokines and of IL-6, but not of other Th2 (IL-4 and IL-10) or the pro-inflammatory (TNF-α) cytokines.</p> <p>These results suggest that augmentation of hypothalamic-pituitary hormones leads to the increase of T and B cell responses, unlike the facts previously observed in hypothyroid conditions.</p>	<p>B6-112 2,4-Dichlorophenoxyacetic acid (2,4-D) effects on mRNA expression of myelin proteins. Konjuh, C.; Evangelista de Duffard, A.M. and Duffard R.O. <i>LATOEX – Facultad de Ciencias Bioquímicas y Farmacéuticas. UNR. Suipacha 531. 2000 - Rosario. e-mail: ckonjuh@fbioyf.unr.edu.ar</i></p> <p>Myelination is a critical process in the maturation of the nervous system is especially susceptible to perturbations such as toxic insult, nutritional deficiencies, and other environmental factors. 2,4-D is a phenoxyherbicide used for selective control of broadleaf weeds. Unfortunately, 2,4-D produces different harmful effects on mammals, including humans, which range from embryotoxicity and teratogenicity to neurotoxicity. Very little is known about the cellular mechanisms underlying its neurotoxicity. In previous works, we found hypomyelination in rats exposed to 2, 4-D. These rats present a decrease in several myelin components (cholesterol, phospholipids, myelin proteins) and by electron microscopy we observed myelin compaction problems and mitochondrial and reticular swelling in oligodendrocytes. The aim of this work was to evaluate the effect of 2,4-D on mRNA of the major myelin protein expression. Two experimental groups were used: 1- control rats and 2- rats exposed to the herbicide from postnatal day 9 to 22. After the exposure period rats were sacrificed, brains were dissected and RNA was extracted. Myelin protein expression quantification of relative genic expression of major myelin proteins (PLP, MBP and CNPase) were realized by RT-PCR. We found no significant difference in the expression of the mRNA of the proteins studied respect to controls. We can conclude that 2,4-D do not affects the expression of mRNA of myelin proteins studied and the decrease found in these proteins could then be due to alterations in their transport, translation or increased degradation.</p>

AUTORES

A	B	C	D	E	F	G	H	I	J	K	L	M	N
Ñ	O	P	Q	R	S	T	U	V	W	X	Y	Z	

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		B4-40	Albarellos G.					B2-15	B2-14			Anesini C.	
		B3-33	Albarracín R						B3-32			Aón L.	
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		B1-11	Alovero F.						B6-65			Artillo Guida RD	
		B6-104	Alvarez E						B4-39			Asprea M.	
B4-47	B1-07	B1-04	Alvarez L						B4-49			Auad J	
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		B3-79									B5-51	Borda E	
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		B4-89						B4-86	B4-39			Bramuglia GB.	
		O1-05	Baratti CM				B6-107	B6-106	OIII-18			Brandan N	
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		B6-65	Barreiro KA						B4-87			Breda S	
		B6-111	Barreiro Arco S						B1-13			Brizuela NY	
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		B4-43	Bartel LC						B2-26			Bruno MA	
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		B2-18	Bianchi M							B4-44		Bulffer R.F.	
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		O1-05	Boccia MM										
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		OI-05	Carcaboso AM			B3-78	Codagnone M
		B3-35	Cardamone L			B6-104	Cointry G
		B6-103	Casas S			B2-24	Colareda G.
		B5-57	Castagnino J			B5-92	Coll CT
		B6-109	Castillo G			B5-92	Coll SG
		B4-82	Castro E.			B5-92	Coll TA
	B4-44	B4-43	Castro JA		B5-100	B5-52	Collia N
		OII-13	Catania VA	B1-01	OIII-20	OII-08	Confalonieri A
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		OII-09	Celuch S.M		B5-95	B3-35	Contini M de C
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		B5-100	Cerquetti MC		B3-30	B3-29	Cuesta S.
		B1-05	Cerra M.			B6-63	Cuis N
		B6-109	Chanampa Y				
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	B5-53	B2-20	Dadé M			B5-98	Demurtas S
		B6-64	Daich M		B1-07	B1-04	Denegri G
		OIII-19	Dalfovo MC			B4-86	Di Gennaro SS
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		B2-26	Errasti ME				
		B1-10	Errecalde J				
	B1-09	B1-08	Errecalde J.				
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		B6-65	Faletti AG			B5-92	Filinger EJ
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		B5-92	Fernández MA			B1-05	Formentini E.
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		B5-57	Garce S			OII-10	Girardi E
		B2-16	Garcia Aseff S			B5-96	Giron S
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		B1-09	Lambertini A.		B5-58	B5-57	Lipszyc P
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		B3-38	Maldonado H			B3-35	Millen N
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B4-87	B1-11	OII-08	Manzo R			B2-28	Miño J.
		B4-91	Manzo R.			B5-51	Miozza V
	B1-09	B1-08	Marchetti M.L			B2-27	Mitjans N
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		B4-48	Marder M.			O1-06	Molina V.A.
	B6-67	OIII-19	María AO			B1-10	Moncada Cárdenas LA.
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		B2-28	Marrassini C.	B4-81	B4-80	B4-46	Monfrinotti A.
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		B1-12	Martins E			B4-45	Monti D
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		B5-94	Medina M			B4-47	Moreno L
		B5-52	Medina V			B6-108	Moreno LE
		B5-98	Meirovich CI			OII-13	Mottino AD
B1-09	B1-08	B1-10	Mestorino N.			B3-79	Moutinho L
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		B5-100	Noto Llana M						
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	B4-87	OII-08	Olivera M						
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RECONOCIMIENTO A INSTITUCIONES Y EMPRESAS

La Reunión Anual de SAFE 2009 se realiza con el aporte, auspicio y declaración de interés de las siguientes Instituciones y empresas:

Apoyo Económico

ANPCYT, FONCYT

CONICET

COLEGIO DE FARMACÉUTICOS 2DA

CIRCUNSCRIPCIÓN DE LA PROVINCIA DE SANTA FE

UNIVERSIDAD NACIONAL DE ROSARIO

FACULTAD DE CS BIOQUÍMICAS Y FARMACÉUTICAS UNR

GE Healthcare

BAGO SA

ETC INTERNACIONAL SA

MONTPELLIER SA

CHEMICAL CENTER

JENK SA

Cafés LA VIRGINIA SA

RICARDO BUELONI Y CIA.

Declaración de Interés y Beneplácito

- Universidad Nacional de Buenos Aires, Facultad de Medicina.

- Universidad Nacional de Buenos Aires, Facultad de Farmacia y Bioquímica, UBA

Auspicio/ Adhesiones

- Academia Nacional de Farmacia y Bioquímica

- Universidad Nacional de San Luis

- Universidad Católica de Córdoba

- Universidad Nacional del Litoral, Facultad de Ciencias Veterinarias.

- Universidad Nacional del Centro de la Provincia de Buenos Aires, Facultad de Ciencias Veterinarias

- Universidad Nacional de Buenos Aires, Facultad de Ciencias Veterinarias.

Universidad Nacional de Río Cuarto-Facultad de Cs Exactas Físicoquímicas y Naturales

Universidad Nacional de Rosario -Facultad de Cs Bioquímicas y Farmacéuticas

Rectorado de la Universidad Nacional de Río Cuarto

.Rectorado de la Universidad Nacional de Rosario

Declaración de Interés Provincial

- Evento declarado de interés provincial para la Provincia de Santa Fe por el Sr. Gobernador por Decreto N 1749/2009..

Declaración De Interés Municipal

emitida por el CONSEJO MUNICIPAL DE ROSARIO Decreto Nro.32521/2009

Declaración De Interés Académico

- emitida por la FACULTAD DE CS VETERINARIAS DE LA UNIVERSIDAD NACIONAL DEL NORDESTE

.-emitida por la FACULTAD DE CS VETERINARIAS DE LA UNIVERSIDAD NACIONAL DE ROSARIO